13th INTERNATIONAL CONFERENCE

TYPHOID & OTHER INVASIVE SALMONELLOSES

DECEMBER 5–7, 2023 | KIGALI, RWANDA

SABIN VACCINE INSTITUTE

COALITION AGAINST TYPHOID

CATALYZING CHANGE

The Urgency of Expanding Impact-Driven Solutions

On behalf of the Coalition against Typhoid, housed at the Sabin Vaccine Institute, it is our great pleasure to welcome you to the 13th International Conference on Typhoid & Other Invasive Salmonelloses. We extend our deepest gratitude to the Bill & Melinda Gates Foundation for their generous support of this highly anticipated event.

We return to an in-person gathering after a four-year hiatus, exhilarated that we can once again benefit from the collaborative environment of researchers, healthcare professionals, and policymakers from diverse backgrounds discussing innovative tools and strategies to combat typhoid and other invasive non-typhoidal *Salmonella* (iNTS). These meetings have consistently fostered research collaborations and knowledge exchange that have been instrumental in advancing important progress within this field. We will also be celebrating our achievements, including the introduction of the typhoid conjugate vaccine in six endemic countries, where it has now become part of their routine vaccination schedules.

It's essential to note that despite our progress, there were an estimated 9–24 million cases of typhoid fever in 2019, leading to 110,000 deaths. Additionally, antimicrobial resistance continues to erode our treatment arsenal. This year, our conference theme is "Catalyzing Change: The Urgency of Expanding Impact-Driven Solutions." Aligned with this theme, over the next three days, our aim is to address the current challenges in typhoid and iNTS control and prevention, discuss impactful tools and potential solutions, and collectively explore approaches to forge a pathway forward.

We are delighted to welcome more than 300 attendees to this conference, representing over 325 people from 44 countries. The conference will feature plenary sessions to address the urgency for solutions, delve into the tools at our disposal, and chart a course forward. Solid symposia will provide the intellectual foundation for the critical discussions and decisions that lie ahead. In addition, 96 oral and 120 poster presentations will capture a broad array of research, showcasing the remarkable progress we've made and the discoveries guiding our way.

As we gather here, let us remember that we share a common objective: to achieve tangible impact. We have the tools, and we have the knowledge to catalyze progress. Yet it is our shared commitment that will truly set the course for change, shaping the direction of future studies, and encouraging innovative approaches. Let's address these challenges with sobriety, enthusiasm, and unity. This conference goes beyond a mere gathering; it's a celebration of your unwavering commitment to the fight against enteric fever and iNTS in a time of growing need. Together, we can make a meaningful difference.

Sincerely,

Denise Garrett, M.D., M.Sc.

Vice President, Applied Epidemiology
Sabin Vaccine Institute
Director, Coalition against Typhoid

Anuradha Gupta

President, Global Immunization
Sabin Vaccine Institute

Amy Finan

Chief Executive Officer
Sabin Vaccine Institute

SCIENTIFIC COMMITTEE & ABSTRACT REVIEW PANEL

Scientific Committee	Affiliation
Jason Andrews	Stanford University
Adwoa Bentsi-Enchill	World Health Organization
Lucy Breakwell	U.S. Centers for Disease Control and Prevention
John Crump	University of Otago
Denise Garrett	Sabin Vaccine Insitute
Melita Gordon	Malawi-Liverpool Wellcome Programme
Taufique Joarder	Duke-NUS Global Health Institute
Jacob John	Christian Medical College, Vellore
Hope Johnson	Gavi, The Vaccine Alliance
Samuel Kariuki	Kenya Medical Research Institute
Stephen Luby	Stanford University
Kathleen M. Neuzil	University of Maryland School of Medicine
Duncan Steele	Bill & Melinda Gates Foundation
Eunice Ubomba-Jaswa	Water Research Commission

Abstract Review Panel	Affiliation
Buddha Basnyat	Nepal Academy of Science and Technology
Isaac Bogoch	University Health Network
Megan Carey	International AIDS Vaccine Initiative and London School of Hygiene & Tropical Medicine
Ali Carter	Sabin Vaccine Insitute
Richelle C. Charles	Massachusetts General Hospital-Harvard University
Kate Doyle	Sabin Vaccine Insitute
Antonio Gonzalez Lopez	Sabin Vaccine Insitute
Leslie Jamka	University of Maryland School of Medicine
Dolly Katz	Consultant, Sabin Vaccine Institute
Supriya Kumar	Bill & Melinda Gates Foundation
Ashley Latimer	PATH
James Meiring	University of Sheffield
Nginache Nampota	University of Malawi
Iruka Okeke	University of Ibadan
Alphonse Ouedraogo	Groupe de Recherche Action en Santé
Ellis Owusu-Dabo	Kwame Nkrumah University of Science and Technology
Christopher Parry	Liverpool School of Tropical Medicine
Virginia Pitzer	Yale University
Andrew J. Pollard	Oxford University
Jyotshna Sapkota	FIND
Jessica Seidman	Sabin Vaccine Insitute
Amanda Tiffany	U.S. Centers for Disease Control and Prevention
Tahir Yousafzai	Aga Khan University

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BILL & MELINDA GATES *foundation*

TyVAC Typhoid Vaccine Acceleration Consortium
CENTER FOR VACCINE DEVELOPMENT • OXFORD VACCINE GROUP • PATH

Together we have reached more than 56 million children with typhoid conjugate vaccines (TCV) in 6 countries.

But the work to Take on Typhoid is not over.

Drug resistance is increasing rapidly.

Typhoid burden is increasing with more severe weather events and population movements.

Displaced populations and rapidly urbanized communities lack access to safe water.

We must continue to Take on Typhoid together.

Single dose TCVs are highly effective in children, offer durable protection, and may be given with other vaccines as part of campaigns or routine immunization.

Now is the time to introduce TCVs to protect children, families, and communities against typhoid.

The Typhoid Vaccine Acceleration Consortium (TyVAC) is available to support countries with TCV introduction. TyVAC can help review and collate burden data, generate health economic evidence, develop advocacy materials, assist with the Gavi application, and provide technical assistance for TCV campaign planning.

Materials, data, and messages at

TakeonTyphoid.org

It's time for YOU to TakeonTyphoid

TyVAC Typhoid Vaccine Acceleration Consortium

CENTER FOR VACCINE DEVELOPMENT • OXFORD VACCINE GROUP • PATH

AGENDA

TUESDAY, DECEMBER 5

8:30–8:45 Opening Session

KILIMANJARO BALLROOM

Welcome Remarks and Housekeeping Items
Denise Garrett, Sabin Vaccine Institute

8:45–9:45 Global Challenges in the Fight Against Typhoid and Invasive Salmonelloses: The Urgency to Act

KILIMANJARO BALLROOM

PLENARY SESSION MODERATED BY:
Denise Garrett, Sabin Vaccine Institute & Eileen Quinn, PATH

Fighting Typhoid: The Importance of Evidence for Effective Prevention and Control Amid Urgency to Act
Anuradha Gupta, Sabin Vaccine Institute

Non-Typhoidal Salmonella Invasive Disease as a Leading Cause of Child Death in Africa — Challenges and Opportunities for Management and Control
Samuel Kariuki, Kenya Medical Research Institute

The Challenge of Sustainable Access to Effective Antibiotics for Enteric Infections
Ramanan Laxminarayan, One Health Trust

Confronting the Challenge of Data Inequity
Kathleen M. Neuzil, University of Maryland School of Medicine

Discussion

9:45–10:15 Coffee Break & Poster Viewing

FOYER

10:15–12:15 Vaccine Voyage I: Navigating the Advancements in Vaccine Research

KILIMANJARO BALLROOM

ORAL ABSTRACT SESSION MODERATED BY:
Kirsten Vannice, Bill & Melinda Gates Foundation
& Sushant Sahastrabuddhe, International Vaccine Institute

Serological Response Using ELISA Anti-Vi-IgG After Single Dose of Typhoid Conjugate Vaccine Against *Salmonella* Typhi Among Children in Hyderabad, Pakistan
Farah N. Qamar, Aga Khan University

The Validity of Different Study Designs in Estimating the Protection of Typhoid Conjugate Vaccine
Xinxue Liu, Oxford Vaccine Group, Department of Paediatrics, University of Oxford, and the NIHR Oxford Biomedical Research Centre

TyVAC Nepal: Two Dose and Extended Immunogenicity
Mila Shakya, Patan Academy of Health Sciences, Patan Hospital

Effectiveness of Typhoid Conjugate Vaccine (TCV): A Systematic Review
Amira Mahboob, World Health Organization Regional Office for the Eastern Mediterranean

Efficacy of Typhoid Conjugate Vaccine Against Culture-Confirmed *Salmonella* Typhi — A Systematic Review and Meta-Analysis
Rabab Batool, Aga Khan University

Safety of Typhoid Conjugate Vaccine Booster Vaccination in Malawian Children
Osward Nyirenda, Blantyre Malaria Project, Kamuzu University of Health Sciences

Test-Negative Design: An Efficient Method to Assess Typhoid Conjugate Vaccine Effectiveness
Matthew Laurens, University of Maryland School of Medicine

A Phase IV Clinical Study to Evaluate the Immunogenicity and Safety of Typhoid Conjugate Vaccine (Typbar TCVA®) in Elderly Population
Raches Ella, Bharat Biotech International

12:15–13:30 Lunch

SOKO RESTAURANT

13:30–15:00 Maximizing Learnings from Clinical Trials and Public Sector Use — the Full Public Health Value of Typhoid Conjugate Vaccines

KILIMANJARO BALLROOM

SYMPOSIUM SESSION CHAIRED BY:
Megan E. Carey, International AIDS Vaccine Initiative and London School of Hygiene & Tropical Medicine & Kathleen M. Neuzil, University of Maryland School of Medicine

Longer-Term Efficacy of Typhoid Conjugate Vaccine in Malawi
Priyanka Patel, Malawi-Liverpool-Wellcome Trust

New findings on Immunogenicity of TCV: Booster Dose in School-Aged Children and 1 Versus 2 Dose Regimens in HIV-Exposed Infants
Osward Nyirenda, Blantyre Malaria Project

Typhoid Fever Surveillance in Urban Dhaka, Bangladesh: Risk Factors and Antimicrobial Resistance Pattern
Farhana Khanam, icddr,b

Impact Assessment of National TCV Introduction in Pakistan
Tahir Yousafzai, Aga Khan University

The Impact of a TCV Mass Campaign on Typhoid Fever Cases and Antimicrobial Use in Harare, Zimbabwe
Ioana Diana Olaru, London School of Hygiene & Tropical Medicine

Measuring the Impact of Typhoid Conjugate Vaccines on Antimicrobial Usage from Pivotal Efficacy Studies
James E. Meiring, Department of Infection, Immunity and Cardiovascular Disease, University of Sheffield

15:00–15:30 Coffee Break & Poster Viewing

FOYER

#TakeOnTyphoid

15:30–17:30 Comprehensive Exploration of iNTS: From Vaccine Trials to Global Epidemiology

KILIMANJARO BALLROOM

ORAL ABSTRACT SESSION MODERATED BY:
James Meiring, University of Sheffield
& Raphael Zellweger, International Vaccine Institute

Study Design & Initial Data from Phase 1 RCT to Evaluate the Safety, Reactogenicity & Immunogenicity of a Vaccine Against iNTS & Typhoid Fever in Healthy Adults
Yasir Shitu Isa, GSK Vaccines Institute for Global Health

Age-Specific Incidence and Associated Mortality of Invasive Non-Typhoidal *Salmonella* in Mozambican Children, 2001 – 2019
Inacio Mandomando, Centro de Investigação em Saúde de Manhiça

Severe Anaemia Increases Risk Of Invasive Non-Typhoidal *Salmonella* Bacteraemia In Kenyan Children
Kelvin Mokaya Abuga, KEMRI-Wellcome Trust Research Programme

Modelling the Global Prevalence of Antimicrobial Resistant Invasive Non-Typhoidal Salmonella Infections, 2000 to 2019
Frederick Fell, University of Oxford

IgG and IgA Antigen-Specific B Memory Responses in Healthy U.S. Adults Immunized with a Parenteral Trivalent Salmonella Conjugate Vaccine (TSCV)
Marcelo Sztein, University of Maryland School of Medicine

Antimicrobial Resistance and Intestinal Shedding of Non-Typhoidal Salmonella Among Children Under Five Years and Carriage in Asymptomatic Hosts in Kenya
Celestine Wairimu, Kenya Medical Research Institute

Acquisition of Immunity to Non-Typhoidal Salmonella in Malawian Children to Inform Vaccine-Derived Immunity; a Serological Catalytic Model
Helen Dale, University of Liverpool

The Burden of Invasive Non-Typhoidal Salmonella Disease in Six Sites in Africa: Results from the Severe Typhoid Fever Surveillance in Africa Program
Hyonjin Jeon, International Vaccine Institute

18:00–19:30 Evening Welcome Reception

MALAIKA GARDEN

WEDNESDAY, DECEMBER 6

7:45–8:30 Sunrise Symposium: *Salmonella* Controlled Human Infection Models — Insights, Opportunities and Challenges

ISARO ROOM

SYMPOSIUM SESSION CHAIRED BY:
Malick Gibani, Imperial College London

Preliminary Results From an Oral Vaccine in the Paratyphoid Human Challenge Model
Naina McCann, Oxford Vaccine Group, Department of Paediatrics, University of Oxford

A Typhoid Fever Challenge Model in India? — Opportunities and Challenges
Rakesh Aggarwal, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry

Development of a Non-Typhoidal *Salmonella* Challenge Model
Christopher Smith, Department of Infectious Disease, Imperial College London

8:30–9:30 Amplifying Impact: Tools and Solutions to Accelerate Progress

KILIMANJARO BALLROOM

PLENARY SESSION MODERATED BY:
Julie Bines, University of Melbourne & Andrew J. Pollard, University of Oxford

Accelerating Impact Through Mindful Management of Innovation
Jerome Kim, International Vaccine Institute

Enhancement and Utilization of Laboratory Infrastructure to Mitigate Enteric Disease Threats
Proscovia Nalumyima, Makerere University, Walter Reed Uganda

Integrating Artificial Intelligence to Analyze Typhoid and Other Invasive Salmonelloses Data: From Zero to Hero!
Bráulio Roberto Gonçalves Marinho Couto, Biobyte Sistemas Ltda

Progress and Challenges Towards Typhoid Diagnostics
Jyotshna Sapkota, FIND

Discussion

9:30–9:45 Recognition Ceremony

KILIMANJARO BALLROOM

9:45–10:15 Coffee Break & Poster Viewing

FOYER

10:15–12:15 Concurrent Oral Abstract Sessions

Inside Out: Genomic and Antimicrobial Resistance in *Salmonella*

ISARO ROOM

ORAL ABSTRACT SESSION MODERATED BY:
Iruka Okeke, University of Ibadan
& Christopher Parry, Liverpool School of Tropical Medicine

Role of Bacteriophage Defence Systems in the Spread of Drug-Resistant *Salmonella* Typhi
Yogesh Hooda, Child Health Research Foundation

Genomic Analysis and Antimicrobial Resistance Profiling for the Global Collection of *Salmonella* Paratyphi B Isolates
Junaid Iqbal, Aga Khan University

Assessing the Global Risk of Typhoid Outbreaks Caused by Extensively Drug Resistant *Salmonella* Typhi
Jo Walker, Yale School of Public Health

Recent Emergence of Cephalosporin Resistant Salmonella Typhi Carrying IncFIB(K) Plasmid Encoding blaCTX-M-15 Gene in India
Tharani Priya Thirumoorthy, Christian Medical College, Vellore

A 24-Year Passive Surveillance Study Reveals Trends in Antimicrobial Resistance Amongst *Salmonella* Typhi and Paratyphi A Cases in Bangladesh
Arif Mohammad Tanmoy, Child Health Research Foundation

Genetic Heterogeneity in the *Salmonella* Typhi Vi Capsule Locus: A Population Genomic Study from Fiji
Aneley Getahun Strobel, Peter Doherty Institute for Infection and Immunity, University of Melbourne

The Genetic Landscape of *Salmonella* Enterica Serovar Typhi in Zimbabwe Before the Introduction of Typhoid Conjugate Vaccine (TCV)
Tapfumanei Mashe, Ministry of Health and Childcare, World Health Organization

Genomic Characterization of Invasive *Salmonella* Enterica Isolated in Severe Typhoid in Africa Surveillance in Ibadan, Nigeria
Oyeniyi Stephen Bejide, Chrisland University

Vaccine Voyage II: Navigating the Advancements in Vaccine Research

KILIMANJARO BALLROOM

ORAL ABSTRACT SESSION MODERATED BY:
Myron "Mike" Levine, University of Maryland School of Medicine & Farah Qamar, Aga Khan University

Vaccines for All: The Malawi National Integrated Typhoid Conjugate Vaccine Campaign
Latif Ndeketa, Malawi Liverpool Wellcome Programme

Antimicrobial Susceptibility Patterns of *Salmonella* Typhi Isolates Following Mass-Targeted Typhoid Conjugate Vaccine Immunization in Harare City, Zimbabwe, 2023
Kudzai Patience Takarinda, National Microbiology Reference Laboratory Zimbabwe

Modeling Typhoid Vaccination in Nepal: TCV Impact and Booster Dose Strategy
Virginia Pitzer, Yale University

Trend of anti-Vi-IgG and anti-Vi-IgA Antibody Responses Induced in Vi-TT Recipients Over the Period of Five Years Among Bangladeshi Children
Farhana Khanam, icddr,b

Assessing the Medium-Term Impact of a Typhoid Conjugate Vaccine in Preventing Typhoid Infections in Bangladesh
Firdausi Qadri, icddr,b

The Association Between Vaccine Coverage and Herd Protection: Exploratory Analyses of a Cluster-Randomised Trial of Vi Conjugate Vaccine
Yiyuan Zhang, Oxford Vaccine Group and National Institute for Health and Care Research Oxford Biomedical Research Centre

Durability of Anti-Vi IgG and IgA Responses in 15-month-old Children Vaccinated with a Typhoid Conjugate Vaccine in Burkina Faso
Alphonse Ouedraogo, Groupe de Recherche Action en Santé

Introduction of Typhoid Conjugate Vaccine — A Successful Implementation in Strengthening National Immunization Program of Nepal
Navneet Bichha, Indian Institute of Health Management Research

12:15–13:30 Lunch

SOKO RESTAURANT

13:30–15:00 Bridging the Gap: Environmental and Sero-Surveillance for Estimating Typhoid Burden and Supporting Vaccine Introduction

KILIMANJARO BALLROOM

SYMPOSIUM SESSION CHAIRED BY: Kristen Aiemjoy, University of California Davis & Mahidol University Faculty of Tropical Medicine, Richelle C. Charles, Massachusetts General Hospital-Harvard University & Nick Grassly, Imperial College London

Latest Advances in Seroepidemiology for Enteric Fever
Kristen Aiemjoy, University of California Davis & Mahidol University Faculty of Tropical Medicine

Quick and Informative: Schools as a Platform for Rapid Typhoid Seroepidemiological Assessments
Shiva Naga, Dhulikhel Hospital, Kathmandu University and Sira Jam Munira, Child Health Research Foundation

Mapping Typhoid Transmission: Geospatial Analysis and Seroepidemiology for TCV Prioritization
Momin Kazi, Aga Khan University

A Target Product Profile for Wastewater Surveillance of *S.* Typhi
Supriya Kumar, Bill & Melinda Gates Foundation

Seroincidence of Enteric Fever based on Targeted Serosurveillance in Blantyre, Malawi
Jonathan Mandolo, Liverpool School of Tropical Medicine

Wastewater Surveillance of *S.* Typhi in India and Comparison with Clinical and Serological Surveillance
Dilip Abraham, Christian Medical College, Vellore

Direct Sequencing of *S.* Typhi in Wastewater Samples to Determine Antimicrobial Resistance and Genotype
Catherine Troman, Imperial College London

15:00–15:30 Coffee Break & Poster Viewing

FOYER

15:30–17:30 Eyes on Surveillance: Illuminating the Path to Effective Monitoring

KILIMANJARO BALLROOM

ORAL ABSTRACT SESSION MODERATED BY:
Adidja Amani, World Health Organization Regional Office for Africa
& Jessica Seidman, Sabin Vaccine Institute

Development of a Low-Cost Environmental Surveillance Method for Effective Typhoid Fever Control
Shuborno Islam, Child Health Research Foundation

Leveraging Paired Serology to Estimate the Incidence of Typhoidal *Salmonella* Infection in the STRATAA Study
Jo Walker, Yale School of Public Health

Estimating the Burden of Environmental *Salmonella* Typhi in the Asante Akim North District of Ghana: The Role of Novel Techniques
Michael O. Owusu, Kwame Nkrumah University of Science and Technology

The Burden and Trend of Typhoid Fever in Low- and Middle-Income Countries: An Updated Meta-Regression Approach
Harsh Vivek Harkare, Swiss Tropical and Public Health Institute and University of Basel

Blood Culture Positive Typhoid and Paratyphoid Cases in Children Presenting to Patan Hospital, Nepal, Over a 14-Year Period (2009-2022)
Shrijana Shrestha, Patan Academy of Health Sciences

The Ty-FIVE Project — Strengthening Typhoid Surveillance Around a Mass Vaccination Campaign in the Northern Division of Fiji
Alumita Vuakanisakea, Ty-FIVE Project, International Vaccine Institute

Typhoid-Associated Ileal Perforations Following the Introduction of the Typhoid Conjugate Vaccine in Pakistan: Findings from a Multi-Center Surveillance Study
Saqib Hamid Qazi, Aga Khan University

Molecular Surveillance of Non-Typhoidal *Salmonella* from Environmental Sources in Disease Endemic Informal Settlement in Nairobi, Kenya
Michael Muraya Mugo, Kenya Medical Research Institute

THURSDAY, DECEMBER 7

7:45–8:30 Sunrise Symposium: How Data Drive Decision-Making: Reflections from TCV Introductions in Pakistan and Malawi and the Role of Data Moving Forward

ISARO ROOM

SYMPOSIUM SESSION CHAIRED BY: Emmanuel Mugisha, PATH

Optimizing Surveillance and Interventions to Advance National XDR Typhoid Control: The Pakistan Experience
Nada Taqi, World Health Organization

From Decision-Making to Introduction: How Persistence, Partnership, and Planning Led to the Introduction of Typhoid Conjugate Vaccine in Malawi
Esau Mkisi, PATH

The MENA Typhoid Project: New Insights on Typhoid Burden and Antibiotic Resistance
Kristen Heitzinger, U.S. Centers for Disease Control and Prevention

8:30–10:00 Landscape, Strategy, and Progress Update for iNTS Vaccines in Clinical Development

KILIMANJARO BALLROOM

SYMPOSIUM SESSION CHAIRED BY: Melita Gordon, Malawi-Liverpool Wellcome Programme & Samuel Kariuki, Kenya Medical Research Institute

Prevalence and Distribution of Non-Typhoidal *Salmonella* enterica Serogroups and Serovars Isolated from Normally Sterile Sites: A Global Systematic Review
John Crump, University of Otago

Sero-Epidemiology of iNTS in Large Field Cohorts from Malawi, Burkina Faso, Kenya and Ghana
Helen Dale, University of Liverpool

Economic Burden of iNTS and Cost-Effectiveness Analysis for a Hypothetical iNTS Vaccine in Ghana, Burkina Faso and Malawi
Jung-Seok Lee, International Vaccine Institute

The Public Health Need for iNTS Vaccines, and Preferred Vaccine Characteristics
Adwoa Bentsi-Enchill, World Health Organization

A LMIC Perspective on iNTS Vaccine Strategy, and Lessons from Recent Vaccine Introductions
Mike Chisema, Malawi Ministry of Health

Current Status of the Clinical Development of Trivalent *Salmonella* Conjugate Vaccine (TSCV)
Wilbur Chen, Center for Vaccine Development, University of Maryland School of Medicine

Development of iNTS Conjugate and Preclinical Study for a Novel Trivalent iNTS/Typhoid Vaccine
SoJung An, International Vaccine Institute

Development of GMMA-Based Vaccines Against iNTS: Current Status
Rocio Canals Alvarez, GSK Vaccines Institutes for Global Health

10:00–10:30 Coffee Break & Poster Viewing

FOYER

10:30–12:30 Mosaic of Insights: An Exploration of Diverse Salmonelloses Topics

KILIMANJARO BALLROOM

ORAL ABSTRACT SESSION MODERATED BY:
Nicholas Feasey, Liverpool School of Tropical Medicine
& Calman A. MacLennan, Bill & Melinda Gates Foundation

Impact of COVID-19 Pandemic on Enteric Fever Diagnosis in Nepal: Findings from the Surveillance of Enteric Fever Asia Project Study
Dipesh Tamrakar, Dhulikel Hospital-Kathmandu University Hospital

The Application of Machine Learning with High-Content Imaging to Infer Antimicrobial Resistance Phenotypes in *Salmonella* Typhimurium
Sushmita Sridhar, Universidad Peruana Cayetano Heredia and University of New Mexico

Evaluation of a Point-of-Care Multiplex Immunochromatographic Assay (DPP Typhoid Assay) for the Diagnosis of Typhoid
Zahida Azizullah, Aga Khan University

Design and Initial Data from a Phase 1 RCT to Evaluate the Safety and Immunogenicity of a Vaccine Against *S.* Typhi and *S.* Paratyphi A in Healthy European Adults
Usman Nasir Nakakana, GSK Vaccines Institute for Global Health

From Rarity to Clarity: The Potential of Seroepidemiology for Monitoring Typhoid Vaccine Impact
Kristen Aiemjoy, University of California Davis & Mahidol University Faculty of Tropical Medicine

Role of Gallstones in *Salmonella* Typhi Stool Carriage and Shedding in an Urban Typhoid Endemic Setting in Nairobi, Kenya
Samuel Kariuki, Kenya Medical Research Institute

The Impact of Surgical Interventions for Severe Typhoid on Families and Healthcare Systems in Rural South Central Niger
Yakoubou Sanoussi, Hopital de la SIM Galmi, Niger

Safety and Immunogenicity of a Bivalent Paratyphoid A-Typhoid Conjugate Vaccine: Phase I Study
Andrew J. Pollard, University of Oxford

12:30–13:45 Lunch

SOKO RESTAURANT

13:45–15:45 The Late-Breakers: Unveiling the Latest in Enteric Fever and iNTS Research

KILIMANJARO BALLROOM

ORAL ABSTRACT SESSION MODERATED BY:
Jason Andrews, Stanford University & Anna Minta, World Health Organization

Assessing the Protective Efficacy of an Intranasal Vaccine Candidate, rCTB-T2544, Against Typhoid and Paratyphoid Infection Using Iron Overloaded Murine Model
Suparna Chakraborty, ICMR National Institute of Cholera and Enteric Diseases

Diversity and Antimicrobial Resistance of *Salmonella* Paratyphi A: A Collaborative Global Typhoid Genomics Consortium Initiative
Zoe Anne Dyson, London School of Hygiene & Tropical Medicine

Pan-genome clustering Reveals the Role of Prophage Elements in the Evolution and Adaptation of *Salmonella* Enteritidis
Jobin John Jacob, Christian Medical College, Vellore

Initial Immunogenicity and Safety Data From a First-in-Human Randomised Controlled Trial of an Invasive Non-Typhoidal *Salmonella* GMMA Vaccine: the SALVO Trial
Peter D. Skidmore, Oxford Vaccine Group, NIHR Oxford Biomedical Research Centre, Department of Paediatrics, University of Oxford

Forecasting iNTS for the Global Burden of Disease Study
Jeffrey Stanaway, The Institute for Health Metrics and Evaluation, University of Washington

Unmasking Typhoid Vaccine Hesitancy: A Study of Myths Surrounding TCV in Immunisation Programs Within Refugee Communities in Southwestern Uganda
Muhumuza Umar, Africa Centers for Disease Control

Bacterial Profile of Suspected Typhoid Intestinal Perforation Cases, Regional Hospital Centre, Maradi, Niger
Maman Laminou Sani, Regional Hospital Centre, Maradi

Impact of TCV Introduction on Ileal Perforations in Pakistan: A Comparative Analysis
Huma Syed Hussain, Aga Khan University

15:45–16:15 Coffee Break & Poster Viewing

FOYER

16:15–17:15 Closing Plenary: Forging a Path Forward: The Roadmap to Expand Solutions and Catalyze Change

KILIMANJARO BALLROOM

PLENARY SESSION MODERATED BY:
Robert F. Breiman, Emory University
& Eunice Ubomba-Jaswa, Water Research Commission

Charting a Comprehensive and Innovative Path to Fight Typhoid and Invasive Salmonelloses: The Importance of Multi-Sectorial Collaboration, Resource Mobilization, Health Systems Strengthening and Political Will
Robert Agyarko, African Risk Capacity

From Data to Action: Leveraging Existing Primary Healthcare Systems for Solutions
Samba Sow, Center for Vaccine Development-Mali

Accelerating the Fight Against Invasive *Salmonella* Diseases: Perspectives From WHO
Adwoa Bentsi-Enchill, World Health Organization

Looking Ahead — What Do We Need for Successful Enteric Fever Control?
Duncan Steele, Bill & Melinda Gates Foundation

Discussion

17:15–17:30 Closing Session

KILIMANJARO BALLROOM

Closing Remarks
Meeting Adjournment
Denise Garrett, Sabin Vaccine Institute
& Anuradha Gupta, Sabin Vaccine Institute

PROGRAM

TUESDAY, DECEMBER 5

8:30–8:45 Opening Session

KILIMANJARO BALLROOM

Welcome Remarks and Housekeeping Items
Denise Garrett, Sabin Vaccine Institute

8:45–9:45 Global Challenges in the Fight Against Typhoid and Invasive Salmonelloses: The Urgency to Act

KILIMANJARO BALLROOM

PLENARY SESSION MODERATED BY:
Denise Garrett, Sabin Vaccine Institute & Eileen Quinn, PATH

Addressing the paramount global challenges posed by typhoid and iNTS is of utmost importance. As the opening plenary, this session holds a central role for the entire conference, shedding light on the pressing global challenges that demand our immediate attention and emphasizing the need to expand impact-focused solutions. Topics to be explored during this session include the need for evidence to implement effective solutions, addressing data inequality, combating antimicrobial resistance, and dealing with iNTS. Through insightful presentations, we will navigate the intricate landscape of these problems, charting a course toward actionable strategies that lead to real-world impact.

Fighting Typhoid: The Importance of Evidence for Effective Prevention and Control Amid Urgency to Act
Anuradha Gupta, Sabin Vaccine Institute

Non-Typhoidal *Salmonella* Invasive Disease as a Leading Cause of Child Death in Africa — Challenges and Opportunities for Management and Control
Samuel Kariuki, Kenya Medical Research Institute

The Challenge of Sustainable Access to Effective Antibiotics for Enteric Infections
Ramanan Laxminarayan, One Health Trust

Confronting the Challenge of Data Inequity
Kathleen M. Neuzil, University of Maryland School of Medicine

Discussion

9:45–10:15 Coffee Break & Poster Viewing

FOYER

10:15–12:15 Vaccine Voyage I: Navigating the Advancements in Vaccine Research

KILIMANJARO BALLROOM

ORAL ABSTRACT SESSION MODERATED BY: Kirsten Vannice, Bill & Melinda Gates Foundation & Sushant Sahastrabuddhe, International Vaccine Institute

Serological Response Using ELISA Anti-Vi-IgG After Single Dose of Typhoid Conjugate Vaccine Against *Salmonella* Typhi Among Children in Hyderabad, Pakistan

Farah N. Qamar, Aga Khan University

Sonia Qureshi[1], **Farah Naz Qamar[1],** Zoya Haq[2], Mohammad Tahir Yousufzai[1], Ibtisam Qazi[1], Momin Kazi[1], Seema Irfan[1], Najeeha Iqbal[1], Zohra Malik[1], Mehreen Adnan[1], Aneeta Hotwani[1], Najeeb Rahman[1]

[1]Aga Khan University Hospital, [2]Liaquat National Hospital

Typhoid is a potentially life-threatening infection caused by the bacterium *Salmonella* Typhi, affects 11-21 million people annually and can be prevented through immunization with Typhoid Conjugate Vaccine (TCV). This study aimed to measure the serologic response following immunization with Typbar-TCV against *Salmonella* typhi using ELISA anti-Vi-antibodies at several time points over a period of 4 years among children from Hyderabad, Pakistan. A subsample of children aged 6 months-10 years, vaccinated during the outbreak response for extensively drug resistant typhoid fever in Hyderabad were enrolled and followed from March 2018-January 2023. Blood samples were collected at baseline and after administration of Typbar-TCV at 4-6 weeks, 6 months, 1 year, 2 years, 3 years and 4 years post vaccination to measure ELISA anti-Vi-IgG levels and estimate seroconversion rates. Seroconversion was defined as a 4-fold rise in anti-Vi-IgG titer from baseline to 4-6 weeks. Febrile cases were identified through biweekly phone followups and blood cultures were offered to any child with fever ≥3 days within the last 7 days of at the nearest AKU satellite laboratory. At enrolment, the mean age of the study participants was 46.5 (SD ± 29.7) months. Most participants (501/958; 52.3%) were male. Most participants seroconverted (777/837; 92.8 %) at 4-6 weeks following a single dose of Typbar -TCV. The mean geometric titers (GMT) of anti-Vi-IgG antibodies at 4-6 weeks for children aged 6 months-5 years were 1014.3 U/mL (95% CI: 825.2, 1166.9) and for children aged >5-10 years were 991.2 U/mL (95% CI: 549.0, 1274.8). The drop in GMT below 4-fold from the baseline was observed in only 126/588 (21.4%) participants 4 years post Typbar-TCV vaccination. During the 4 years of follow-up, 12 children had culture confirmed typhoid (11 = *S.* Typhi, 1 = *S.* Paratyphi). Around 91.7% (11/12) enteric fever cases seroconverted at 4-6 weeks post Typbar -TCV vaccination and 8 (66.7%) of them remained seroconverted at 4-year time point following Typbar -TCV. They had Geometric mean (95% CI) antibody titers of 24.4 (11.3 – 52.9) (U/ml) at the time of infection. Our study shows successful seroconversion (92.8%) immediately following a single dose of Typbar -TCV. Elevated anti-Vi-IgG titers were maintained above the baseline at 4 years in 408/579 (70.5%) of the cohort.

The Validity of Different Study Designs in Estimating the Protection of Typhoid Conjugate Vaccine

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BACKGROUND

Typhoid conjugate vaccines (TCVs) has been introduced in five countries by 2023. Inconsistent vaccine effectiveness (VE) has been reported following the introduction using different study designs. This methodology study aims to evaluate the validity of different designs in estimating VE.

METHODS

We utilised the data from a cluster-randomised controlled trial (CRCT) conducted in Bangladesh between 2018-2020. 150 clusters were randomised (1:1) to receive either TCV or Japanese encephalitis (JE) vaccine. The vaccination rate during the 2-year follow-up period was 64%. We compared the VE against typhoid estimated by CRCT (TCV vaccinees vs. JE vaccinees), cohort design (TCV vaccinees vs. non-vaccines in TCV clusters), and test-negative design (TND, typhoid cases vs non-typhoid infections in TCV clusters). We conducted bias indicator analysis among JE clusters as well as the analysis using blood cultured confirmed non-typhoid infections as the endpoint. Adjusted Poisson regression was used in the CRCT and cohort analysis, while logistic regression was used in the TND analysis adjusting for the same confounders.

RESULTS

The CRCT analysis revealed a typhoid incidence of 614 (per 100,000 person-years) in JE vaccinees and 70 in TCV vaccinees, resulting in a VE of 88% (95%CI: 80-93). In the cohort analysis, the incidence was 282 among non-vaccinees in the TCV clusters with a VE of 77% (95%CI:

58-88), while the TND yielded a VE of 85% (95%CI: 75-90), which closely aligned with the gold standard of CRCT analysis. In the JE clusters, the cohort analysis (JE vaccinees vs non-vaccinees) showed a 2.2-fold increased risk of typhoid (95%CI:1.4-3.3) in JE vaccinees compared with non-vaccinees, whereas the TND analysis found no significant association (odds ratio: 0.97, 95%CI: 0.70-1.36) between JE vaccination and typhoid. Similar patterns were observed when using non-typhoid infection as the endpoint. Compared with non-vaccinees, a significantly increased risk (around 2-fold) in TCV or JE vaccinees was seen in the cohort analysis, though no significant association was found in the TND.

CONCLUSIONS

The cohort design for estimating TCV effectiveness following its introduction may lead to biased estimations. Our findings confirm earlier work from Malawi suggesting that the TND may be useful for evaluating the effectiveness of TCV.

TyVAC Nepal: Two Dose and Extended Immunogenicity

Mila Shakya, Patan Academy of Health Sciences, Patan Hospital

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BACKGROUND

In a previous study, a single dose of Vi-typhoid conjugate vaccine (Vi-TCV) was found to be highly efficacious in Nepalese childrenless than 16 years of age. We have reported a 99% anti-Vi IgG and a 97% anti-Vi IgA seroconversion at day 28 and persistence of antibodies at 18 months following vaccination with a Vi-TCV.

Here we describe the medium term immunogenicity of a single dose typhoid conjugate vaccine and also assess the immunogenicity of Vi-TT at 9 or12 months of age, with a booster dose at 15 months of age.

METHODS

In 2017, we conducted a participant-and-observer blinded randomized controlled trial (RCT) where 20,019 children 9 months -< 16 years, were randomized 1:1 to receive either Vi-TCV or meningococcal conjugate vaccine (MenA). Participants were offered the alternate vaccine at the final visit of the RCT 2 years later. Depending upon the timing of TCV, there were three cohorts: the early cohort vaccinated at the beginning of the trial (2017/2018) and the two late cohorts vaccinated in 2020 and 2021. Among the study participants, 1500 participants were randomized to participate in the immunogenicity sub-study. The current immunogenicity study is an observational study of RCT participants were followed for another 2 years and were offered twoblood draws scheduled at 42-50 months and 50-60 months.

A prospective cohort study was also included consisting of infants outside the RCT, were receivedan initial dose of Vi-TCV at 9 or 12 months of age, with a booster dose at 15 months of age and antibody titres were measured.

Anti-Vi IgG titers were measured using a commercial ELISA kit and anti-Vi IgA titers were assessed with Vi-coated plates and reagents supplied by The Binding Site using a protocol adapted from the commercial VaccZyme assay. Here we present the analysis of first blood sampling at 42-50 months following vaccination in the RCT andone month following the initial and booster doses in infants.

RESULTS

From the immunogencity cohort, a total of 761 blood samples were collected at 42 -50 months post-initial vaccination (507 from the early cohort and 253 from the late cohort).The median time of sample collection in the early cohort was 49.2(48.2-50.2) months and the late cohort was 13.73(10.8-24.0) months post vaccination with TCV . The geometric mean concentration (GMC) at 95% CIs of the IgA titers in the early and late cohort were 13.02 EU/ml(11.76-14.42) and 22.33 EU/ml (19.29-25.84) respectively, while the GMC of IgG titers were 146.46(132.3-162.0) EU/ml and 241.29(208.5-279.23).

Fifty participants recruited in the 9- and 12-month groups attained 100% seroconversion (4-fold antibody titre) of IgG 1 month after the initial dose. Post-booster, the 9-month group showed significantly higher IgG seroconversion than the 12-month group. All participants who attended visits per protocol (n=27 in the 9-month and n=32 in the 12-month groups) showed IgG seroconversion following the first dose. However, after the second dose, 80% of the participants of 9-month group showed a four-fold rise in antibody levels, while none of the participants of 12-month group showed the four-fold rise (p<0.001).

CONCLUSIONS

High levels of anti Vi IgG and anti Vi IgA titers persisted in both the early and late cohorts. Vi-TCV is highly immunogenic at both 9 and 12 months of age. There may be a stronger response to a booster at 15 months of age in those individuals receiving their first dose at 9 months of age rather than 12 months, likely as a result of the longer interval between doses.

Effectiveness of Typhoid Conjugate Vaccine (TCV): A Systematic Review

Amira Mahboob, World Health Organization Regional Office for the Eastern Mediterranean

Amira Mahboob, Muhammad Tayyab, Shaza Mohammed, Sherein Elnossery, Paiman Akbar, Abdinasir Abubakar

WHO/EMRO

BACKGROUND

Typhoid fever is a worldwide public health problem. In 2018, WHO recommended the programmatic use of Typhoid Conjugate Vaccine (Typbar-TCV) for children in endemic countries after its prequalification in 2017. This review aims to assess the effectiveness of the TCV from campaign settings conducted in line with WHO recommendations.

METHODOLOGY

We conducted an electronic search in the relevant databases (PubMed, Embase, Scopus, Web of Science, and google scholar) in addition to gray literature search and manual search by citation chaining. Eligibility criteria included post TCV campaign observational studies (2018-2023) with culture confirmed typhoid cases among children and limited to English language.

RESULTS

A total of 206 articles were retrieved using the search strategy, five articles met the eligibility criteria and were included in the systematic review, comprising a total of 2,708 participants (aged from 6 months to 15 years). One study was from AFR (Zimbabwe), three from EMR (Pakistan), and one from SEAR (India). The vaccine effectiveness (VE) against culture confirmed typhoid infection ranged from 56% to 98% in four studies, while in the fifth study the VE was calculated against two control groups (facility controls and community controls) with VE of 54% (-21%-82%) and 74% (42%-89%), respectively. Extensively drug resistant typhoid (XDR) was addressed in one study in which 85% of the culture confirmed cases had antimicrobial resistance and the vaccine showed 97% effectiveness against XDR. One study addressed the VE by time in which VE was higher during the 1st year compared to the 2nd and 3rd years after the campaign. The difference in VE within the included studies is probably attributed to the different context, study design, sample size, sampling strategy, criteria of selection, and the time period between the campaign and the study.

CONCLUSIONS

A single dose of typhoid conjugate vaccine (Typbar-TCV) administered in campaign settings showed effectiveness in prevention of culture confirmed typhoid infection among children. To the best of our knowledge, this is the first systematic review to study the real- world effectiveness of TCV. Further studies are needed to evaluate VE against the antimicrobial resistant typhoid as well as the duration of protection.

Efficacy of Typhoid Conjugate Vaccine Against Culture-Confirmed *Salmonella* Typhi — A Systematic Review and Meta-Analysis

Rabab Batool, Aga Khan University

Rabab Batool[1], Rehana A. Salam[2], Zoya Qamar Haq[3], Sonia Qureshi[1], Per Ashorn[4], Farah Naz Qamar[5]

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After the emergence of extensively drug resistant strains, Typhoid has become a serious public health threat in many low- and middle-income countries. Typhoid immunization can substantially reduce typhoid fever burden in high-risk settings. We performed a systematic review and meta-analysis to estimate vaccine efficacy (VE) of typhoid conjugate vaccine against culture confirmed Samnonella Typhi. A systematic literature search was conducted in electronic databases including Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, and Embase upto 5 January 2023. Randomized control trials comparing efficacy of typhoid conjugate vaccine with control in adults and children were eligible for inclusion.

Certainty of evidence for key outcome was assessed using the GRADE methodology. The outcome of interest was typhoid fever confirmed by the isolation of *Salmonella* enterica serovar Typhi in blood. We calculated pooled risk ratios (RRs) and efficacy (1 – RR as a percentage) with associated 95% confidence intervals (CIs).

In total, four RCTs (Mitra 2016, Shakya 2019, Patel 2021, Qadri 2021) contributed to the quantitative analysis in this review, all of the trials were conducted in typhoid endemic countries (India, Bangladesh, Nepal and Malawi), trial participants age ranged from 6 months to 16 years.

The VE of the typhoid conjugate vaccine at 1 year among the participants aged 6 months to 16 years was found to be 85% (95% CI: 79%, 89%; moderate certainty); TCV likely results in a large reduction in the incidence of Typhoid fever. At two years typhoid conjugate vaccine likely results in a large reduction in the incidence of Typhoid fever (VE: 80%; 95%CI: 69, 87%; I^2: 0%; moderate certainty). The random-effects pooled vaccine efficacy of typhoid conjugate at one to two years was 83% (95% CI: 77%, 88%, I^2: 0%; high certainty).

We conducted subgroup analysis by age, as three trials (Patel 2021, Qadri 2021, Shakya 2021) evaluated the efficacy of the typhoid conjugate vaccine vaccine and stratified VE results according to the age groups. The vaccine efficacy of typhoid conjugate vaccine among the participants aged ≥ 5 years was significantly higher than the vaccine efficacy observed in participants aged < 5 years, 87% (95% CI: 80%, 91% ; I^2:0; moderate certainty) versus 73% (95% CI: 53%, 85% ; I^2: 37% ; moderate certainty).

The existing data provides promising results on the efficacy of typhoid conjugate vaccine in typhoid endemic countries. Future research on long term efficacy of conjugate vaccines and their impact on enteric infection and shedding is warranted.

Safety of Typhoid Conjugate Vaccine Booster Vaccination in Malawian Children

Osward M. Nyirenda, Blantyre Malaria Project, Kamuzu University of Health Sciences

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BACKGROUND

Typhoid conjugate vaccines (TCV) are being introduced into routine immunization programs in Malawi and other countries. Safety data for booster dose vaccination is essential to inform decision-making for vaccine schedule changes. We report the safety of a booster dose of a typhoid Vi polysaccharide tetanus toxoid conjugate vaccine (Vi-TT) given to children at 5 years who initially received Vi-TT or control vaccine at 9-11 months of age.

METHODS

A phase 3 trial of Vi-TT in Malawi randomized children 1:1 to receive either Vi-TT or meningococcal capsular group A conjugate vaccine. From this study population, we recruited and enrolled children vaccinated at 9-11 months of age into a booster substudy to receive Vi-TT as a first or booster dose at approximately 5 years of age. Safety outcomes included solicited and unsolicited adverse events (AE) within 7 and 28 days of vaccination, respectively.

RESULTS

We enrolled 136 children: 64 received first and 72 booster Vi-TT.

Local reactions on day one post-vaccination were mostly mild/moderate and occurred at a similar rate in first (40/43, 93%) and booster Vi-TT (52/55, 94.5%) recipients– p-value 1.00. The most common local reaction on day one was mild/moderate pain (90% and 89.1%), followed by mild/moderate swelling (20.9% and 18.2%), in first and booster Vi-TT recipients, respectively. By day five post-vaccination, all local reactions had resolved.

The rate of systemic AEs on day one post-vaccination did not differ significantly between first (10/43, 23.3%) and booster Vi-TT (19/55, 34.6%) – p-value 0.27. Reported fever was the most common systemic AE, occurring in 11.63% of first and 30.91% of booster Vi-TT participants. Mild/moderate malaise occurred in 14.0% of first and 9.1% of booster Vi-TT participants. On day 7, one participant in each group reported fever, and all other symptoms had resolved.

Unsolicited AEs occurred at a similar rate between the two groups (24/64, 37.5% in first and 23/72, 31.9% in booster Vi-TT – p-0.59). One AE each in both arms was considered related to vaccination.

CONCLUSION

TCV caused few AEs after first or booster dose administration, which were mostly mild and moderate. Reactogenicity of first and booster doses of TCV at age 5 years were similar.

Test-Negative Design: An Efficient Method to Assess Typhoid Conjugate Vaccine Effectiveness

Matthew Laurens, University of Maryland School of Medicine

Yuanyuan Liang[1], Amanda Driscoll[1], Priyanka Patel[2], Shrimati Datta[1], Merryn Voysey[3], Neil French[4], Leslie Jamka[1], Marc Henrion[2], Latif Ndeketa[2], Matthew Laurens[1], Robert Heyderman[5], Melita Gordon[4], Kathleen Neuzil[1]

[1]University of Maryland School of Medicine, [2]Kamuzu University of Health Sciences, [3]University of Oxford, [4]University of Liverpool, [5]University College London

BACKGROUND

As typhoid conjugate vaccines (TCVs) are introduced in low-income and middle-income countries to prevent typhoid illness in children via national immunisation programmes, post-introduction monitoring is important to understand how they perform under real-world conditions. Although the test-negative design (TND) is used to evaluate the effectiveness of other vaccines, its suitability for TCV has been questioned due to the potential for false negative cases resulting from low blood culture sensitivity. Using data from a randomised controlled trial (RCT) in Malawi, we evaluated the appropriateness of the TND as a method to assess typhoid Vi polysaccharide-tetanus toxoid conjugate vaccine (Vi-TT) effectiveness.

METHODS

Using blood culture surveillance data from a RCT of Vi-TT in Malawi, we simulated three TND samples to derive vaccine effectiveness estimates using three different approaches (participant-based with or without censoring and specimen-based approaches proposed by De Serres et al. 2013) and compared these to RCT efficacy results. In the RCT, 27 882 children aged 9 months to 12 years were randomly assigned (1:1) to receive a single dose of Vi-TT or meningococcal capsular group A conjugate vaccine between 02/21/2018 and 09/27/2018, and were followed up for blood culture-confirmed typhoid fever until 09/30/2021.

RESULTS

For all three approaches, TND vaccine effectiveness estimates (80·3% [95% CI: 66·2%, 88·5%] vs 80·5% [66·5%, 88·6%] vs 80·4% [66·9%, 88·4%]) were almost identical to the RCT results (80·4% [66·4%, 88·5%]). Receipt of Vi-TT did not affect the risk of non-typhoid fever (vaccine efficacy against non-typhoid fever −0·4% [−4·9%, 3·9%] vs −1% [−5·6%, 3·3%] vs −2·5% [−6·4%, 1·3%] for the three approaches, respectively). Importantly, the effect of blood culture sensitivity was minimal for vaccine effectiveness estimation accuracy when typhoid-positive cultures comprised fewer than 10% of all blood cultures.

CONCLUSIONS

This study validated the TND core assumption that TCV has no effect on febrile illnesses that are not caused by typhoid. Furthermore, this study showed that the TND produced accurate and precise estimates of vaccine effectiveness compared with RCT vaccine efficacy results in a Malawian pediatric population. These results suggest that TND is well-suited for post-introduction assessments of TCV effectiveness in similar settings.

A Phase IV Clinical Study to Evaluate the Immunogenicity and Safety of Typhoid Conjugate Vaccine (Typbar TCV®) in Elderly Population

Raches Ella, Bharat Biotech International

Krishna Mohan, Siddharth Reddy, Sandhya Rani, Vinay Aileni

Bharat Biotech International

BACKGROUND

Typhoid risk is higher in the children but adults and elderly adults also significantly infected with *Salmonella* Typhi1,2. Among these, 1 to 6 % becomes chronic biliary carriers of *Salmonella* Typhi. These carriers are potential factors in the continued transmission of the disease3,4. Vaccination to the adult population could help in reducing the carriers and disease transmission. BBIL conducted a Phase 4 study to evaluate the safety and immunogenicity of the Typbar TCV® vaccine in adults ages 45 to 65 years compared to younger population.

METHODS

In this study, a total of 300 participants were enrolled in to two groups. in Group 1 younger adults (n=100) ages between 18-45 years and in Group 2 (n=200) elderly adults ages between 45-65 years were enrolled and vaccinated with single dose Typbar TCV® vaccine. The vaccine safety and immunogenicity was previously assessed in younger adults (18-45Years) age group5, hence this was used as control group in the study. Safety was monitored during the study and blood samples before and 4 weeks after the vaccination were collected to assess the vaccine safety and immunogenicity in elderly adults compared to younger adults.

RESULTS

Overall 94 AEs were reported in 58 subjects (19.33%) of the total enrolled subjects. The proportion of subjects who reported AEs were similar across the treatment groups with 28 (28%) in group I and 30 (15%) in group II. The distribution of AEs is similar across the treatment groups for solicited and unsolicited AEs. No SAEs occurred during the study period. Anti Vi IgG GMTs at baseline were 12.0 U/ml and 13.01 U/ml, which increased to 1468.81 U/ml (95% CI 1260.52, 1711.51) and 1568.21 U/ml (95% 1378.58, 1783.93) post-vaccination in group I and group II, respectively. Seroconversion (4-fold) was observed in 99% (95% CI 94.55, 99.97) and 97% (95% CI 94.26, 99.18) in group I and group II respectively.

CONCLUSIONS

Typbar TCV® is well tolerated in elderly adults and safety with regard to solicited and unsolicited AEs were comparable across the two groups. Typbar TCV® vaccine induces comparable and equivalent immune response in the two treatment groups. Typbar TCV® can be safely administered to elderly population to prevent typhoid infection. Our next objective is to extend this study to ages 65 years and above.

12:15–13:30 Lunch — SOKO RESTAURANT

13:30–15:00 Maximizing Learnings From Clinical Trials and Public Sector Use — The Full Public Health Value of Typhoid Conjugate Vaccines

KILIMANJARO BALLROOM

SYMPOSIUM SESSION CHAIRED BY:
Megan E. Carey, International AIDS Vaccine Initiative and London School of Hygiene & Tropical Medicine & Kathleen M. Neuzil, University of Maryland School of Medicine

Salmonella enterica serovar Typhi (*S.* Typhi) caused an estimated 9.24 million (95% UI 5.94–14.1) cases of typhoid fever in 2019, resulting in 110,000 deaths (52,800–191,000) and 8.05 million (3.86–13.9) disability-adjusted life years (DALYs).[1] When treated appropriately, typhoid fever has a mortality rate <1%, but mortality rates exceeded 20% in the pre-antimicrobial era.[2] Increasing prevalence and severity of antimicrobial resistance (AMR) jeopardizes effective typhoid fever control, particularly in South Asia, where resistance to all oral antimicrobials has been reported [3] and disease incidence is highest.

This is a pivotal moment for typhoid fever control. We have two safe and effective World Health Organization-prequalified vaccines, funding from Gavi, the Vaccine Alliance, and growing drug-resistance — now is the time for countries to introduce TCVs and *Take on Typhoid*. Six countries have introduced TCV into their national immunization programs, and work is underway to determine the feasibility of typhoid elimination. As decision-makers weigh the value of TCVs against other cost-effective, live-saving interventions, it is important to measure the full public health value of vaccines, including the potential impact on AMR. TCVs can mitigate the burden of AMR by preventing infections caused by drug-resistant pathogens and by lowering selection pressure by preventing unnecessary antimicrobial use.

Ongoing surveillance continues at Typhoid Vaccine Acceleration Consortium (TyVAC) sites in Bangladesh, Malawi, and Nepal to answer additional policy questions. We will present data on vaccine efficacy over more than four years, alternative vaccine schedules (including booster doses), and illustrate how data inform country decision-making on TCV introduction. We will also present available evidence on the impact of TCVs on AMR and discuss ongoing efforts and considerations for how best to measure the impact of TCV on AMR, moving from clinical trials and outbreak response campaigns to large-scale TCV introduction.

Longer-Term Efficacy of Typhoid Conjugate Vaccine in Malawi
Priyanka Patel, Malawi-Liverpool-Wellcome Trust

New Findings on Immunogenicity of TCV: Booster Dose in School-Aged Children and 1 Versus 2 Dose Regimens in HIV-Exposed Infants
Osward Nyirenda, Blantyre Malaria Project, Kamuzu University of Health Sciences

Typhoid Fever Surveillance in Urban Dhaka, Bangladesh: Risk Factors and Antimicrobial Resistance Pattern
Farhana Khanam, icddr,b

Impact Assessment of National TCV Introduction in Pakistan
Farah N. Qamar, Aga Khan University

The Impact of a TCV Mass Campaign on Typhoid Fever Cases and Antimicrobial Use in Harare, Zimbabwe
Ioana Diana Olaru, London School of Hygiene and Tropical Medicine

Measuring the Impact of Typhoid Conjugate Vaccines on Antimicrobial Usage From Pivotal Efficacy Studies
James E. Meiring, Department of Infection, Immunity and Cardiovascular Disease, University of Sheffield

15:00–15:30 Coffee Break & Poster Viewing

FOYER

15:30–17:30 Comprehensive Exploration of iNTS: From Vaccine Trials to Global Epidemiology

KILIMANJARO BALLROOM

ORAL ABSTRACT SESSION MODERATED BY:
James Meiring, University of Sheffield & Raphael Zellweger, International Vaccine Institute

Study Design and Initial Data From Phase 1 RCT to Evaluate the Safety, Reactogenicity and Immunogenicity of a Vaccine Against iNTS and Typhoid Fever in Healthy Adults

Yasir Shitu Isa, GSK Vaccines Institute for Global Health

Yasir Shitu Isa[1], Kanchanamala Withanage[2], Antonio Lorenzo Di Pasquale[1], Alimamy Serry-Bangura[3], Giulia Luna Cilio[3], Omar Rossi[1], Beatrice Grossi[1], Chiara Crispino[1], Rita La Gaetana[1], Valentino Conti[1], Usman Nasir Nakakana[1], Rocio Canals[1], Ashwani Kumar Arora[1]

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BACKGROUND

Invasive nontyphoidal *Salmonella* (iNTS) disease and typhoid fever are major public health concerns causing a significant socioeconomic burden particularly in resource-limited settings of sub-Saharan Africa (sSA). In 2017, an estimated 535 000 iNTS disease cases were reported with >400 000 in sSA. More than 50% of the 59 100 deaths in the same year occurred in children under 5 years of age with a case fatality rate of 14.5%. *S.* Enteritidis and *S.* Typhimurium are the most common *Salmonella enterica* serovars causing iNTS disease in sSA accounting for >90% of cases. There is currently no licensed vaccine available for iNTS disease and typhoid conjugate vaccines (TCVs) are not widely used in Africa. iNTS-causing *Salmonella* strains are usually associated with multidrug resistance particularly in sSA. A novel trivalent iNTS-TCV vaccine aimed at preventing iNTS disease and typhoid fever is under development by GSK Global Health Vaccines R&D (GVGH). The first stage of the clinical development is a first-time-in-human (FTIH) study aimed to evaluate the safety and immunogenicity profile of the vaccine in healthy European adults aged 18 to 50 years.

METHODS

50 healthy adults were randomized in a 2:2:1 ratio to receive either iNTS-TCV vaccine and concomitant saline in opposite arms, or separate iNTS-GMMA and TCV vaccines in opposite arms, or placebo and saline in opposite arms intramuscularly on Days 1, 57 and 169. The study followed a 2-step staggered design with a sentinel and dose-escalation approach starting with the low dose and progressively administering the full dose.

RESULTS

After at least two administrations with the low or full doses or controls, the majority of adverse events (AEs) observed are of mild to moderate intensity. Injection site pain is the most reported local solicited AE while myalgia, fatigue and headache are the most frequent systemic solicited AEs. Severe unsolicited AEs considered related to vaccination were reported in 2 subjects overall. No serious AE considered related to vaccination has been reported.

CONCLUSIONS

Based on available safety data, clinical development is planned to progress into healthy adults in an endemic African country, to further assess safety and immunogenicity of the iNTS-TCV vaccine.

Age-Specific Incidence and Associated Mortality of Invasive Non-Typhoidal *Salmonella* in Mozambican Children, 2001–2019

Inacio Mandomando, Centro de Investigação em Saúde de Manhiça

Inacio Mandomando[1], Marcelino Garrine[2], Llorenc Quintò[3], Augusto Messa Jr[4], Sergio Massora[4], Charfudin Sacoor[4], Quique Bassat[3], Pedro Alonso[5]

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BACKGROUND

Despite the decline in the incidence of invasive non-typhoidal *Salmonella* (iNTS) over the past years in sub-Saharan Africa, iNTS remain a significant problem, particularly among children younger than 5 years of age, calling for alternative preventive and therapeutic tools to decrease iNTS-associated morbidity and mortality, particularly in light of the limited access to the most expensive second-line antibiotics to treat infections caused by multidrug-resistant iNTS strains.

METHODS

We estimated the age stratified incidence of iNTS among children admitted to the Manhiça District Hospital and with blood cultures performed between January 2001 and December 2019. Incidences were determined for small

age group brackets (0-7 weeks; 8-15 weeks; 4-8 months; 9 months; 10-11 months; 12-23 months; 24-59 and 5-15 years) for a more detailed understanding of risks in the first months of life and to tailor guidance for vaccine strategies and best age for vaccination. Overtime incidence rate trends and associated mortality were calculated for cases using the demographic surveillance system for accurate denominators.

RESULTS

Over the study period, iNTS was isolated in 1.2% (674/57755) of blood cultures, with S. Typhimurium (68%, 458/674) and S. Enteritidis (20.5%, 138/674) being the most common serovars circulating. The overall minimum community-based incidence rate was 42.60 episodes (95% CI: 38.20 - 47.51), peaking at 9 months of age (478.52; 95% CI: 315.08 - 726.73), 5.98-fold higher than that of the baseline age-group (0-7 weeks); while it was 129.29 episodes (95% CI: 58.09 - 287.79) among the 4 months old. Children aged 4 months old infected by serovars other than S. Typhimurium and Enteritidis had the second major incidence (64.45; 95% CI: 20.85 - 200.44 episodes per 100,000 child-years), immediately following the 9 months old group (86.69; 95% CI: 32.65 - 231.78, episodes per 100,000 child-years). Children infected by iNTS were likely to have severe malnutrition (WAZ <-3): OR=5.51 (95% CI: 4.48 - 6.76) or anemia (OR=8.92; 95% CI: 6.69 - 11.89), diarrhea (OR=3.09; 95% CI: 2.58 - 3.71), or splenomegaly (OR=4.33; 95% CI: 3.61 - 5.20) compared to those of whom blood cultures were negative for iNTS. iNTS-associated mortality was 12% (67/569) being significantly higher in children younger than 7 months of age (6/17; 35%).

CONCLUSIONS

Our findings demonstrate that despite a decline of iNTS incidence over the past years, the burden of iNTS remains high and life-threatening, and warrants the urgent development of non-typhoidal conjugate vaccines to immunize African infants.

Severe Anaemia Increases Risk of Invasive Non-Typhoidal *Salmonella* Bacteraemia in Kenyan Children

Kelvin Mokaya Abuga, KEMRI-Wellcome Trust Research Programme

Kelvin Mokaya Abuga[1], John Muthii Muriuki[1], Reagan Mogire[1], Johnstone Makale[1], Alex Macharia[1], Esther Muthumbi[1], Shebe Mohammed[1], Salim Mwarumba[1], Neema Mturi[1], Philip Bejon[1], Thomas Williams[1], J. Anthony G. Scott[1], Manfred Nairz[1], Calman MacLennan[2], Sarah Atkinson[1]

[1]KEMRI-Wellcome Trust Research Programme, [2]University of Oxford

BACKGROUND

Severe anaemia and invasive non-typhoidal *Salmonella* (iNTS) bacteraemia are important causes of death and morbidity for children living in sub-Saharan Africa, but few studies have investigated their association and the underlying mechanisms of this association. We hypothesized that severe anaemia increases the risk of iNTS by disrupting iron homeostasis and impairing immune responses.

METHODS

We investigated the relationship between severe anaemia and iNTS in all paediatric admissions aged <14 years over a 21-year period between 1st August 1998 and 31st March 2020. We then assayed hepcidin, iron biomarkers, and cytokine levels in hospitalized children with 1) severe anaemia and iNTS (n=28), 2) severe anaemia alone (n=52), and 3) iNTS alone (n=45).

RESULTS

Among the 91,261 admissions during the study period, 16,053 (17.6%) had severe anaemia and 4,687 (5.1%) had bacteraemia, of which 448 (9.6%) were iNTS (148 serovar Typhimurium, 154 Enteritidis, 39 not typeable, and 107 not tested). Severe anaemia was associated with a four-fold increased risk of iNTS bacteraemia (OR 4.54 [95% CI 3.76, 5.50], P<0.0001). The risk of iNTS bacteraemia increased along the spectrum of anaemia severity, with each 1g/dL decrease in haemoglobin increasing the risk of iNTS by 30% (OR 1.30 [95% CI 1.26, 1.34]; P<0.0001). Severely anaemic children with iNTS had lower hepcidin/ferritin ratios and higher erythroferrone levels (0.03 [IQR 0.01, 0.09] and 7.2 ng/mL [IQR 4.2, 17.6], respectively) than those with NTS alone (0.11 [IQR 0.06, 0.23]; P=0.005 and 3.7 ng/mL [IQR 1.7, 10.6]; P=0.02, respectively), indicating suppressed hepcidin production. Hepcidin/ferritin ratios and erythroferrone levels were not different in severely anaemic children with or without iNTS. Proinflammatory and anti-inflammatory cytokine levels were similar across the three groups.

CONCLUSION

Severe anaemia contributes to the burden of iNTS in African children. Since hepcidin degrades ferroportin on the *Salmonella*-containing vacuole, we hypothesize that reduced hepcidin in children with severe anaemia might contribute to iNTS risk by modulating iron availability for bacterial growth. Further studies are needed to understand how the hepcidin-ferroportin axis might mediate susceptibility to NTS in severely anaemic children.

Modelling the Global Prevalence of Antimicrobial Resistant Invasive Non-Typhoidal *Salmonella* Infections, 2000–2019

Frederick Fell, University of Oxford

Frederick Fell[1], Benn Sartorius[1], Ben Cooper[1], Annie Browne[2], Michael Chipeta[3], Christiane Dolecek[1]

[1]University of Oxford, [2]Telethon Kids Institute, [3]The African Institute for Development Policy

BACKGROUND

There are approximately half a million cases of invasive Non-typhoidal *Salmonella* (iNTS) disease annually. iNTS has a case-fatality of approximately 15%, with the elderly, those with HIV or malaria, and the malnourished most at risk. Antimicrobial resistance (AMR) makes treatment for iNTS

even more challenging especially with the rise of multi-drug resistant (MDR) infections. As part of the GRAM (Global Burden of Disease–Antimicrobial Resistance) project, we aimed to estimate the percentage of iNTS infections that were fluoroquinolone non-susceptible (FQNS), third-generation cephalosporin resistant (3GCR) and MDR (defined as concurrent resistance to ampicillin/amoxicillin, chloramphenicol and trimethoprim-sulfamethoxazole) in 204 countries between 2000 and 2019.

METHODS

We used a two-stage spatiotemporal modelling framework to estimate the percentage of iNTS infections that were FQNS, 3GCR and MDR. The analysis made use of data from public health surveillance networks, large multi-country studies and a systematic review.

RESULTS

Data were included from 149 sources with over 54,000 isolates of iNTS covering 60 countries within 16 global regions over 19 years. We estimated that, between 2000 and 2019, FQNS increased by 8.47% [95% uncertainty interval 4.5–13.9%] across the world with prevalence of resistance in south Asia increasing by 18.3% [12.9–23.8%]. MDR remained high across the study period with the highest prevalence in sub-Saharan Africa (SSA). In 2019, the estimated prevalence in east SSA was 55% [41.9–67.4%], the corresponding estimates for central, western, and southern SSA were 46.5% [34.7–58.8%], 43.8% [30.5–57.9%] and [21.2–44.2%], respectively. Based on limited data, there were small increases in estimated 3GCR prevalence between 2000 and 2019.

CONCLUSIONS

This study presents a detailed analysis of AMR iNTS infections globally over the last 20 years and highlights trends and the regions most affected by MDR, FQNS and 3GCR. Results from this analysis will help identify those locations where improvements in water, sanitation and hygiene (WASH) are most urgently needed. The study also identifies areas where additional data and research is needed to improve our understanding of AMR in iNTS across space and time.

IgG and IgA Antigen-Specific B Memory Responses in Healthy U.S. Adults Immunized with a Parenteral Trivalent *Salmonella* Conjugate Vaccine (TSCV)

Marcelo Sztein, University of Maryland School of Medicine

Rezwanul Wahid[1], Wilbur Chen[2], Sharon Tennant[2], Rekha Rapaka[2], Gangadhara Naidu[3], Myron Levine[2], **Marcelo Sztein[2]**

[1]Center for Vaccine Development, University of Maryland School of Medicine, [2]Center for Vaccine Development and Global Health, University of Maryland School of Medicine, Baltimore, Maryland, USA, [3]Bharat Biotech International Limited, Hyderabad, Telangana, India

BACKGROUND

Invasive non-typhoidal (iNTS) serovars *S.* Typhimurium (STm) and *S.* Enteritidis (SE) cause fatal infections in infants and young children in sub-Saharan Africa. To prevent these infections, a novel Trivalent *Salmonella* Conjugate Vaccine (TSCV) was developed using core+O polysaccharide (COPS) from STm and SE conjugated to serovar-homologous flagellin subunits (FliC), in combination with Typbar TCV the first WHO pre-qualified *S.* Typhi Vi-Tetanus toxoid vaccine (Vi-TT) licensed in many countries. In a phase-1 clinical trial, we evaluated whether intramuscular administration (IM) of this vaccine could elicit memory B cells (BM) against TSCV antigens.

METHODS

Cryopreserved PBMCs from vaccinees immunized with quarter-strength TSCV (6.25 µg per conjugate, cohort A, n=8) and half-strength TSCV (12.5 µg per conjugate cohort B, n=10) TSCV or Placebo recipients (n=4) obtained before and after vaccination at days 29, D57 and D450/412 were expanded with B cell mitogens in vitro and subjected to antigen specific ELISPOT assays.

RESULTS

The percentages of volunteers among vaccinees (Cohort A and B: N=18) showing post-vaccination increases in IgG and/or IgA BM cells specific for Vi (72%), Lipopolysaccharide (LPS)-SE (67%) and LPS-STm (72%) were significantly higher than those observed in Placebo controls (n=4). The magnitude and rate of BM responses peaked at day 29 post-vaccination and gradually declined over a year. No such responses were observed against an LPS control from *S.* Choleraesuis. There were no significant differences of either isotype (IgG or IgA) between the volunteers who received quarter-strength versus half-strength TSCV doses. A COVID-19 lockdown prevented vaccination with the full-strength TSCV (25 µg per conjugate) and precluded Day 180 follow-up visits of some enrolled volunteers.

CONCLUSIONS

TSCV was able to induce B_M cells against vaccine antigens which could be detected in circulation at least 2 months post-vaccination. B_M cells are also being measured in a follow-on study in which adults received full-strength TSCV doses to confirm the magnitude and kinetics of the B_M cells response against vaccine antigens.

Antimicrobial Resistance and Intestinal Shedding of Non-typhoidal *Salmonella* Among Children Under Five Years and Carriage in Asymptomatic Hosts in Kenya

Celestine Wairimu, Kenya Medical Research Institute

Kelvin Kering[1], **Celestine Wairimu[1],** Georgina Odityo[1], Kariuki Njaanake[2], Marianne Mureithi[2], Cecilia Mbae[1], Samuel Kariuki[1]

[1]Kenya Medical Research Institute, [2]Univeristy of Nairobi,

BACKGROUND

Nontyphoidal *Salmonella* (NTS) infection is characterized by self-limiting enterocolitis, but can become invasive resulting in bacteremia. *Salmonella enterica* serovars Typhimurium and Enteritidis (*S.* Typhimurium and *S.* Enteritidis) are the most common causes of NTS with the highest incidences reported in sub-Saharan Africa and in children ≤ 5 years. Since intestinal shedding could serve as a potential source of new infections in vulnerable individuals, this study aimed to determine rates of post-convalescent shedding in children under five years of age and corresponding age-matched controls in the community.

METHODS

This was a prospective case-control study in children from the Mukuru Informal settlement in Nairobi, between June 2021 and April 2023. Children presenting with fever for > 24 hours with or without diarrhoea were recruited. Blood and stool were collected, subjected to culture for NTS isolation, and identified through serology and PCR. Disk diffusion method was used to determine the antimicrobial susceptibility to 14 commonly used antibiotics. Fourteen days post-treatment, index cases, their household contacts, and randomly selected controls were followed-up for a minimum of one month. Thereafter, follow-up was stopped after three consecutive negative cultures from the stool.

RESULTS

Of the 3,057 participants, 1.5% (46) were NTS-positive with 58.7% (27/46) being male. The positivity rate per age group was: ≤ 12 months (1.7%), 13-24 months (1.7%), 25-36 months (1.1%), 37-48 months (0.7%), and 49-60 months (2.2%). Intermittent intestinal shedding was observed in 26.1% (12/46) of the index cases with 66.7% (8/12) of those being male. The longest duration of intestinal shedding was three months post-treatment. Among the healthy individuals, 3.7% were found to be shedding NTS. Resistance to Azithromycin, the current drug of choice for the treatment of invasive NTS, was observed in 13.8% of *S.* Typhimurium and 8.9% of *S.* Enteritidis with reduced susceptibility in 72.4% of *S.* Typhimurium and 82.2% of *S.* Enteritidis.

CONCLUSION

The presence of NTS carriage in children within informal settlements is a risk as they can be sources of transmission to vulnerable and immunosuppressed populations. This study demonstrates the need for vaccine introduction in the prevention of invasive NTS infections especially among young children in endemic settings.

Acquisition of Immunity to Non-Typhoidal *Salmonella* in Malawian Children to Inform Vaccine-Derived Immunity; A Serological Catalytic Model

Helen Dale, University of Liverpool

Helen Dale[1], Esmelda Chirwa[1], Priyanka Patel[2], Theresa Misiri[2], Paul Kambiya[2], Richard Wachepa[2], Maurice Mbewe[2], Innocent Kadwala[2], Niza Silungwe[2], Kenneth Chizani[2], Happy Banda[2], Maria Grazia Aruta[3], Daniele De Simone[3], Rocio Canals Alvarez[3], Georgina Makuta[2], Neil French[1], Omar Rossi[3], Tonney Nyirenda[4], Melita Gordon[1], José Lourenço[5]

[1]University of Liverpool, [2]Malawi-Liverpool Wellcome Research Program, [3]Global Vaccines for Global Health, [4]Kamuzu University of Health Sciences, 5University of Oxford

BACKGROUND

Children exposed to enteric nontyphoidal *Salmonella* (eNTS) develop effective natural immunity against invasive disease, which can inform vaccine-derived immunity. Understanding the age-stratified natural acquisition of immunity in relation to age-stratified asymptomatic eNTS infections and invasive disease incidence in different settings can identify correlates of protection (COP) and inform vaccine impact and implementation.

METHODS

Paired serum from 2428 healthy children recruited in the community was tested for O-Ag (O4) immunoglobulin G (IgG) and high throughput luminescent serum bactericidal activity (L-SBA) to *Salmonella* Typhimurium. We designed a serotype-specific catalytic serological model assuming an exponential decay of maternal antibodies with age from birth, and exposure to eNTS leading to induction of immunity (anti-O-Ag (O4) IgG) through a Gompertz function relationship by age. We compared two models; model 1 assumed a constant force of infection (FOI) throughout ages from birth to 60 months, model 2 assumed FOI changed with age in a sigmoidal relationship with age. Both models were fitted to the serological data per age-bin using a Markov-chain Monte-Carlo (MCMC) approach, and models were compared by Pareto smoothed importance sampling (PSIS) and Widely applicable information criterion (WAIC).

RESULTS

Model 2 was selected as the best-fit model, supporting the hypothesis that the relationship of exposure to eNTS is consistent with a changing (sigmoidal) FOI with age, as reflected in O4 OAg IgG responses in children. This model estimated that on average at birth children were experiencing 0.2 (0.18–0.22) eNTS average infections capable of inducing a serotype-specific serological response, increasing to 2 (95% CI 1.1 to 3.0) by 6 months of age and 4 (95% CI 2.1 to 5.7) by 12 months of age, plateauing at 5 (95% CI 2.2 to 7.1) eNTS infections cumulatively by age 20–60 months.

CONCLUSIONS

Model fit was improved assuming FOI increased around age of weaning (4-6 months); this is consistent with the observed age-stratified point prevalence of eNTS detected on stool microbiology in the same study cohort. Next steps include modeling age-stratified serological responses versus disease incidence and cross-validation considering risk factors and epidemiological setting.

The Burden of Invasive Non-Typhoidal *Salmonella* Disease in Six Sites in Africa: Results from the Severe Typhoid Fever Surveillance in Africa Program

Hyon Jin Jeon, International Vaccine Institute

Hyon Jin Jeon

International Vaccine Institute

BACKGROUND

Within the Severe Typhoid in Africa program (SETA), the burden of invasive, symptomatic non-typhoidal *Salmonella* infections (iNTS disease) were assessed in six African countries: Burkina Faso, the Democratic Republic of the Congo (DRC), Ethiopia, Ghana, Madagascar, and Nigeria.

METHODS

A hybrid design, hospital-based prospective surveillance with population-based healthcare utilization surveys, was implemented. Patients suffering acutely from fever (≥37·5°C axillary or ≥38·0°C tympanic) or reporting fever for three consecutive days within the previous seven days were enrolled. A Bayesian mixture model was used to estimate population disease incidence.

RESULTS

A total of 99% (27,540/27,866) of recruited participants received a blood culture. Clinically-significant organisms were detected in 7% (2,055/27,540) of these cultures and non-typhoidal *Salmonella* serovars grew in 49% (1,011/2,055) of them. The adjusted incidence per 100,000 person-years of observation (PYO) was highest in the Kavuaya/Nkandu-1 DRC site (840, 95% Credible Interval (95%CI) [675; 1,054], followed by Nioko1/Polesgo, (118, 95%CI [95; 149]) in Burkina Faso. No iNTS case was reported in Madagascar. Overall, 13% (104/834) of all hospitalized culture confirmed iNTS cases were severe. Around 90% (756/843) of all iNTS isolates tested for antimicrobial susceptibility were multidrug resistant.

CONCLUSIONS

The circulation of increasingly resistant isolates and the high incidence of infection (defined as equal or higher than 100/100,000 PYO) in two of the six African countries evaluated, indicates the need for development of iNTS vaccines following the successful pathway of the development and use of typhoid conjugate vaccines.

18:00–19:30 Evening Welcome Reception

MALAIKA GARDEN

WEDNESDAY, DECEMBER 6

7:45–8:30 *Salmonella* Controlled Human Infection Models — Insights, Opportunities and Challenges

ISARO ROOM

SUNRISE SYMPOSIUM SESSION CHAIRED BY:
Malick Gibani, Imperial College London

Controlled human infection models (CHIM) for typhoid fever have been in existence for over sixty years. In the six years since we last hosted this symposium — at the 10th International Conference on Typhoid and Other Invasive Salmonelloses in Kampala, Uganda — the use of *Salmonella* challenge studies has continued to grow.

Salmonella challenge models have provided a platform to test novel vaccine candidates and to study host-pathogen interactions in a biologically relevant model. Notable successes include demonstrating efficacy of a Vi-TT conjugate vaccine (Typbar-TCV) prior to the delivery of field studies; describing the role of the typhoid-toxin in human disease and the identification of several putative correlates of protection.

The use-case of *Salmonella* challenge studies continues to evolve in the era of new Vi-conjugate vaccines. Important unmet needs include the development and testing of new vaccines for *Salmonella* Paratyphi A and invasive non-typhoidal *Salmonella*. In addition, the expansion of these models to regions where invasive Salmonelloses are endemic offer the potential to expand capacity and to study the disease in an epidemiologically relevant context.

In this symposium, we will present rapidly emerging data from human challenge models for enteric fever and invasive non-typhoidal *Salmonella*. In particular, we will summarise the background for paratyphoid vaccine development and present new data from a vaccine efficacy study utilizing the paratyphoid challenge model, comparing the response to challenge in a group of healthy volunteers vaccinated with a novel oral *Salmonella* Paratyphi A vaccine against placebo. We will discuss nascent plans to develop a *Salmonella* Typhi challenge model in India and the steps taken to set up a regulatory pathway for such studies. We will present data generated from the application of a systems biology approach to better understand early and innate responses to human enteric fever challenge. Finally, we will present the rationale, the design and preliminary data from the first Non-Typhoidal *Salmonella* challenge model.

It is hoped that these data could build on the successes of the typhoid challenge model and generate momentum to accelerate vaccine development for other invasive Salmonelloses.

Preliminary Results From An Oral Vaccine in the Paratyphoid Human Challenge Model
Naina McCann, Oxford Vaccine Group, Department of Paediatrics, University of Oxford

A Typhoid Fever Challenge Model in India? — Opportunities and Challenges
Rakesh Aggarwal, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry

Development of a Non-Typhoidal *Salmonella* Challenge Model
Christopher Smith, Department of Infectious Disease, Imperial College London

8:30–9:30 Amplifying Impact: Tools and Solutions to Accelerate Progress

KILIMANJARO BALLROOM

PLENARY SESSION MODERATED BY:
Julie Bines, University of Melbourne & Andrew J. Pollard, University of Oxford

Cutting-edge technologies have become pivotal in the control and prevention of infectious diseases. In this session, we will explore the latest tools available to combat typhoid and iNTS, unveiling a realm of strategies with the power to catalyze changes and amplify impact. Topics encompass promising advancements in the field of vaccines, emerging diagnostic technologies, artificial intelligence, and the latest developments in laboratory capacity building. Through presentations and discussions, attendees will gain a profound understanding of the new strategies and tools reshaping the landscape of public health.

Accelerating Impact Through Mindful Management of Innovation
Jerome Kim, International Vaccine Institute

Enhancement and Utilization of Laboratory Infrastructure to Mitigate Enteric Disease Threats
Proscovia Naluyima, Makerere University, Walter Reed Uganda

Integrating Artificial Intelligence to Analyze Typhoid & Other Invasive Salmonelloses Data: From Zero to Hero!
Bráulio Roberto Gonçalves Marinho Couto, Biobyte Sistemas Ltd

Progress and Challenges Towards Typhoid Diagnostics
Jyotshna Sapkota, FIND

Discussion

9:30–9:45 Recognition Ceremony

KILIMANJARO BALLROOM

9:45–10:10 Coffee Break & Poster Viewing

FOYER

10:15–12:15 Inside Out: Genomic and Antimicrobial Resistance in *Salmonella*

ISARO ROOM

CONCURRENT ORAL ABSTRACT SESSION MODERATED BY: Iruka Okeke, University of Ibadan & Christopher Parry, Liverpool School of Tropical Medicine

Role of Bacteriophage Defence Systems in the Spread of Drug-Resistant *Salmonella* Typhi

Yogesh Hooda, Child Health Research Foundation

Yogesh Hooda, Shuborno Islam, Rathindranath Kabiraj, Rajan Saha, Hafizur Rahman, Arif Tanmoy, Samir Saha, Senjuti Saha

Child Health Research Foundation

BACKGROUND

Salmonella Typhi transmission is dictated by its interaction with humans, other microbes within the host and/or the environment and the circulating bacteriophages. While previous studies have identified molecular mechanisms that dictate interaction of *Salmonella* Typhi and humans, limited information is available regarding the other interactions, specifically that of *Salmonella* Typhi with bacteriophages. Typhi-specific phages have been reported in the literature and before the advent of molecular and genomic techniques, phages were extensively used for typing *Salmonella* Typhi isolates. However, little is known about the abundance and diversity of Typhi-specific phages or presence of phage defence systems in *Salmonella* Typhi, and the role of phages in the spread of drug-resistant strains.

METHODS

We analyzed over 5000 *Salmonella* Typhi whole genome sequences sequenced by our group and available in public databases and searched for the presence of phage defence systems in their genomes using PADLOC. Based on the results, we selected strains of *Salmonella* Typhi with diverse genomic backgrounds. To test the phenotypic resistance to bacteriophages, and the correlation of genomic phage defense systems to phenotypic phage resistance, we used our library of Typhi phages collected from environmental samples. In total, the killing activity of 83 Typhi phages were tested on 19 *Salmonella* Typhi strains using the double layer agar method.

RESULTS

Through bioinformatic analysis, we identified a total of six different phage defence systems in *Salmonella* Typhi — CRIPSR-Cas (two sub-types), BREX, Duarantia III, AbiL, CBASS and dXTPase. Two of these systems: CRISPR-Cas1E and Druantia type III are present in all isolates including the laboratory strain Ty2. The Bacteriophage Exclusion (BREX) anti-phage defence system is exclusively found in the plasmids that also contain antimicrobial resistance genes in the extensively drug-resistant (XDR, 4.3.1.1.P1) lineage of Pakistan, and the ciprofloxacin resistant Bdq lineage (4.3.1.3.Bdq) of Bangladesh. On examining phenotypic phage resistance of strains belonging to the 4.3.1.3 lineage with or without the plasmid, we found that strains with the plasmid with the BREX system are much more likely to be resistant to bacteriophages.

CONCLUSIONS

Our data suggest that drug-resistant isolates such as those within the 4.3.1.P1 (XDR) and 4.3.1.3.Bdq lineages contain active phage defence systems, and they are often on plasmids that carry antimicrobial resistance genes. Thus, phage defence systems may play a consequential role in the survival of *Salmonella* Typhi in the environment, thereby determining which lineages spread in a geographical location. In addition, as phage defence systems are often found in plasmids that also often contain antimicrobial resistance genes, phage resistance may be a contributing factor for maintenance of multi-drug resistance plasmids in *Salmonella* Typhi and the spread of drug resistance.

Genomic Analysis and Antimicrobial Resistance Profiling for the Global Collection of *Salmonella* Paratyphi B Isolates

Junaid Iqbal, Aga Khan University

Safina Abdul Razzak, **Junaid Iqbal,** Sidra Tahir, Farah Naz Qamar

Aga Khan University

BACKGROUND

Salmonella Paratyphi B (SPB) is a clinically significant pathogen associated with both invasive paratyphoid fever and non-invasive gastroenteritis worldwide. It comprises of two variants *senso stricto* (dt^-) and *Java* (dt^+). Understanding the genetic diversity, antimicrobial resistance (AMR) patterns, and genotypic profiles of the SPB complex is crucial for effective surveillance and control measures. This study aimed to investigate genomics characteristics of SPB complex from different geographical regions and collection sources.

METHODS

Genomic data from 1,510 *S.* Paratyphi B strains isolated from clinical, food, and environmental samples were obtained from various studies conducted in Africa, America, Asia, and Europe. In silico analysis was conducted on these

genomes to identify AMR-related genes, mutations, and plasmids present in the strains. Phylogenetic relationships were determined using multilocus sequence typing (MLST) and consensus SNP-sites. Multiple correlation analysis was performed to assess the relationship between the strains' AMR patterns, plasmids, and geographic distribution.

RESULTS

Among the SPB isolates, approximately 78.40% exhibited resistance to one or more antimicrobial classes, while the remaining strains were pan-sensitive. Multi-drug resistance was detected in 58% of the isolates obtained from all sources, with 32% originating from clinical sources. Aminoglycoside resistance genes were the most prevalent, followed by genes conferring resistance to tetracycline and β-lactam antibiotics, with clinical isolates showing higher resistance rates compared to food isolates. Multiple aminoglycoside resistance gene variants suggest evolving and diversifying resistance mechanisms. Regional variations in AMR were observed, with different countries in Asia and Europe displaying distinct prevalence and distribution patterns of AMR genes. Notably, plasmid-mediated quinolone resistance mutations in *gyr*A (Ser83Phe, Asp87Gly) and *par*C (Ser80Arg) genes were detected in isolates from Asia and America. Phylogenetic analysis of the dt+ and dt- variants of the *S.* Paratyphi B complex revealed the formation of two distinct clades, suggesting significant genetic differentiation and the emergence of separate clusters.

CONCLUSION

This research provides insights into antimicrobial resistance and genetic profiles of SPB isolates, emphasizing the role of clinical and non-clinical sources in resistant strain transmission. It enhances our understanding of the molecular characteristics of SPB, aiding in the development of effective AMR surveillance and infection control measures.

Assessing the Global Risk of Typhoid Outbreaks Caused by Extensively Drug Resistant *Salmonella* Typhi

Jo Walker, Yale School of Public Health

Jo Walker[1], Chrispin Chaguza[1], Nathan Grubaugh[1], Megan Carey[2], Stephen Baker[2], Kamran Khan[3], Isaac Bogoch[4], Virginia Pitzer[1]

[1]Yale School of Public Health, [2]University of Cambridge School of Clinical Medicine, [3]BlueDot Global, [4]University of Toronto Department of Medicine

BACKGROUND

Since its emergence in 2016, extensively drug resistant *Salmonella enterica* serovar typhi (*S.* Typhi) has become the dominant cause of typhoid fever in Pakistan. The establishment of sustained transmission of extensively drug resistant *S.* Typhi represents a major public health threat. Identifying countries at high risk of outbreaks of extensively drug resistant typhoid could facilitate the targeting of surveillance and control measures.

METHODS

We quantify the country-level risk of outbreaks of extensively drug resistant typhoid along two axes: the risk of importation from Pakistan (represented by the annual volume of incoming air travel from Pakistan), and the risk of efficient local transmission following the introduction of cases (represented by previously published typhoid burden estimates). To validate the association between air travel and the risk of *S.* Typhi importation, we compare the volume of air travel from Pakistan to countries that have and have not imported extensively drug resistant *S.* Typhi in the past. We also use a phylogeographic model to evaluate the role of air travel in the global emergence of multidrug resistant *S.* Typhi.

RESULTS

The 15 countries with known importations of extensively drug resistant *S.* Typhi importations received a median of 104,829 (IQR: 25,171 to 221,937) air travelers from Pakistan in 2019, while the other 185 countries received a median of only 259 annual passengers (IQR: 26 to 3,010). We also detected a significant positive association between air travel volume and the rate of between-country movement of the multidrug resistant H58 *S.* Typhi haplotype across multiple phylogeographic models. Finally, we identify the countries which, on the basis of air travel patterns, may be most likely to import extensively drug resistant *S.* Typhi in the future, both overall and specifically among countries with endemic typhoid transmission.

CONCLUSIONS

Air travel patterns strongly predict the international movement of emerging *S.* Typhi lineages. Public health activities to track and mitigate the spread of extensively drug resistant *S.* Typhi should be prioritized in typhoid endemic countries with strong travel connections to Pakistan.

Recent Emergence of Cephalosporin Resistant *Salmonella* Typhi Carrying IncFIB(K) Plasmid Encoding $bla_{CTX\text{-}M\text{-}15}$ Gene in India

Tharani Priya Thirumoorthy, Christian Medical College, Vellore

Tharani Priya Thirumoorthy[1], Jobin John Jacob[2], Aravind V[2], Monisha Priya T[2], Yesudoss M[2], Bhavini Shah[3], Anand Shah[4], Anushree Gaigawale[5], Pooja Patel[6], Ankur Mutreja[7], Jacob John[2], Gagandeep Kang[2], Balaji Veeraraghavan[2]

[1]Christian Medical College, Vellore, [2]Christian Medical College, Vellore, Tamilnadu, [3]Neuberg Supratech Reference Laboratories, Ahmedabad, Gujarat, [4]Zydus Hospitals, Ahmedabad, Gujarat, [5]Suburban Diagnostics India Pvt. Ltd, Andheri (w), Mumbai, [6]Pathocare Pathology Laboratory, Vadodara, Gujarat, [7]Cambridge Institute of Therapeutic Immunology and Infectious Disease, Jeffrey Cheah Biomedical Centre, Cambridge

INTRODUCTION

Over the past decades, the increasing rates of MDR and fluoroquinolone-resistant *Salmonella* Typhi led to the use of third-generation cephalosporins and azithromycin as the drug of choice. However, increasing reports on

cephalosporin-resistant *S.* Typhi pose a serious threat and challenge the therapeutic management of typhoid fever.

METHODS

Clinical isolates of twelve cephalosporin-resistant *S.* Typhi strains isolated from India were subjected to the phenotypic and genotypic characterization of the antimicrobial resistance profiles.

RESULTS

Comparative genome analysis of study isolates revealed the emergence of a new clone of ceftriaxone-resistant *S.* Typhi containing three plasmids of the incompatibility group IncFIB(K), IncX1 and IncFIB(pHCM2). Among the three, IncFIB(K) plasmid confers resistance to third-generation cephalosporins by means of $bla_{CTX\text{-}M\text{-}15}$ gene, as well as other resistance determinants such as *aph(3")*, *aph(6')*, *sul2*, *dfrA14* and *tetA*. Phylogenetic analysis of strains revealed that a single isolate belongs to a clade corresponding to genotype 4.3.1 and isolates from Ahmedabad (*n=11*) belong to a distinct subclade within genotype 4.3.1.2 (H58 lineage II). SNP-based phylogenetic analysis of the core genes in IncFIB(K) revealed the plasmid backbone is closely related to that of IncFIB(K) from other Enterobacterales.

CONCLUSION

The findings suggest that H58 lineage II can acquire MDR plasmids from other Enterobacteriales if compensatory evolution reduces the cost of carrying the plasmids. Though, like previously reported, exposure to the third generation cephalosporins during the treatment may have selected these variants, this could indicate the beginning of a new wave of ceftriaxone-resistant *S.* Typhi in India. The implementation of control measures such as vaccination, improved water, sanitation, etc., could be undertaken in areas where MDR or XDR *S.* Typhi strains are prevalent.

A 24-Year Passive Surveillance Study Reveals Trends in Antimicrobial Resistance Amongst *Salmonella* Typhi and Paratyphi A Cases in Bangladesh

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BACKGROUND

Typhoid and paratyphoid fever, collectively known as enteric fever, are common bloodstream infections in areas with suboptimal water and sanitation infrastructure. These two diseases are often clinically indistinguishable, and consequently, similar treatment strategies are followed. This study aims to assess AMR patterns for *Salmonella* Typhi and Paratyphi A, the causative agents for typhoid and paratyphoid fever, respectively, before the introduction of typhoid-conjugate vaccine (TCV) in the country.

METHODS

A 24-year surveillance of typhoid and paratyphoid fever was conducted in Dhaka, Bangladesh, encompassing two major pediatric hospitals and one private clinic from 1999 to 2022. Blood cultures were performed at physicians' discretion, and confirmed cases were determined through microbiological, serological, and biochemical tests. Antimicrobial susceptibility testing was conducted following the CLSI guidelines. National annual antibiotic consumption data for azithromycin, ciprofloxacin, and cotrimoxazole were collected.

RESULTS

The surveillance identified 12,489 typhoid and 2,725 paratyphoid fever cases from 1999-2022. Multidrug resistance (MDR) and resistance to individual first-line drugs (amoxicillin, chloramphenicol, cotrimoxazole) for *Salmonella* Typhi isolates showed a declining trend, accompanied by a decrease in cotrimoxazole consumption. Over 97% of *Salmonella* Paratyphi A isolates remained susceptible to all first-line antimicrobials, ampicillin, chloramphenicol, and cotrimoxazole.

Ciprofloxacin resistance remained high for both pathogens, while its consumption remained stable. Resistance to ceftriaxone has remained low for both *Salmonella* Typhi and Paratyphi A. The minimum inhibitory concentration (MIC) for ceftriaxone showed a slight increase over the years but remained much lower than the resistant level. Azithromycin resistance has also remained low, although an increasing trend in azithromycin consumption was observed.

CONCLUSIONS

This 24-year surveillance study provides the baseline data to assess the impact of TCVs and other interventions on AMR amongst *Salmonella* Typhi and Paratyphi A isolates in Bangladesh. The resistance against the first-line antimicrobial drugs is decreasing amongst *Salmonella* Typhi but has remained low for *Salmonella* Paratyphi A in Bangladesh. *Salmonella* Paratyphi A overall exhibits a higher susceptibility to most antibiotics compared to *Salmonella* Typhi. Taken together, this study suggests that TCV introduction might allow for evidence-based changes to the empirical treatment of enteric fever in Bangladesh.

Genetic Heterogeneity in the *Salmonella* Typhi Vi Capsule Locus: A Population Genomic Study From Fiji

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BACKGROUND

Northern Division typically reports the highest incidence of typhoid fever in Fiji and will implement a mass vaccination with typhoid conjugate vaccine as a public health control measure during 2023. Our study was conducted to define the genomic epidemiology of *S.* Typhi in the Division prior to commencing vaccination.

METHODS

Between 1 January 2017 and 31 December 2019, a total of 240 S. Typhi isolates from 217 patients (88% of the total cases) from the Northern Division were whole genome sequenced (WGS). For comparative analyses, a further 179 *S.* Typhi isolates from the Central Division (2017-2019) were WGS and 367 Fijian genomes were obtained from public repositories. Phylogenomic and phylodynamic analyses were undertaken.

RESULTS

A total of 246 culture-confirmed typhoid fever patients were reported during in the Northern Division during 2017-2019. The majority, (93.8%) were from the indigenous iTaukei ethnic group, 58.1% were males and 83% resided in rural areas. The median age was 26 years (IQR 17-41) and children (<15 year of age) represented 22% of the overall patients. Phylogenetic analysis of Fijian *S.* Typhi isolates revealed that 99% belong to genotype 4.2, encompassing two dominant sub-lineages, 4.2.1 and 4.2.2. We found sporadic importation of multidrug resistant 4.3.1 and 3.5 genotypes with no evidence of subsequent transmission in the community. Genome clustering identified multiple transmission clusters within and between the Northern and Central Divisions of Fiji. To identify markers of genomic selection, we plotted single nucleotide polymorphism (SNP) accumulation rates in *S.* Typhi genotypes. A total of 1265 mutational events (SNPs/ small indels) were observed in the population, of which the *viaB* operon encoding for the Vi-capsular polysaccharide synthesis genes had higher than expected density of mutations. The *viaB* operon SNPs accounted for 2.6% of all events (n=30) with most across two particular genes, *tviE* and *tviD*. These mutations encoded for protein coding changes, suggesting selective pressure may be acting to maintain mutations that cause changes to amino acid sequence in these genes. Some strains of *S.* Typhi with *tvi* mutations persisted throughout the study period with evidence of ongoing community transmission and localised outbreak suggesting that mutations in *tvi* genes can be maintained in the population with new infections. Evidence of selection of several of these *tvi* mutations was also evident in a global population dataset of 12,382 *S.* Typhi genomes, indicating independent selection across the global *S.* Typhi population. Maintenance of *S.* Typhi sub-lineages carrying *tvi*mutations indicate that these mutations persist in an expanding *S.* Typhi population.

CONCLUSION

Our study showed that typhoid in Fiji is derived from clonal expansion, evolution, or replacement of local *S.* Typhi strains over time, rather than through importation of new strains from international sources. The abundance of non-synonymous SNPs in viaB operon suggests there is higher selective pressure and potential adaptive mutation in this locus. The impact of the viaB mutations on the Vi-capsular structure and other phenotypic characteristics are presently unknown. However, given the central role of the Vi-capsular polysaccharide in vaccination, further integrated epidemiological, genomic, and phenotypic surveillance is required to determine the functional implications of these mutations.

The Genetic Landscape of *Salmonella Enterica* Serovar Typhi in Zimbabwe Before the Introduction of Typhoid Conjugate Vaccine (TCV)

Tapfumanei Mashe, Ministry of Health and Child Care Zimbabwe/ World Health Organization

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BACKGROUND

In nations where typhoid is an endemic disease, vaccination is required due to the persistent rise of drug-resistant *Salmonella enterica* serovar Typhi (*S.* Typhi). An outbreak of typhoid fever in Harare, Zimbabwe, in 2018 was due to a multidrug- and ciprofloxacin-resistant strain of *S.* Typhi. In response, Zimbabwe started a typhoid conjugate vaccination program. The population structure, gene flux, and sequence polymorphisms of strains that were isolated before the widespread typhoid vaccination campaign were examined to better understand the historical origin and evolution of drug resistance in endemic *S.* Typhi strains in Zimbabwe. This data will serve as a baseline for later assessments of the immunization program's success and impact on transmission.

METHODS

We analyzed the population structure, gene flux, and sequence polymorphisms in the context of the genome sequence of 1904 *S.* Typhi strains isolated from 65 countries to reconstruct the evolution of antimicrobial resistance (AMR) and the historical spread of endemic strains into Zimbabwe.

RESULTS

The majority of *S.* Typhi strains in Zimbabwe were of the multidrug-resistant genotype 4.3.1.1 (H58), which spread to the country from neighbouring countries around 2009. Within Zimbabwe, these strains have evolved to become even more resistant to antibiotics, acquiring an IncN plasmid carrying a *qnrS* gene and a mutation in the quinolone resistance-determining region of the *gyrA* gene. A minority of *S.* Typhi strains in Zimbabwe are of the susceptible genotype 3.3.1, but these strains are becoming increasingly rare.

CONCLUSIONS

The most common strain of *S.* Typhi in Zimbabwe is genotype 4.3.1.1. This strain spread to Zimbabwe from neighbouring countries around 2009 and has since acquired additional antibiotic resistance through the acquisition of a plasmid and a mutation in the *gyrA* gene. This study provides a baseline for future evaluation of the impact of the typhoid conjugate vaccine program in Harare.

Genomic Characterization of Invasive *Salmonella Enterica* Isolated in Severe Typhoid in Africa Surveillance in Ibadan, Nigeria

Oyeniyi Stephen Bejide, Chrisland University

Odion O. Ikhimiukor[1], **Oyeniyi Stephen Bejide[2]**, Ibilola Olatimbo Ogunleye[3], Aderemi Kehinde[4], Ini Adebiyi[5], Veronica Kayinebi Dada[3], Oluwafemi John Adewusi[6], Olabisi C. Akinlabi[7], Sarah Agbi[6], Chukwuemeka Nwimo[8], Oluwafemi Popoola[9], Trevor Toy[10], Ondari D. Mogeni[10], Florian Marks[10], Iruka N. Okeke[7]

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INTRODUCTION

Typhoid is endemic in Nigeria but little is known about circulating lineages and their antimicrobial resistance. We whole genome-sequenced *Salmonella enterica* serovar Typhi and invasive non-typhoidal *Salmonella* (iNTS) recovered between 2017 and 2021 by the Severe Typhoid in Africa node in Ibadan, Nigeria.

METHODS

Fifty-seven isolates were available for antimicrobial susceptibility profiling and whole genome sequencing. Antimicrobial susceptibility testing was done using Vitek2 system. Genomic DNA was extracted from the isolates and whole genome sequenced using the Illumina platform. Bioinformatic analysis of the genomes was done using publicly available bioinformatic tools.

RESULTS

S. Typhi isolates were all serotype D1 strains and belonged to genotypes 3.1.1 (33/38 isolates), 2.3.1 (4/38) and 0.0.3 (1/38). Eight of the 38 isolates had an antimicrobial

resistance genotype consistent with multidrug resistant (MDR) Typhi. All *S.* Typhi 0.0.3 and 2.3.1 and 28/33 3.1.1 isolates were susceptible to ciprofloxacin, however 24 of the phenotypically susceptible *S.* Typhi isolates carried single S83Y or S83F *gyrA* substitutions. Isolates with quinolone resistance-determining region SNPs carried *dfrA14* or *dfrA15*, *sul1* or *sul2*, *tetA*, bla_{TEM1} (except one) and *aph-6-1d*, and an IncY plasmid replicon. The iNTS isolates belonged to serovars Enteritidis (9), all ST11, Weltevreden (6), all ST365, Typhimurium (3), all ST313, and Stanleyville (1) belonging to ST2562. *S.* Weltvreden has not previously been reported from clinical cases in Nigeria and the isolates identified did not represent an outbreak cluster. *S.* Weltevreden and *S.* Stanleyville isolates were generally pan-susceptible but *S.* Enteritidis and *S.* Typhimurium isolates, all from well-established invasive lineages, were multiply resistant.

CONCLUSION

Salmonella Typhi in Ibadan predominantly belong to the 3.1.1 West Africa lineage and are multidrug-resistant. Circulating iNTS serovars include Enteritidis, Typhimurium and Weltevreden, which also carry multiple resistance genes. Antimicrobial resistance containment strategies, including Typhoid Conjugate Vaccines need urgent deployment to protect Nigerians at risk of invasive salmonellosis.

10:15–12:15 Vaccine Voyage II: Navigating the Advancements in Vaccine Research

KILIMANJARO BALLROOM

CONCURRENT ORAL ABSTRACT SESSION MODERATED BY: Myron "Mike" Levine, University of Maryland School of Medicine & Farah Qamar, Aga Khan University

Vaccines for All: The Malawi National Integrated Typhoid Conjugate Vaccine Campaign

Latif Ndeketa, Malawi Liverpool Wellcome Programme

Brenda Mhone[1], Theresa Misiri[2], **Latif Ndeketa[2],** Priyanka D. Patel[2], Esau Mkisi[3], Aziza Mwisongo[3], Emmanuel Mugisha[3], Mavuto Thomas[1], Boston Mzimba[4], Donnie Mategula[2], Jonna Jeurlink[5], Ghanashyam Sethy[6], Chukwuemeka Agbo[7], Maureen Maguza[8], Storn Kabuluzi[1], Melita A Gordon[9], Mike Chisema[1]

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BACKGROUND

In May 2023, Malawi conducted a GAVI-supported integrated national campaign and introduction of Typhoid Conjugate Vaccine (TCV), targeting 9 million children aged 9 months to 15 years—nearly half the population. Malawi had heavy burden of recent urgent vaccination campaigns; COVID-19, polio and cholera. The campaign. was unique due to its integration of 3 vaccines and vitamin A (4 interventions), and stands out as Malawi's largest campaign to date.

METHODS

The integrated campaign spanned seven days in May 2023, with three additional days for mop-up activities. Four interventions were integrated during the campaign: TCV (09 months-14 years), Measles-Rubella (09-59 months), Oral Polio Vaccine (0-59 months), and Vitamin A (06-59 months). Vaccinations took place at static sites, (schools and health facilities), outreach and mobile clinic sites, and Internally Displace Person camps (IDP) post-Cyclone Freddy. Several methods were employed to sensitize the community, including print communication materials, text messaging, TV and radio programmes and mobile vans with jingles and invitations.

RESULTS

Overall, the national coverage for the four integrated interventions demonstrated notable achievements. Daily vaccination tally sheets captured the daily count for delivery of each intervention. Estimated national coverage rate for TCV was 76.% of the target population, while the MR vaccination reached 83%. Administrative coverage rates of OPV were 86% and of Vitamin A were 105% (6-11 months) and 78.3% (12-59 months). Post-campaign vaccine coverage survey is pending. The successful collaboration with schools played a significant role in facilitating vaccine administration and community engagement. However, the campaign faced challenges, including vaccinator fatigue due to consecutive vaccine campaigns, community fatigue resulting from frequent vaccination drives, integration of 4 interventions, and infrastructure damage from the recent tropical cyclone Freddy.

CONCLUSIONS

The Malawi National Integrated Vaccine Campaign represents a major milestone in public health. The strategic integration of multiple interventions demonstrates the country's commitment to enhancing immunization coverage. Challenges related to vaccinator and community fatigue, and highlight the importance of addressing vaccine hesitancy. Malawi's integrated vaccination campaign will serve as a model and provide learnings for other countries. Ongoing research is assessing the effectiveness and real-life impact of the campaign and introduction.

Antimicrobial Susceptibility Patterns of *Salmonella* Typhi Isolates Following Mass-Targeted Typhoid Conjugate Vaccine Immunization in Harare City, Zimbabwe, 2023

Kudzai Patience Takarinda, National Microbiology Reference Laboratory Zimbabwe

Kudzai Patience Takarinda[1], Tapfumanei Mashe[2]

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BACKGROUND

Typhoid fever is a life-threatening disease that has been endemic in Zimbabwe, particularly in Harare, since 2010. Ciprofloxacin has been the antibiotic of choice for diarrheal cases in Zimbabwe, adopted by the Ministry of Health and Child Care, from current World Health Organisation (WHO) guidelines. However, due to the emergence and spread of multidrug resistance against ciprofloxacin and conventional antibiotics for the treatment of typhoid, the Ministry of Health and Child Care (MOHCC), Zimbabwe, organized the first typhoid conjugate vaccination (TCV) campaign in 2019. This was a response to recurring typhoid outbreaks in Harare. The campaign was conducted in nine high-density suburbs and was targeted at all children aged 6 months to -15 years. The target age range was extended up to 45 years in one suburb due to the past high attack rate among adults. In 2021, a second nationwide mass TCV was conducted which led to the incorporation of TCV in the country's routine immunization program, There are limited studies on antimicrobial susceptibility patterns of *Salmonella* Typhi post-vaccine introduction. We conducted a cross-sectional study aimed to determine antimicrobial susceptibility patterns of *Salmonella* enterica serotype Typhi isolated in Harare City from October 2022 to May 2023 following the introduction of the typhoid conjugate vaccine.

METHODS

We conducted this study at the National Microbiology Reference Laboratory (NMRL) at Sally Mugabe Central Hospital in Zimbabwe. Out of 55 suspected blood culture isolates received, a total of 31 were confirmed as *Salmonella* typhi using the BioMerieux VITEK® MS which uses Matrix Assisted Laser Desorption Ionisation Time-of-Flight (MALDI-TOF) Technology. Antimicrobial susceptibility testing was performed using the VITEK® 2 COMPACT antimicrobial susceptibility (AST) cards which use the broth micro-dilution minimum inhibitory concentration technique. Interpretations were verified using the Clinical and Laboratory Standards Institute (CLSI) guidelines.

RESULTS

From October 2022 to May 2023, 31 (56%) isolates received at NMRL were confirmed as *Salmonella* Typhi. Only 1 (3%) isolate was resistant to ciprofloxacin which is the first-line drug for typhoid treatment. All 31 (100%) were resistant to ampicillin, while 28(90%) were resistant to cotrimoxazole and 14 (45%) were resistant to tetracycline. No resistance was observed against ceftriaxone as all 31 (100%) isolates were susceptible to this second-line treatment.

CONCLUSIONS

Our study suggests that there is increased susceptibility to ciprofloxacin following the introduction of a typhoid conjugate vaccine in Harare City. Previous studies conducted in Zimbabwe have shown increased resistance to ciprofloxacin of up to 75%. Limitations of our study include inference based on small sample size. We recommend enhanced surveillance and continued integration of TCV in the National Immunization Program. Additionally, molecular studies and phylogenetic relatedness may need to be established using whole-genome sequencing to identify the presence and mechanism of antimicrobial resistance. We recommend mathematical modeling studies to determine the effect of vaccination on antimicrobial-resistant *Salmonella* Typhi.

Modeling Typhoid Vaccination in Nepal: TCV Impact and Booster Dose Strategy

Virginia E. Pitzer, Yale University

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BACKGROUND

Typhoid conjugate vaccines (TCV) have addressed several challenges faced by earlier typhoid vaccines, with increased efficacy, longer-lasting protection, and safety and immunogenicity in children under 2 years of age in a single-dose vaccine. As TCVs are integrated into national immunization programs, questions remain regarding whether a pediatric booster dose is needed to sustain protection and which potential booster strategies might maximize impact. In Nepal, TCV was introduced in April 2022, with a national catch-up campaign vaccinating children 15 months to 15 years of age, followed by on-going routine vaccination of children at 15 months of age. This modeling study explores the potential impact and cost-effectiveness of different strategies for TCV booster vaccination compared to the current one-dose strategy in Nepal.

METHODS

We fit an age-stratified compartmental typhoid transmission model to data from Patan hospital in Kathmandu, Nepal. Using the fitted model, we explored the impact of vaccination strategies including catch-up vaccination plus routine vaccination at 15 months (i.e., the current strategy), the current strategy plus a booster dose at 5 years of age (i.e., school-entry booster dose) or 10 years of age (i.e. 10-year booster dose), and the school-entry booster dose plus a second booster dose at 10 years of age. We calculated the number of typhoid fever cases, deaths, and disability-adjusted life-years averted for each scenario and identified the optimal strategy across a range of willingness-to-pay thresholds.

RESULTS

The impact of each vaccination strategy was highly dependent on assumptions regarding waning immunity dynamics among vaccinated and naturally-infected individuals. Across most immunity dynamics, a booster dose at 5 or 10 years of age led to further reductions in typhoid burden among key high-incidence groups of individuals. However, the optimal strategy in terms of cost-effectiveness depended upon the functional form of waning immunity.

CONCLUSIONS

This study provides valuable insight into the potential impact of the current vaccination program in Nepal as well as key considerations for informing the value of addition of booster doses in endemic settings. Further understanding of the dynamics of waning immunity is needed to inform the need and timing of booster doses.

Trend of Anti-Vi-IgG and Anti-Vi-IgA Antibody Responses Induced in Vi-TT Recipients Over the Period of Five Years Among Bangladeshi Children

Farhana Khanam, icddr,b

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BACKGROUND

A cluster-randomized trial of Vi-tetanus toxoid conjugate (Vi-TT) vaccine revealed 83% efficacy among Bangladeshi children after 2 years of vaccination. The Japanese Encephalitis (JE) vaccine was used as a control vaccine for this trial. The vaccine induced a robust anti-Vi-IgG antibody response after single dose of Vi-TT, which persisted even after 2 years of vaccination. Here, we present the results of measurement of anti-Vi-IgG at later time points and anti-Vi-IgA responses across a five-year study period.

METHODS

Blood specimens were collected from a subset of 1,500 children who were randomly selected on 2:1 basis (Vi-TT vs JE) before vaccination and then at day 28, at 18 months (day 545), and at two years (day 730), four years (day 1,460), and five years (day 1,825) post-vaccination. a A commercial ELISA kit (VaccZyme), The Binding Site, Birmingham, UK) was used to measure the anti-Vi IgG titres. The laboratory assay to measure the anti-Vi IgA titre in specimens collected from the same participants of the immunogenicity study is under way with Vi-coated plates and reagents supplied by The Binding Site by following a protocol adapted from the commercial VaccZyme assay.

RESULTS

Immunogenicity of Vi-TT on day 28 post-vaccination and persistence of anti-Vi-IgG antibodies induced by Vi-TT at 18 and 24 months have been previously reported. In this presentation, we will show the decline pattern of anti-Vi-IgG titres at later time points (four years and five years) and the anti-Vi-IgA antibody responses of all time points. The antibody responses within different age cohorts (<2 years, 2-4 years and 5 to <16 years) is also being assessed. We will report the responses induced in participants with breakthrough infection. We will attempt to determine the association of IgA and IgG titres with protection against natural *Salmonella enterica* serotype Typhi infection and disease severity.

CONCLUSIONS

The evaluation of Vi IgA and IgG responses in Bangladeshi children who received Vi-TT can assist to inform the policy makers for introduction of typhoid conjugate vaccines in the national immunization programme for eradicating typhoid disease in endemic situations.

Assessing the Medium-Term Impact of a Typhoid Conjugate Vaccine in Preventing Typhoid Infections in Bangladesh

Firdausi Qadri, icddr,b

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BACKGROUND

The efficacy and effectiveness of the typhoid conjugate vaccine (TCV) have been established through randomised controlled trials and observational studies. However, most of these studies had a follow-up period of less than 2 years. The medium-term protection provided by TCV remains unknown, while the decay of Vi-IgG antibodies has been reported after 2 years of vaccination.

METHODS

We conducted an observational study by following the participants of a cluster randomized controlled trial (CRCT) for 2.5 years in Dhaka, Bangladesh. In the original CRCT conducted between 2018 and 2020, 150 geographical clusters were randomly assigned (1:1) to receive either TCV or Japanese encephalitis (JE) vaccine. Children aged 9 months to <16 years were offered the vaccine assigned to their cluster of residence. The final visit of the CRCT took place between January and March 2021, during which the JE recipients were offered a single dose of TCV. This visit serves as the baseline for our observational study. In this study, we will compare the incidence of typhoid between children who received TCV in 2018-2019 (previous-TCV cohort) and those vaccinated in 2021 with TCV (recent-TCV cohort). Participants will be censored at the earliest date among

migration, death, loss of follow-up, or the end of the study. The incidence rate ratio (IRR) will be estimated using mixed-effect Poisson regression, adjusting for cluster (random effect) and other covariates as fixed effects, with the recent-TCV cohort as the reference. If the IRR is significantly higher than one, it indicates that the medium-term TCV protection has decreased compared to the short-term protection.

RESULTS

Between 2018-2019, a total of 33,909 children received TCV, while 33,486 children received the JE vaccine. Among the JE recipients, 24,073 children attended the final visit and received a TCV vaccine, comprising the recent-TCV cohort. For the children who received TCV in 2018-2019, 26,672 attended the final visit and will be included as the previous-TCV cohort. Up to date, 64 typhoid fever cases have been reported in the study population. The final analysis will be conducted upon completion of the study in August 2023.

CONCLUSIONS

This study will provide key data on medium-term protection following single-dose TCV.

The Association Between Vaccine Coverage and Herd Protection: Exploratory Analyses of a Cluster-Randomised Trial of Vi Conjugate Vaccine

Yiyuan Zhang, Oxford Vaccine Group and National Institute for Health and Care Research Oxford Biomedical Research Centre

Yiyuan Zhang[1], Farhana Khanam[2], Sarah Kelly[1], Firdausi Qadri[2], Andrew Pollard[1], John Clemens[2], Xinxue Liu[1]

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BACKGROUND

The evidence regarding herd protection from typhoid vaccines remains conflicting, despite the direct protection being established by several randomised controlled trials. While significant indirect protection has been reported for the Vi polysaccharide vaccine, it has not been observed for the typhoid conjugate vaccine (TCV). One possible explanation is the difference in vaccine coverage. This study aims to evaluate the impact of vaccine coverage on indirect vaccine effectiveness (iVE).

METHODS

Between April 2018 and March 2020, a participant- and observer-blind cluster randomised trial was conducted in Dhaka, Bangladesh. 150 clusters were randomised to a single-dose of TCV or Japanese encephalitis (JE) vaccine and children aged 9 months to <16 years were invited for vaccination. The 150 clusters were divided into four groups based on quartiles of the average vaccine coverage across the trial. For each group, the iVE was estimated by comparing the incidence of typhoid among non-vaccinees in the TCV clusters with that in the JE clusters, using Poisson regression adjusting for randomisation stratification variables and demographics. TCV coverage was also collected from 35 schools with a size of >100 students in the study area. Since these schools cover both TCV and JE clusters, coverage was defined as the percentage of TCV vaccinees among all children (including JE vaccinees). The association between coverage and the incidence of typhoid in non-TCV recipients was modelled by adjusted Poisson regression.

RESULTS

During the 24-month follow-up, the vaccine coverage ranged from 54% to 72% in children aged 9 months to <16 years across the 150 clusters. The iVE were 12% [95%CI: -72, 55], 12% [95%CI: -131, 67], 6% [95%CI: -97, 55], and -24% [95%CI: -245, 56] in the four quartiles, respectively. No significant correlation was found between coverage and herd protection (p for interaction=0.75). TCV coverage across the 35 schools varied between 8% and 55%. The incidence of typhoid among non-TCV recipients was 209 (per 100,000 person-years) [95%CI: 100, 384] and 337 [95%CI: 168, 602] in the low-coverage schools (≤median) and high-coverage schools (>median), respectively, with no significant difference (p=0.97).

CONCLUSIONS

Our study did not find an association between vaccine coverage and herd protection. Vaccinating children may not result in a detectable level of herd protection.

Durability of Anti-Vi IgG and IgA Responses in 15-month-old Children Vaccinated with a Typhoid Conjugate Vaccine in Burkina Faso

Alphonse Ouedraogo, Groupe de Recherche Action en Santé

Alphonse Ouedraogo[1], Amidou Diarra[1], Issa Nebie[1], Leslie P Jamka Mem[2], Kathleen M. Neuzil[2], Sodiomon B. Sirima[1], Matthew B. Laurens[2]

[1]Groupe de Recherche Action en Santé (GRAS), [2]Center for Vaccine Development and Global Health, University of Maryland School of Medicine, Baltimore, MD, USA

BACKGROUND

A single dose of typhoid conjugate vaccine (TCV) has demonstrated efficacy against typhoid fever. In a controlled human infection model, TCV induces high anti-Vi IgA and IgG responses to *Salmonella Typhi* that correlate

with protection. In this study, we measured longer-term immunogenicity of Vi-TCV co-administered with Expanded Programme on Immunization vaccines at 28 days and 30-35 months post-vaccination in children aged 15-23 months in Burkina Faso.

METHODS

Children were randomized 2:1 in a double-blind trial to receive TCV or inactivated polio vaccine (IPV; control) alongside routine measles-rubella and meningococcal serogroup A vaccines. Anti-Vi IgG and IgA were measured by ELISA at baseline, day 28, and 30-35 months post-vaccination. Seroconversion was defined as ≥4-fold increase in titer.

RESULTS

At day 28 post-vaccination (n=150), anti-Vi IgG seroconversion was 94.9% (95%CI 88.4-98.3%) in TCV recipients compared to 3.9% (95%CI 0.5-13.5%) in the IPV group. Anti-Vi IgG geometric mean titer (GMT) at day 28 in the TCV group was 3210.1 EU/ml (95%CI 2311.7-4457.6) compared to 5.3 EU/ml (95%CI 4.1-6.9) in the IPV group. At 30-35 months (n=115), anti-Vi IgG seroconversion was 88.7% versus 6.8% in TCV and IPV recipients, respectively; GMT decreased compared to Day 28 to 79.3 EU/ml (95%CI 63.1-99.6) in the TCV group versus 5.7 EU/ml (95%CI 4.4-7.3) in the IPV group . Participants receiving TCV achieved higher anti-Vi IgA GMT at day 28 (41.1 EU/ml, 95%CI 33.8-49.9) compared to IPV recipients (1.7 EU/ml, 95%CI 1.5-1.8). Anti-Vi IgA GMT decreased compared to day 28 to 5.1 EU/ml (95%CI 4.1-6.4) in TCV recipients and remained unchanged at 1.7 EU/ml (95%CI 1.5-2.0) in the control group 30-35 months after vaccination.

CONCLUSIONS

TCV induces durable IgA and IgG immune responses for at least 2.5 years. TCV conferred similarly strong anti-Vi IgA and IgG responses at 28 days and 30-35 months post-vaccination in children vaccinated at 15-23 months of age. Sustained immunogenicity informs vaccination schedule planning in endemic areas.

Introduction of Typhoid Conjugate Vaccine—A Successful Implementation in Strengthening National Immunization Program of Nepal

Navneet Bichha, Indian Institute of Health Management Research

Navneet Bichha[1], Bibek Kumar Lal[2], Sagar Dahal[3]

[1]IIHMR University (WHO/TDR), [2]Family Welfare Division, Ministry of Health and Population, [3]Child Health and Immunization Service Section, Family Welfare Division, Ministry of Health and Population

BACKGROUND

Nepal is estimated to have one of the highest burdens of typhoid in the world with increasing treatment failure due to drug resistant typhoid strain since 1992. Global Burden of Disease study in 2017 estimated that there were 351 typhoid cases per 100,000 people in Nepal. Nepal successfully conducted a typhoid catch up vaccination campaign with the WHO prequalified vaccine ,TYPHIBEV manufactured by Biological E Limited targeting 15 months to 15 years children in 2022 before its introduction in the routine immunization program. The aim of this campaign was to reach 7.4 million children to significantly reduce the morbidity and mortality caused by typhoid in the country specifically, among children under 15 years and identify missed dose children for basic routine vaccines. This was a school-based vaccination program with the establishment of 50,000 session sites to deliver the vaccine across the country.

METHODOLOGY

A cross sectional survey was done by the National Family Welfare Division of Nepal. Immunization Information data was collected during the typhoid vaccination campaign among (n= 7837623) children from 15 months to 15 years old in all seven provinces of Nepal from April 2022 to May 2022.

RESULTS

A national achievement of 95% coverage with all provinces exceeding 90% coverage was seen with the implementation of Typhoid conjugate Vaccine in Nepal. However, the gap was seen in youngest age-group about 40% missed in 15–23-month-old age-group.

CONCLUSION

Nepal was the fourth country in the world to introduce the Typhoid Conjugate vaccine in its routine immunization program in 2022 with the support from Gavi after Pakistan in 2018, Liberia and Zimbabwe in 2019. This survey provided the accurate vaccination coverage estimates to assess the program performance, monitoring and planning and evidence-based decision-making capacity. This survey also helped in understanding the effectiveness of supplementary immunization activity mechanism to strengthen routine immunization in identifying missed dose children for basic routine vaccines recommended to young children in Nepal.

12:15–13:30 Lunch

SOKO RESTAURANT

13:30–15:00 Bridging the Gap: Environmental and Sero-Surveillance for Estimating Typhoid Burden and Supporting Vaccine Introduction

KILIMANJARO BALLROOM

SYMPOSIUM SESSION CHAIRED BY:
Kristen Aiemjoy, University of California Davis & Mahidol University Faculty of Tropical Medicine, Richelle C. Charles, Massachusetts General Hospital-Harvard University & Nick Grassly, Imperial College London

Despite the existence of effective typhoid conjugate vaccines, many high-risk communities remain unvaccinated due to the lack of precise, locally relevant epidemiological data. Our symposium seeks to bridge this data gap by delving into the latest advancements in serological and environmental surveillance—affordable, scalable approaches that may help support public health decision making by providing estimates of the incidence of infection and identifying circulating antimicrobial resistant strains.

We will present some of the latest findings from research institutes in Asia and Africa that are implementing these novel surveillance methods. We will discuss technical and logistic challenges and host a roundtable discussion on the use of these surveillance tools by the public health community to support vaccine introduction and monitoring.

Latest Advances in Seroepidemiology for Enteric Fever
Kristen Aiemjoy, University of California Davis & Mahidol University Faculty of Tropical Medicine

Quick and Informative: Schools as a Platform for Rapid Typhoid Seroepidemiological Assessments
Shiva Naga, Dhulikhel Hospital, Kathmandu University and Sira Jam Munira, Child Health Research Foundation

Mapping Typhoid Transmission: Geospatial Analysis and Seroepidemiology for TCV Prioritization
Momin Kazi, Aga Khan University

A Target Product Profile for Wastewater Surveillance of *S.* Typhi
Supriya Kumar, Bill & Melinda Gates Foundation

Seroincidence of Enteric Fever Based on Targeted Serosurveillance in Blantyre, Malawi
Jonathan Mandolo, Liverpool School of Tropical Medicine

Wastewater Surveillance of *S.* Typhi in India and Comparison with Clinical and Serological Surveillance
Dilip Abraham, Christian Medical College, Vellore, India

Direct Sequencing of *S.* Typhi in Wastewater Samples to Determine Antimicrobial Resistance and Genotype
Catherine Troman, Imperial College London

15:00–15:30 Coffee Break & Poster Viewing

FOYER

15:30–17:30 Eyes on Surveillance: Illuminating the Path to Effective Monitoring

KILIMANJARO BALLROOM

ORAL ABSTRACT SESSION MODERATED BY: Adidja Amani, World Health Organization Regional Office for Africa & Jessica Seidman, Sabin Vaccine Institute

Development of a Low-Cost Environmental Surveillance Method for Effective Typhoid Fever Control

Shuborno Islam, Child Health Research Foundation

Rathindranath Kabiraj[1], Yogesh Hooda[1], **Shuborno Islam[1],** Hafizur Rahman[1], Kesia E. da Silva[2], Rajan Saha Raju[1], Stephen P Luby[2], Jason R Andrews[2], Samir K Saha[1], Senjuti Saha[1]

[1]Child Health Research Foundation, [2]Stanford University

BACKGROUND

Typhoid-conjugate vaccines (TCVs) provide an opportunity to reduce the burden of typhoid fever, caused by *Salmonella* Typhi, in endemic areas. As policymakers develop vaccination strategies, accurate and high-resolution data on disease burden is crucial. However, traditional blood culture-based surveillance is resource extensive, prohibiting its large scale and sustainable implementation. *Salmonella* Typhi is a water-borne disease, and we investigated the potential of Typhi-specific bacteriophage surveillance in surface water bodies as a low-cost technique for determining where *Salmonella* Typhi circulates in the environment.

METHODS

From August 2021 till July 2022, surface water samples were collected from different environmental sources (sewage drains, rivers, ponds, lakes, and stagnant water) from three sites in Bangladesh: Dhaka, Mirzapur and Chittagong. 10 ml water sample was collected from each source that was filtered using a sterile 0.22 µm syringe filter. The filtered water sample was enriched with phage-sensitive *Salmonella* Typhi Ty2 liquid culture and Luria Broth media. By using the Double-Layer Agar method, the enriched sample was lawned to observe the presence of phages through plaque formation.

RESULTS

Salmonella Typhi-specific bacteriophages were found in 66 out of 211 (31%) samples in Dhaka, in comparison to 4 out of 315 (1.2%) samples in Mirzapur while 23 of 275 samples (8.3%) came out positive for phages in Chittagong. During the same year, 4,620 blood cultures at the two largest pediatric hospitals of Dhaka yielded 215 (5%) culture-confirmed typhoid cases, and 3,788 blood cultures in the largest hospital of Mirzapur yielded 2 (0.05%) cases. Furthermore, in Chittagong hospital, out of 2,789 blood cultures, 16 (1%) were positive for *Salmonella* Typhi.

CONCLUSION

Our pilot investigation found that the frequency of phage positivity was higher in Dhaka and Chittagong compared to Mirzapur, which correlates with the typhoid clinical cases in respective areas. These findings suggest a link between the presence of Typhi-specific phages in the environment and the prevalence of typhoid fever, as well as the possibility of using environmental phage surveillance as a low-cost and sustainable tool to aid policy decisions on typhoid control such as vaccine implementation.

Leveraging Paired Serology to Estimate the Incidence of Typhoidal *Salmonella* Infection in the STRATAA Study

Jo Walker, Yale School of Public Health

Jo Walker[1], Paula Russell[2], Leanne Kermack[2], Tan Trinh Van[3], Nga Tran Vu Thieu[3], James E. Meiring[4], Farhana Khanam[5], Mila Shakya[6], Deus Thindwa[7], Melita A. Gordon[7], Buddha Basnyat[8], Firdausi Qadri[5], Andrew J. Pollard[6], Merryn Voysey[6], Stephen Baker[2], Virginia E. Pitzer[1]

[1]Yale School of Public Health, [2]University of Cambridge School of Clinical Medicine, [3]Oxford University Clinical Research Unit, Ho Chi Minh City, [4]University of Sheffield Medical School, [5]International Center for Diarrhoeal Disease Research, Bangladesh, [6]Oxford Vaccine Group, University of Oxford, [7]Malawi Liverpool Wellcome Trust, [8]Oxford University Clinical Research Unit-Nepal

BACKGROUND

Traditional typhoid diagnostics require considerable laboratory infrastructure, which is often not available in endemic areas. As a result, public health authorities often lack the local surveillance data needed to make informed policy decisions. Serologic surveillance of at-risk populations could be used to directly estimate the incidence of typhoidal *Salmonella* infection across a variety of settings, including those without access to facility-based clinical surveillance, enabling more representative burden estimates.

METHODS

Paired blood samples were collected 3 months apart from an age-stratified random sample of community participants in Bangladesh, Malawi, and Nepal as part of the Strategic Typhoid Alliance Across Asia and Africa (STRATAA) study. We measured the concentration of IgG antibodies against a panel of typhoid antigens in each sample, and identified recently infected participants by fitting a regression mixture model to the change in IgG concentration between participants' samples. Finally, we estimated the seroincidence of infection in a Bayesian framework for each study site, age group, and antigen target.

RESULTS

When estimated using a combination of IgG against HlyE and LPS09, seroincidence was >10x higher than the incidence of clinical typhoid fever across all study sites and age groups, even after adjusting for underdetection of typhoid cases due to blood culture sensitivity, testing practices, and care-seeking. Clinical incidence declined more sharply with age than seroincidence, implying that acquired immunity reduces the severity and likelihood of symptoms upon reinfection. Our seroincidence estimates are consistent with patterns of culture-confirmed cases across different settings, age groups, and time periods, and are comparable to previously published estimates generated using cross-sectional serology data as an alternative approach.

CONCLUSIONS

Our results indicate that a high fraction of typhoidal *Salmonella* infections are mild or asymptomatic, and that this fraction increases with age due to acquired immunity. Consequently, adults may play a greater role in transmission than clinical surveillance would suggest. Ours is the first study to estimate typhoid seroincidence with paired samples, and takes advantage of data on multiple antigen targets, which we modeled in combination. This approach could be used to evaluate the local burden of typhoid in settings where facility-based clinical surveillance is impractical.

Estimating the Burden of Environmental *Salmonella* Typhi in the Asante Akim North District of Ghana: The Role of Novel Techniques

Michael O. Owusu, Kwame Nkrumah University of Science and Technology

Michael O. Owusu[1], Sampson Twumasi-Ankrah[1], Michael Owusu-Ansah[1], Debora Akortia[1], Gifty Nkrumah[1], Eric Darko[1], Christopher B. Uzzell[2], Jonathan Rigby[2], Catherine M. Troman[2], Nicolette A Zhou[3], John Scott Meschke[3], Nicholas Grassly[4], Yaw Adu-Sarkodie[5], Ellis Owusu-Dabo[5]

[1]Kwame Nkrumah University of Science and Technology, [2]Department of Infectious Disease Epidemiology, Imperial College London, [3]Department of Environmental and Occupational Health Sciences, School of Public Health, University of Washington, [4]Department of Infectious Disease Epidemiology, Imperial College London, London, [5]Kwame Nkrumah University of Science and Technology

BACKGROUND

The Asante Akim North District of Ghana is a high typhoid burden community with estimated incidence above the WHO threshold of 100 per 100,000 PYO. Blood culture is the gold standard for confirmation of typhoid, however this method is of limited availability in resource poor countries. Environmental surveillance (ES) offers an alternative low-cost approach for estimating the extent of *Salmonella* enterica serovar Typhi circulation. We conducted a cluster-based longitudinal study to evaluate detection methods for *S.* Typhi and determine the utility of ES and its association with typhoid incidence in Ghana.

METHODS

We used standardized protocols developed by the ES consortium for selection of surveillance sites. Grab and Moore swab (MS) methods were used to collect wastewater every month from 40 validated sites and transported to the laboratory for testing. Samples were filtered using membrane filtration and DNA extracted following standard protocols. Real-time PCR was then performed to detect *S.* Typhi target genes (ttr [pan-*Salmonella* target], staG, tviB) and human-restricted Bacteroides (HF183).

RESULTS

We collected 417 samples made up of 208 Grab and 209 MS samples over a 5-month period. The rates of detection of *S.* Typhi in MS [42.6% (95%CI = 35.3-50%)] was higher than Grab [10.6% (95%CI = 6.4% - 17%)] (mixed effects regression $p < 0.001$). We observed a low intracluster correlation coefficient (ICC) of 0.03 for MS detections compared to Grab (0.15). The detection rate of HF183 was higher (95.2%; 95%CI = 91%-98%) in MS compared to Grab samples (66.3%; 95%CI = 57% – 75%). For all *Salmonella* genes tested, only the ttr target was significantly associated with HF183 (p=0.000195). From a concurrent blood culture surveillance in the same area, we recorded low prevalence (0.19%, 95%CI = 0.004 - 0.72) of *S.* Typhi.

CONCLUSION

Our preliminary data has demonstrated the usefulness of ES in providing information about *S.* Typhi distribution. Few typhoid fever cases were reported during the study period, despite relatively high detection of *S.* Typhi in the environment. Additional data from ongoing ES, as well as seroprevalence studies, could help provide further evidence about the incidence of *S.* Typhi infection and utility of ES as a surveillance tool.

The Burden and Trend of Typhoid Fever in Low- and Middle-Income Countries: An Updated Meta-Regression Approach

Harsh Vivek Harkare, Swiss Tropical and Public Health Institute and University of Basel

Harsh Vivek Harkare[1], Ottavia Prunas[2], Virginia Elizabeth Pitzer[3], Marina Antillon[2]

[1](1) Swiss Tropical and Public Health Institute AND (2) University of Basel, [2](1) Swiss Tropical and Public Health Institute, (2) University of Basel, [3](1) Public Health Modeling Unit, Yale School of Public Health, Yale University; (2) Department of Epidemiology of Microbial Diseases, Yale School of Public Health, Yale University

BACKGROUND

In the absence of up-to-date incidence data of typhoid fever in low- and middle-income countries (LMICs), policymaking for informing vaccination campaigns can be misguided. Since most LMICs lack surveillance data, model-estimated incidence can offer an insight into the true disease burden. Data on the trends in overall incidence of the typhoid fever in LMICs is also not widely available.

METHODS

We updated the original mixed-effects model developed by Antillón et al (2017) to estimate typhoid (*Salmonella* Typhi only) incidence in LMICs. The original model was compared to recently published data from 20 countries. We then updated the model and fitted it to data from 83 population-based studies conducted in 57 locations across 27 countries (compared to 14 in the original model). The set of environmental and economic variables (n = 11) used to predict typhoid incidence have also been updated and their contribution to incidence prediction tested using a stochastic search variable selection algorithm.

RESULTS

Except for a few countries in sub-Saharan Africa (SSA) where no surveillance data was previously available, the original model provided a good fit to the new out-of-sample typhoid incidence data. Including more data points allowed for a better fit and provided more granular estimates of age-specific incidence in children in SSA and India. We also identified potential new important predictors of typhoid incidence.

CONCLUSION

Our analysis provides an updated estimate of the overall as well as age-specific incidence of typhoid fever in LMICs. We also identify certain widely available indicators of health development that may be used to estimate typhoid incidence in the absence of population-based surveillance data. The new model allows for a comparison with the original study to track variation in cases and disease burden over time.

Blood Culture Positive Typhoid and Paratyphoid Cases in Children Presenting to Patan Hospital, Nepal Over a 14 Year Period (2009–2022)

Shrijana Shrestha, Patan Academy of Health Sciences

Shrijana Shrestha[1], Meeru Gurung[1], Sanjeev Bijukchhe[1], Bhishma Pokhrel[1], Saugat Bhandari[1], Madav Chandra Gautam[1], Ganesh Prasad Shah[1], Andrew Pollard[2]

[1]Patan Academy of Health Sciences, [2]Oxford Vaccine Group, University of Oxford

BACKGROUND

The relative burden of paratyphoid fever compared to typhoid fever varies depending upon the geographical location. Paratyphoid fever is reportedly increasing especially in South Asia. There are concerns that the increase may be associated with vaccination against typhoid. In Nepal, a nationwide TCV (Typhoid conjugate Vaccine) campaign targeting children aged 15 months to 15 years was conducted in April/May 2022 followed by TCV introduction into the National immunization program from May 2022.

We aimed to assess the relative burden of Paratyphoid fever among children visiting Patan hospital and to look for any changes post TCV introduction.

METHODS

In a long-running study on invasive bacterial disease in children at Patan Hospital, Patan Academy of Health Sciences in Nepal, the record of all positive blood culture isolates, including *Salmonella* Typhi and Paratyphi, from children (1 month-14 years), are available since 2009. Blood culture at the hospital is done using Bac-tec Peds Plus culture bottles. We reviewed the recorded data on culture positive enteric fever cases.

RESULTS

A gradual decline in blood culture positive enteric fever cases (both typhioid and paratyphoid) has been observed over the years (2009-2021), from >200 cases per year (2009-2013) to around 100 cases per year after 2014, till 2019. A significant drop in cases to <50 cases/year was observed during the years affected by COVID-19 pandemic (2020 & 2021) before the TCV introduction. The relative burden of blood culture positive *S.* Paratyphi cases compared to *S.* Typhi varied over these years. From 2015 onwards till 2021, a decline in percentage contribution of *S.* Paratyphi to the total culture positive enteric fever cases has been observed with a median of 9.5% (IQR 3.7- 12.5). In 2022, the first TCV introduction year, the total cases of culture positive enteric fever remained < 50, while culture positive *S.* Paratyphi were more than *S.* Typhi, accounting for 61% of all culture positive enteric fevers.

CONCLUSIONS

Further evaluation of the possibility of an increase in the relative burden of paratyphoid cases after introduction of typhoid vaccine is needed. Development of effective enteric fever vaccines covering both typhoid and paratyphoid is needed for disease control.

The Ty-FIVE Project — Strengthening Typhoid Surveillance Around a Mass Vaccination Campaign in the Northern Division of Fiji

Alumita Vuakanisakea, Ty-Five Project, International Vaccine Institute

Alumita Vuakanisakea[1], Hea Sun Joh[2], Orisi Cabenatabua[3], Matelita Buli[1], Ashweeni Kumar[1], Rachel Pillay[4], Aneley Getahun[5], Raphael Zellweger[2], Richard Strugnell[5], Kim Mulholland[6], Aalisha Sahukhan[4], Florian Marks[2]

[1]Ty-Five Project, International Vaccine Institute, [2]International V accine Institute, [3]Ty-Five project, International Vaccine Institute, [4]Ministry of Health and Medical Services, [5]University of Melbourne, [6]Murdoch Children's Research Institute

BACKGROUND

Fiji has an important typhoid fever burden. Given the sub-optimal water and sanitation infrastructure in Fiji, vaccination could be a valuable control tool. The "Typhoid in Fiji, Vaccination towards Elimination" (Ty-FIVE) consortium has partnered with the Fiji Ministry of Health and Medical Services (FMHMS) to strengthen typhoid surveillance and vaccinate the entire population of Fiji's Northern Division against typhoid using the WHO pre-qualified typhoid conjugate vaccine Typbar-TCV. Clinical and environmental surveillance are being conducted to understand the underlying typhoid epidemiology and assess the impact of vaccination.

METHOD

Since 2020, clinical surveillance has been gradually strengthened and standardized to maximize case detection and improve contact tracing activities. In addition, environmental surveillance has been implemented throughout the island to complement clinical data. Mass vaccination will be conducted by the FMHMS in the Northern Division of Fiji in July-August 2023, with the target population of 9 months to 65 years (~133,000), followed by 2 years of birth cohort vaccination. Post-vaccination coverage will be estimated from vaccination records and medical area population data, and vaccine effectiveness will be assessed by a case-control study (if cases arise).

RESULT

With surveillance strengthening, the number of blood cultures taken has increased from 6350 in 2020 to 7859 in 2022. In parallel, the number of days necessary to investigate a case has decreased. Additionally, the increase in stool collection during contact-tracing activities has improved identification of healthy carriers. In 2022, 78 cases were detected for a total population of 145,172 (~54 per 100'000). Interestingly, 49 cases were in individuals over 20 years of age, and 11 in the over 50 age group, suggesting that typhoid is common in older age-groups in Fiji, supporting the decision to vaccinate the adult population as well. Initial coverage data will be presented if available at the time of the meeting.

CONCLUSION

This project is an example of island-wide typhoid vaccine roll-out, targeting an expanded age-group due to the presence of substantial typhoid burden in the over 20 years of age in Fiji. A successful reduction of typhoid burden locally will hopefully pave the way for a national vaccine introduction in Fiji.

Typhoid-Associated Ileal Perforations Following the Introduction of the Typhoid Conjugate Vaccine in Pakistan: Findings From a Multi-Center Surveillance Study

Saqib Hamid Qazi, Aga Khan University

Saqib Hamid Qazi[1], Muhammad Tahir Yousafzai[2], Irum Fatima Dehraj[2], Humza Thobani[2], Denise O Garrett[3], Surrender Kumar[4], Nasir Saleem Saddal[5], Farah N Qamar[2]

[1]Aga Khan University, [2]Aga Khan University, Karachi, [3]Sabin Vaccine Institute, Washington, DC, [4]Jinnah Post Graduate Medical Center, Karachi, [5]National Institute of Child Health, Karachi

BACKGROUND

As resistance to first- and second-line antimicrobial agents becomes increasingly prevalent amongst typhoidal strains in South Asian nations, the development of the typhoid conjugate vaccine (TCV) is a promising intervention to prevent transmission of the disease. We investigated trends in typhoid-associated ileal perforations following the addition of TCV to Pakistan's childhood immunization program, as part of the "Impact assessment of the Typhoid conjugate vaccine following introduction in the Routine Immunization Program of Pakistan" (ITRIPP) study.

METHODS

We prospectively enrolled patients from 3 tertiary care hospitals in Karachi, Pakistan with non-traumatic ileal perforations with or without laboratory confirmation of typhoidal infection. Patients with clinically suspected or proven TB-associated ileal perforations were excluded. Data on patient sociodemographic and clinical characteristics were compiled by dedicated research staff or treating physicians. Histopathological and laboratory reports were reviewed for the presence of typhoidal strains or other pertinent findings.

RESULTS

266 patients with ileal perforations were enrolled between March 2022 and April 2023. The majority of patients were male (n=223, 85%) and were aged 15-25 years (n=104, 40%) or >25 years (n=100, 35%). Only 9 patients (3.4%) had previously received TCV. Blood culture and other tissue culture reports were available for 234 (88.0%) and 209 (78.6%) patients respectively. Non-typhoidal pathogens including *Staphylococcal sp.*, *E.coli*, *Klebsiella sp.*, *Acinetobacter sp.* and *Enterococcal sp.* were the predominant microorganisms isolated in culture, likely demonstrating contamination with enteral contents following perforation. *S.typhi* and *S.paratyphi* were isolated in only 19 (7.1%) and 1 (0.4%) patients respectively.

CONCLUSION

The burden of ileal perforations remains high in children older than 15 years of age. This contrasts with data from studies prior to the introduction of the TCV, wherein the highest frequency of ileal perforations was reported in children younger than 15 years of age. This is likely attributable to the protective effect of the TCV after its introduction and dissemination to children aged 9 months to 15 years.

Molecular Surveillance of Non-Typhoidal *Salmonella* from Environmental Sources in Disease Endemic Informal Settlement in Nairobi, Kenya

Michael Muraya Mugo, Kenya Medical Research Institute

Collins Kebenei[1], Kelvin Kering[1], **Michael Muraya[1],** Georgina Odityo[1], Cecilia Mbae[1], David Onyango[2], Sam Kariuki[1]

[1]Kenya Medical Research Institute, [2]Maseno University

BACKGROUND

Non-typhoidal *Salmonella* is a major cause of bacteremia in Sub-Saharan Africa, especially in areas with poor water and sanitation infrastructure. However, there is limited knowledge of the spread and environmental carriage of Non-typhoidal *Salmonella* in disease-endemic areas. This study aimed to detect the presence of Non-typhoidal *Salmonella* in various environmental samples and assesses their seasonal fluctuations.

METHODS

The study used a cross-sectional design to detect Non-typhoidal *Salmonella* from environmental samples collected in Mukuru slum throughout 2022. It incorporated secondary data on rainfall patterns. Sanipath protocol was employed in sample collection. Real-time quantitative polymerase chain reaction was used to screen for Non-typhoidal *Salmonella* presence, and seasonal variations were identified by comparing pathogen burden with rainfall patterns.

RESULTS

The study found that 34.6% of analyzed environmental samples had non-typhoidal *Salmonella*, with *Salmonella* Enteritidis being the most prevalent strain (22.8%), followed by *Salmonella* Typhimurium (11.8%). However, there was no critical distinction in occurrence between Enteritidis and Typhimurium (t6=1.469, p=0.192). Raw sewer samples had the highest Non-typhoidal *Salmonella* prevalence (75% *Salmonella* Enteritidis and 68.8% *Salmonella* Typhimurium), followed by effluent (27.6% *Salmonella* Enteritidis and 13.2% *Salmonella* Typhimurium), drinking water (17.4% *Salmonella* Enteritidis and 4.3% *Salmonella* Typhimurium), and soil (11.8% *Salmonella* Enteritidis and 5.3% *Salmonella* Typhimurium). Non-typhoidal *Salmonella* prevalence was higher in wet seasons (Apr-Jun, Oct-Dec) at 46.5% and 45.8% respectively, compared to low precipitation periods, July-Sept (25.0%), and dry periods, Jan-Apr (16.4%). Rainfall partly explains a large proportion (82.9%) of the variations in non-typhoidal *Salmonella* incidence (R2=0.829). However, non-typhoidal *Salmonella* in the environment are influenced by complex and multifactorial factors, and are not solely dependent on rainfall (F1=9.667, P=0.090).

CONCLUSION

This study revealed that non-typhoidal *Salmonella* is widespread in Mukuru, with rainfall patterns affecting its environmental burden. The study suggests a multi-sectoral approach to developing surveillance and control strategies that take seasonality into account. It highlights the importance of metagenomic studies to establish the relationship between environmental disease burden and clinical infections. The study emphasizes the need for environmental sample surveillance in areas with poor water, sanitation, and hygiene infrastructure, and underscores the importance of improving sanitation infrastructure as a disease control measure.

THURSDAY, DECEMBER 7

7:45–8:30 How Data Drive Decision-Making: Reflections From TCV Introductions in Pakistan and Malawi and the Role of Data Moving Forward

ISARO ROOM

SUNRISE SYMPOSIUM SESSION CHAIRED BY:
Emmanuel Mugisha, PATH

Typhoid and drug resistance burden data are crucial to identify prevention interventions. We will discuss how policymakers in Pakistan and Malawi used data to introduce and strategically implement typhoid conjugate vaccine (TCV). We will discuss ongoing data gathering efforts in the Eastern Mediterranean region that support future country decision-making.

Optimizing Surveillance and Interventions to Advance National XDR Typhoid Control: The Pakistan Experience
Nada Taqi, World Health Organization

From Decision-Making to Introduction: How Persistence, Partnership, and Planning Led to the Introduction of Typhoid Conjugate Vaccine in Malawi
Esau Mkisi, PATH/Malawi

The MENA Typhoid Project: New Insights on Typhoid Burden and Antibiotic Resistance
Kristen Heitzinger, U.S. Centers for Disease Control and Prevention

8:30–10:00 Landscape, Strategy, and Progress Update for iNTS Vaccines in Clinical Development

KILIMANJARO BALLROOM

SYMPOSIUM SESSION CHAIRED BY:
Melita Gordon, Malawi-Liverpool Wellcome Programme
& Samuel Kariuki, Kenya Medical Research Institute

iNTS is a high burden, high fatality disease in sub-Saharan Africa. There is now, finally, substantial progress in early clinical development of several candidate vaccines for iNTS. This symposium will (1) update on current vaccine-targeted field-research; (2) evaluate the preferred characteristics for putative iNTS vaccines, including a LMIC African perspective on strategy and experience; (3) give updates on current and imminent clinical trials for 3 leading iNTS vaccines.

Prevalence and Distribution of Non-Typhoidal *Salmonella* Enterica Serogroups and Serovars Isolated From Normally Sterile Sites: A Global Systematic Review
John Crump, University of Otago

Sero-Epidemiology of iNTS in Large Field Cohorts From Malawi, Burkina Faso, Kenya And Ghana
Helen Dale, University of Liverpool

Economic Burden of iNTS and cost-Effectiveness Analysis for a Hypothetical iNTS Vaccine in Ghana, Burkina Faso and Malawi
Jung-Seok Lee, International Vaccine Institute

The Public Health Need for iNTS Vaccines, and Preferred Vaccine Characteristics
Adwoa Bentsi-Enchill,
World Health Organization

A LMIC Perspective on iNTS Vaccine Strategy, and Lessons From Recent Vaccine Introductions
Mike Chisema, Malawi Ministry of Health

Current Status of the Clinical Development of Trivalent *Salmonella* Conjugate Vaccine (TSCV)
Wilbur Chen, Center for Vaccine Development, University of Maryland School of Medicine

Development of iNTS Conjugate and Preclinical Study for a Novel Trivalent iNTS/Typhoid Vaccine
SoJung An, International Vaccine Institute

Development of GMMA-Based Vaccines Against iNTS: Current Status
Rocio Canals Alvarez, GVGH

10:00–10:30 Coffee Break & Poster Viewing

FOYER

10:30–12:30 Mosaic of Insights: An Exploration of Diverse Salmonelloses Topics

KILIMANJARO BALLROOM

ORAL ABSTRACT SESSION MODERATED BY:
Nicholas Feasey, Liverpool School of Tropical Medicine
& Calman A. MacLennan, Bill & Melinda Gates Foundation

Impact of COVID-19 Pandemic on Enteric Fever Diagnosis in Nepal: Findings From the Surveillance of Enteric Fever Asia Project Study

Dipesh Tamrakar, Dhulikel Hospital-Kathmandu University Hospital

Dipesh Tamrakar[1], Shiv Ram Naga[2], Sabin Bikram Shahi[2], Nishan Katuwal[2], Rajeev Shrestha[2], Basudha Shrestha[3], Rabin Pokharel[4], Prativa Bista[5], Ram Prasad Adhikari[6], Kate Doyle[7], Alice S. Carter[7], Jessica Seidman[7], Denise Garrett[7], Jason R. Andrews[8]

[1]Dhulikel Hospital- Kathmandu University Hospital, [2]Dhulikhel Hospital, Kathmandu University Hospital, [3]Kathmandu Model Hospital, [4]Helping Hands Community Hospital, [5]Bir Hospital, [6]Nepal Medical College and Teaching Hospital, [7]Sabin Vaccine Institute, 8Stanford University

BACKGROUND

Over the past decade, population-based studies have demonstrated a very high burden of enteric fever in and around the Kathmandu Valley of Nepal. In April, 2022, Nepal introduced typhoid conjugate vaccination for children under 15 years of age. However, the impact of the COVID-19 epidemic in Nepal on typhoid, prior to vaccine introduction, is unclear.

METHODS

We collected data on blood cultures performed and cases of typhoidal *Salmonella* positivity from October 2016 to April 2022 at five healthcare facilities participating in the Surveillance of Enteric Fever in Asia Project (SEAP) study. We analyzed the trend of blood culture numbers, *Salmonella* positivity rates, and rates of positivity for pathogens other than *Salmonella*. Additionally, a comparison was made between the periods before the COVDI 19 pandemic (October 2016 to March 2020) and during the COVID-19 pandemic (April 2020 to April 2022) prior to the introduction of the typhoid vaccine.

RESULTS

Before the pandemic, a total of 68,724 blood cultures were performed, with an average of 327 cultures per month. During the pandemic, 16,888 blood cultures were conducted, with an average of 133 cultures per month. There was a significant decrease in the number of typhoidal *Salmonella*-positive cases (1325 vs. 65) and the *Salmonella* positivity rate (2.15% vs. 0.4%, p<0.001) between the before pandemic and during pandemic periods. In contrast, the positivity rate for pathogens other than *Salmonella* remained relatively constant (median[IQR] 2.11% [2.14] vs. 2.85% [5.68], p=0.94). Although the number of blood cultures conducted annually has been increasing since the start of the pandemic, reaching approximately two-thirds of the pre-pandemic volume, the typhoidal *Salmonella* positivity rate has remained low or continued to decline.

CONCLUSION

The COVID-19 pandemic had a substantial impact on the diagnosis of enteric fever in Nepal. It resulted in a significant reduction in the number of typhoid cases and the culture positivity rate, while the culture positivity rate for other pathogens remained stable. Potential explanation for these changes include changes in healthcare seeking patterns and reductions in typhoid transmission due to movement restrictions, increased emphasis on hygiene practices, and reductions in eating outside the household, Further studies are needed to clarify the contributions of these potential mechanisms to reduction in typhoid burden.

The Application of Machine Learning with High-Content Imaging to Infer Antimicrobial Resistance Phenotypes in *Salmonella* Typhimurium

Sushmita Sridhar, Universidad Peruana Cayetano Heredia and University of New Mexico

Sushmita Sridhar[1], Tuan-Anh Tran[2], Stephen Reece[3], Octavie Lunguya[4], Jan Jacobs[5], Sandra Van Puyvelde[6], Florian Marks[7], Gordon Dougan[8], Nicholas Thomson[9], Binh Nguyen[10], Pham The Bao[11], Stephen Baker[8]

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BACKGROUND

Antimicrobial resistance (AMR) is a growing public health crisis, and part of this problem arises from the difficulty in accurately and rapidly distinguishing between drug-sensitive and -resistant clinical isolates. Traditional methods rely on extensive culturing and subsequent exposure of a single isolate to the antimicrobial to determine a minimum inhibitory concentration (MIC). *Salmonella* Typhimurium is an enteric pathogen responsible for severe gastrointestinal illness in immunocompetent individuals and severe disease in immunocompromised people, particularly in lower-resource settings. Ciprofloxacin is an important broad-spectrum antimicrobial, often used for the treatment of typhoidal and invasive nontyphoidal *Salmonella*. Ciprofloxacin resistance in nontyphoidal *Salmonella* is most commonly due to mutations in DNA gyrase, and there has been an increase in ciprofloxacin-resistant nontyphoidal *Salmonella* in many parts of the world in recent years. Thus, there is an urgent need for more and improved diagnostics to readily determine drug resistance, particularly to first-line treatments like ciprofloxacin.

METHODS

In this study, we used high-content imaging to examine four isolates of *Salmonella* Typhimurium to quantitatively measure the fluorescence imaging-based differences between isolates grown in culture over 24 hours at four concentrations of ciprofloxacin. These concentrations were: 0x MIC, 1x MIC, 2x MIC, and 4x MIC. Over 50 measurements were captured, including morphological and fluorescence intensity measurements. We applied five comparable machine learning algorithms to the imaging data to determine whether isolates could be computationally differentiated based on imaging measurements. Based on the outcomes of the algorithms, we determined that a random forest classifier could best differentiate isolates and that this could be done using five key imaging data features. We then used a set of 13 additional *Salmonella* Typhimurium isolates to test our random forest algorithm's ability to agnostically distinguish between ciprofloxacin-susceptible and -resistant isolates.

RESULTS

We found that individual isolates display distinct growth and morphological characteristics that could be clustered by timepoint and resistance to ciprofloxacin, independent of ciprofloxacin exposure. We further found that at an isogenic isolate, one containing a GyrA mutation and one without could be clearly differentiated based on imaging parameters, indicating that a GyrA mutation confers bacterial changes that can be captured through imaging. Comparing a total of 16 unique isolates, our algorithm was able to agnostically distinguish between ciprofloxacin-susceptible and -resistant isolates, finding that the random forest classifier could predict ciprofloxacin resistance without any prior knowledge of an isolate's ciprofloxacin susceptibility.

CONCLUSIONS

These results provide proof-of-principle for the use of high-content imaging combined with machine learning algorithms to assess drug susceptibility of clinical isolates. This technique may have myriad applications, including to better understand bacterial biology around drug resistance that has thus far been inaccessible using traditional techniques. Perhaps most importantly, this approach could help to identify drug-resistant bacteria more rapidly and accurately without reliance on traditional culturing and antimicrobial susceptibility testing protocols that are time consuming. This imaging-based approach could be an important tool in addressing the rising spectre of AMR.

Evaluation of a Point-Of-Care Multiplex Immunochromatographic Assay (DPP Typhoid Assay) for the Diagnosis of Typhoid

Zahida Azizullah, Aga Khan University

Zahida Azizullah[1], Rumina Hasan[1], Hina Shams[1], Kevin Tetteh[2], Jason R. Andrews[3], Charles Richelle[4], Sabine Dittrich[5], Jyotshna Sapkota[2]

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BACKGROUND

Typhoid is an acute febrile illness caused by the bacterium *Salmonella* Typhi. The current reference standard for typhoid diagnosis is blood culture, which is resource intensive, has sensitivity ranging from 60 to 80%, and takes 2-5 days for a result. Several point-of-care tests are available, but the performance of these tests is suboptimal. Here, we performed an independent evaluation of the DPP Typhoid (ChemBio) assay, which detects IgA antibodies against LPS and HlyE.

METHODS

We conducted a retrospective, diagnostic substudy nested within a prospective study of patients with acute febrile illness presenting to Aga Khan University Hospital in Karachi, Pakistan. We performed the DPP Typhoid assay on serum samples from 186 culture-confirmed typhoid patients and 199 culture-negative controls. We evaluated the area under the curve and sensitivity and specificity at Youden's optimal threshold, and we performed Bayesian latent class modeling using results from culture and 8 other RDTs to estimate diagnostic assay accounting for these imperfect reference standards.

RESULTS

Using prespecified positivity thresholds of LPS ≥20 and HlyE ≥14 from a small pilot study, sensitivity and specificity of DPP assay were 97.8% and 65.3% respectively. The AUC was 0.926 (95% CI 0.900-0.952). At Youden's optimal threshold,

sensitivity was 91.0% and specificity was 82.4%. In Bayesian latent class analysis, DPP Typhoid sensitivity was 89.7% and specificity was 90.4%, for balanced accuracy of 90%. Balanced accuracy of the other 8 RDTs ranged from 59% to 79%.

CONCLUSION

The results showed that the DPP Typhoid assay exhibited high diagnostic accuracy for typhoid fever. However, although the sensitivity and specificity of the DPP typhoid assay compared favorably with other typhoid diagnostic tests, further modification of the kit and an adjustment to new thresholds is recommended to enhance its performance.

Design and Initial Data From a Phase 1 RCT to Evaluate the Safety and Immunogenicity of a Vaccine Against *S.* Typhi and *S.* Paratyphi A in Healthy European Adults

Usman Nasir Nakakana, GSK Vaccines Institute for Global Health

Usman Nasir Nakakana[1], Ilse De Coster[2], Eleanna Sarakinou[1], Marie-Annick Götze[2], Antonella Silvia Scire[1], Giulia Luna Cilio[3], Alimamy Serry-Bangura[3], Iris Sarah De Ryck De Ryck[3], Martina Carducci[1], Luisa Massai[1], Simona Rondini[1], Valentino Conti[1], Omar Rossi[1], Pierre Van Damme[2], Ashwani Kumar Arora[1]

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BACKGROUND

Despite improved sociosanitary conditions in the last decade, enteric fever remains a major cause of disability and death, with billions of people likely to be exposed to *Salmonella enterica* pathogens causing typhoid and paratyphoid fever. In 2019, there were 13 million cases of enteric fever globally, 28% of these being caused by *Salmonella* Paratyphi A. There is a trend of increased incidence of *S.* Paratyphi A in parts of Asia, estimated as ~35% of cases in India and Nepal and >60% of enteric fever in China, with a similar trend towards rising antimicrobial resistance. A novel Typhoid and Paratyphoid A conjugate vaccine (bivalent), aimed to prevent both typhoid and paratyphoid enteric fever in infants and older age groups, is under development by GVGH. The first step in this development is a first-time-in-human (FTIH) study aimed to evaluate the safety and immunogenicity profile of a low and a full dose , in healthy adults in Europe.

METHODS

In this study, 96 healthy adult participants randomised 2:1 are administered 2 vaccinations using a single priming dose and a booster 6 months later or a comparator vaccine. There is a dose-escalation approach with 2 different doses (low and full), with or without alhydrogel adjuvant. TYPHIM VI will be used as control for the first vaccination, and BOOSTRIX as control for the second. Depending on interim and final results, additional studies will be planned in an endemic setting for enteric fever.

RESULTS

After at least one administration of the low dose or control in participants, most Adverse Events (AEs) reported were of mild to moderate severity. No Serious AEs nor AEs leading to discontinuation have been observed. Headache was the most frequently reported solicited systemic AE and injection site pain was the most frequently reported administration site AE. Follow up of participants in both low and full dose groups is ongoing as well as the immunological assessment both in terms of antigen-specific IgG level and bactericidal activity against *S.* paratyphi A.

CONCLUSIONS

If no safety issues are identified and the vaccine is sufficiently immunogenic, clinical development will progress to younger age groups.

FUNDING

GlaxoSmithKline Biologicals SA (Sponsor); Wellcome Trust

•*Conflict of interest of presenting author: Usman Nasir Nakakana is an employee of GSK and holds shares in GSK*

•*Trial registration number: NCT05613205*

From Rarity to Clarity: The Potential of Seroepidemiology for Monitoring Typhoid Vaccine Impact

Kristen Aiemjoy, University of California Davis & Mahidol University Faculty of Tropical Medicine

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BACKGROUND

Estimating the effect of vaccine interventions is challenging for infectious diseases like typhoid fever that are difficult to measure and/or rare. Recent randomized trials have enrolled more than 20,000 participants to detect fewer than 80 cases of blood-culture-confirmed typhoid fever. Seroepidemiology, an approach using immunological markers of pathogen exposure combined with population sampling strategies, offers a possible alternative method for detecting intervention effects.

METHODS

We simulated quantitative anti-Hemolysin E (HlyE) antibody responses at varying forces of infection of enteric fever

across several age groups. Population antibody responses were generated based on antibody trajectories modeled from a longitudinal cohort of 1420 blood-culture-confirmed enteric fever cases enrolled from Bangladesh, Nepal, and Pakistan. We then simulated vaccine introduction, reducing the force of infection, and assessed the power to detect this effect by age group and time since introduction. We calculated seroincidence rates using maximum likelihood profiles based on the longitudinal antibody kinetics. We simulated each experimental condition 100 times, calculated the seroincidence rate in the control and intervention groups, and defined power as the percentage of iterations where the upper 2.5% of the confidence interval in the intervention group did not include the incidence estimate of the control group.

RESULTS

The power to detect an effect increased over time as antibodies from the pre-intervention phase waned and immune-naïve individuals entered the population. For instance, in a population with a seroincidence rate of 100 per 100,000 person-years and a vaccine that curtails infections by 60%, a sample size of 2600 provided 90% power to detect an intervention effect at 1 year, while a sample size of 1550 gave 90% power to detect the effect at 2 years among a cross-sectional population sample of individuals aged 0-25 years. Young children provided the most informative data for detecting intervention effects, especially within the initial two years post-intervention. In the given example, a sample of 400 children under 5 years was sufficient to detect the intervention effect on infection after 1 year.

CONCLUSION

Using novel seroincidence estimation approaches, we demonstrate that the impact of a vaccine on enteric fever infections can be accurately detected with comparatively small sample sizes. This approach can be used to estimate at what time scale, sample size, and age group a vaccine intervention could be detected in a population.

Role of Gallstones in *Salmonella* Typhi Stool Carriage and Shedding in an Urban Typhoid Endemic Setting in Nairobi, Kenya

Samuel Kariuki, Kenya Medical Research Institute

Peter Muturi[1], Peter Wachira[2], Maina Wagacha[2], Cecilia Mbae[1], Musa Muhammed[3], John Gunn[4], **Samuel Kariuki[1]**

[1]Kenya Medical Research Institute, [2]University of Nairobi, [3]Depart of Medical Services, Nairobi City County, [4]Nationwide Children's Hospital and Ohio State University

BACKGROUND

Salmonella Typhi, the causative agent of typhoid fever, is a human-restricted pathogen. Even after treatment, 3-5% of those infected fail to clear the bacteria within one year and become chronic carriers; and 95% of carriers have gallstones. Asymptomatic carriers shed the infectious bacteria intermittently in their feces for an ill-defined period of time, thus serving as a reservoir of infection.

Little progress has been made in understanding the disease progression, with limited insights into typhoid carriage being generated in recent decades.

The aim of this study was to determine prevalence of chronic typhoid carriers, the longitudinal shedding dynamics, and whether antimicrobial resistance is associated with the duration of shedding.

METHODS

A cohort of typhoid fever patients aged >12 years, identified through blood and stool culture in Mukuru slums, Nairobi, from December 2020 to March 2023 were followed up after treatment with antibiotics. Stool samples were collected once monthly for 12 months to detect *S.* Typhi stool shedding from cases and contacts at home. An abdominal ultrasound scan was used to identify individuals with gallstones. Antimicrobial susceptibility to commonly used antibiotics was tested for all isolates.

RESULTS

Stool shedding was observed in 25.9% (7/27) of cases and five contacts during the first and/or the second month of follow-ups. Only 3/27 of the cases continued to shed *S.* Typhi after the second month; these three cases and one asymptomatic contact had gallstones in their gallbladder.

S. Typhi isolates showed highest resistance to nalidixic acid at 53.8% (7/13) in cases (blood isolates) and 42.3% (11/26) of bacteria isolated during follow-ups. Most of the isolates, 61.5% from blood and 79.6% from stool, were intermediate to ciprofloxacin. Isolates that are MDR, resistant to nalidixic acid, and non-susceptible to ciprofloxacin, were identified in 30.8% of blood isolates and 19.2% of follow-up isolates. Varying susceptibility to ciprofloxacin was also observed in *S.* Typhi strains shed at different time points by three participants.

CONCLUSION

Results obtained show a correlation between duration of *S.* Typhi shedding and presence of gallstones. Presence of asymptomatic carriers at household level is an indication that they may be responsible for persistence and spread of antibiotic-resistant typhoid fever in Nairobi.

The Impact of Surgical Interventions for Severe Typhoid on Families and Healthcare Systems in Rural South Central Niger

Yakoubou Sanoussi, Hopital de la SIM Galmi, Niger

Katherine Shafer[1], **Yakoubou Sanoussi[2],** Yves Mpongo[2], Andrew Avery[2], Audry Banza[2], Noel Ndayisenge[2], Chidi Otuneme[2], Sadock Irankunda[2], Clarisse Giruncuti[2], Emmanuel Ikwutah[2], Louisa Nwachukwu[2], Aminat Fagbenro[2], Brad-lot Igiraneza[2], Aime Mugisha[2], Melance Kabanyegeye[2], Samaila Yusuf[2]

[1]Hopital de la SIM Galmi, Niger, [2]Hopital de la SIM Galmi

BACKGROUND

Surgical complications of severe typhoid, most commonly typhoid intestinal perforations, can have a large financial strain on families and health care systems in Niger. At Hôpital de la SIM Galmi in rural Niger, most typhoid patients seen by the surgical department have a delayed presentation with peritonitis and free fluid on ultrasound, necessitating surgical interventions.

METHODS

We retrospectively reviewed medical records for children (age 3 to 17) who had an initial operative intervention for typhoid intestinal perforations in 2022 and those who needed an ostomy reversal from January 2022 - June 2023. Only those with a history of an acute infectious process, no history of trauma, and intraoperative evidence of a full thickness small bowel perforation were included. We reviewed the cost to families and healthcare systems for hospitalizations and clinic visits.

RESULTS

In 2022, the most common indication for pediatric gastrointestinal emergent surgery at our hospital was typhoid and 191 children required surgery for a perforation (morality rate of 14%). The surgical service is especially overwhelmed post rainy season when 36% of all major operative cases (all ages) in September are related to typhoid and 55% when excluding OB/GYN and orthopedics. Ostomies were created for 105 patients (55%) and eventual ostomy takedown as of June 2023 was 92% with an average length of duration before reversal being 155 days. The average cost for a 7 day hospitalization with surgery for typhoid is estimated at 127, 500 West African CFA franc (CFA) ($211 USD) versus 607 CFA ($1 USD) for the typhoid conjugate vaccine. Once discharged from the hospital, additional clinic visits for ostomy care and wound care mean more costs to families who often struggle to find the money for even transport fees to return to clinic.

CONCLUSIONS

The financial impact of severe typhoid can be catastrophic for rural subsistence farming families with multiple children. With Gavi subsidy, the typhoid conjugate vaccine costs can reduce to 120 CFA (.20 USD). The cost of a vaccine campaign to 15 years of age is fully financed by Gavi. This information is critical to raise awareness of the impact of typhoid in Niger and the necessity of the typhoid conjugate vaccine.

Safety and Immunogenicity of a Bivalent Paratyphoid A-Typhoid Conjugate Vaccine: Phase I Study

Andrew J Pollard, University of Oxford

Prasad S Kulkarni[1], Anirudha Vyankatesh Potey[1], Sandesh Bharati[1], Amy Flaxman[2], Elizabeth Jones[2], Young Chan Kim[2], **Andrew J Pollard[2]**

[1]Serum Institute of India Pvt. Ltd., [2]University of Oxford

BACKGROUND

Despite the introduction of successful vaccination programmes against enteric fever caused by *S.* Typhi, the burden of disease caused by S. Paratyphi A remains an important public health issue. Development of efficacious bivalent vaccines, which can prevent disease caused by both S. Typhi and S. Paratyphi A serotypes will address this need, particularly in low- and middle-income countries. We present the safety and immunogenicity results of a Paratyphoid A-Typhoid Conjugate Vaccine (Sii-PTCV) study.

METHODS

This Phase I double-blind active-controlled study randomized sixty healthy adults in a ratio of 1:1 to receive a single intramuscular dose of Sii-PTCV or comparator vaccine Typbar-TCV®. Participants were followed up for six months after vaccine administration. Solicited adverse events were assessed for one week, unsolicited events for one month and serious adverse events for six months post vaccination. Blood draw at baseline, one month and six months post vaccination was used to assess immunogenicity. Anti-Vi IgG and IgA levels were measured to assess the immunogenicity of the S. Typhi component. Anti-lipopolysaccharide IgG levels were measured to assess the immunogenicity of the S. Paratyphi component along with determining functional antibody activity against S. Paratyphi using serum bactericidal assay.

RESULTS

Solicited adverse events were observed in 90% of participants in Sii-PTCV and 86.7% in Typbar-TCV® groups. There were few unsolicited events in both groups; none were deemed related to study vaccines. No SAEs were reported. At one-month post vaccination, typhoid seroconversion rates for IgG and IgA anti-Vi antibodies were 96.7% and 93.3% respectively with Sii-PTCV and 100% each with Typbar-TCV®; paratyphoid seroconversion rates

for IgG antibodies and SBA titres was 100% and 93.3% with Sii-PTCV and, 3.3% and 0% with Typbar-TCV®, respectively. At six months post vaccination, persistent immune response was observed for the typhoid and paratyphoid components with Sii-PTCV.

CONCLUSIONS

In this first-in-human study of a typhoid-paratyphoid conjugate vaccine, it was safe, well tolerated and immunogenic after a single dose. These results indicate that Sii-PTCV is a strong candidate for progression into further clinical studies, including efficacy testing. In future, Sii-PTCV could combat enteric fever in endemic regions.

12:30–13:45 Lunch

SOKO RESTAURANT

13:45–15:45 The Late-Breakers: Unveiling the Latest in Enteric Fever and iNTS Research

KILIMANJARO BALLROOM

ORAL ABSTRACT SESSION MODERATED BY:
Jason Andrews, Stanford University & Anna Minta, World Health Organization

Assessing the Protective Efficacy of an Intranasal Vaccine Candidate, rCTB-T2544, Against Typhoid and Paratyphoid Infection Using Iron Overloaded Murine Model

Suparna Chakraborty, National Institute of Cholera and Enteric Diseases

Suparna Chakraborty[1], Pujarini Dutta[2], Ananda Pal[1], Swarnali Chakraborty[1], Shin-Ichi Miyoshi[3], Santasabuj Das[4]

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BACKGROUND

Development of safe, efficacious and affordable enteric fever vaccines is a global health priority. Commercialized Typhoid vaccines function through the induction of systemic antibody response, wherein efficacy pertaining to oral tolerance of licensed oral vaccine is compromised. Additionally, no paratyphoid vaccines are available yet. However, considering the entry of the pathogen through the intestinal route, mucosal immune response in the intestine is highly desirable. To overcome this, we constructed an immunogenic formulation, containing the recombinant fusion protein of *Salmonella* Typhi outer membrane protein T2544 (which is already reported to be present in clinical isolates of S. Paratyphi A) and the B subunit of the cholera toxin (CTB) from *Vibrio cholerae*, called rCTB-T2544.

METHODS

CTB was genetically fused with recombinant *Salmonella* Typhi outer membrane protein T2544, through a non-furin linker (GPGP). Later, it was co-expressed and purified using Ni2+affinity chromatography. The immunogenicity and protective capacity of CTB-T2544 was evaluated by administering 60 µg of CTB-T2544 through intranasal route. Iron overloaded mice were used as prototype.

RESULTS

CTB-T2544 immunized mice exhibited enhanced T2544 specific, mucosal IgA and humoral IgG antibodies. Enzyme linked immunospot assay confirmed antigen-specific IgG and IgA secreting plasma cells within mesenteric lymph nodes, spleen, and peyer's patches involving CTBT2544 group. These antibodies were capable of restricting adherence of S. Typhi to HT-29 cell monolayer in vitro and also potentiated bacterial opsanophagocytosis to THP-1 cells. 70% and 80% mice from the rCTB-T2544-immunized group survived the lethal challenge with *Salmonella* Typhi and *Salmonella* Paratyphi A respectively. Cytokine analysis exhibited that CTB-T2544 result in a mixed Th1/Th17 response, essential for the clearance of intracellular S. Typhi. Increased follicular helper T (Tfh) cells along with memory lymphocytes were also generated in the rCTBT2544 group. An adoptive transfer of immunized serum to naïve mice and also by blocking the serum antibody in another immunized subset, our study revealed relative contribution of serum and mucosal antibodies to support the protective response potential against *Salmonella* Typhi and *Salmonella* Paratyphi A.

CONCLUSIONS

In an iron overloaded mouse model, intranasal candidate vaccine shielded against lethal challenges of S Typhi and also S. ParatyphiA; through augmenting intestinal secretory IgA and serum IgG responses

Diversity and Antimicrobial Resistance of *Salmonella* Paratyphi A: A Collaborative Global Typhoid Genomics Consortium Initiative

Zoe Anne Dyson, London School of Hygiene & Tropical Medicine

Zoe Anne Dyson[1], Global Typhoid Genomics Consortium[2], Yogesh Hooda[3], Jaspreet Mahindroo[1]

[1]London School of Hygiene & Tropical Medicine, [2]Global Typhoid Genomics Consortium, [3]Child Health Research Foundation

BACKGROUND

The Global Typhoid Genomics Consortium (GTGC), a group of >200 researchers from >50 different countries, recently reported on the global diversity and antimicrobial resistance patterns of *Salmonella* Typhi from a meta-analysis of >13,000 whole genome sequences (WGS). This study highlighted the global distribution of H58 and other key pathogen genotypes, wide-spread ciprofloxacin non-susceptibility, and emerging resistance to third generation cephalosporins. While Typhi vaccines are now available and being employed for disease prevention across several endemic settings, we lack a licensed vaccine against *Salmonella* Paratyphi A. Antimicrobial treatment of paratyphoid fever is complicated by widespread resistance to ciprofloxacin, and emerging resistance to azithromycin. Moreover, enteric fever cases driven by Paratyphi A have been reported to outnumber those mediated by Typhi in some settings in Asia, and concerns have been raised over the potential for Paratyphi A to replace Typhi following widespread immunisation. Therefore, an updated global understanding of Paratyphi A genotype and AMR frequencies, coupled with trends in transmission dynamics is urgently needed to inform control and intervention strategies, and provide key background data for understanding the impact of future interventions. Standardised, accessible software tools and computational workflows are also required for facilitating straight-forward routine analysis of future Paratyphi A WGS, including long-read Oxford Nanopore Technologies sequencing data.

METHODOLOGY

We have established a working group within the GTGC to draw together >90 researchers aggregating ~3000 WGS and associated standardised metadata that includes the purpose of sampling information. WGS data are being subjected to bioinformatic and phylodynamic analyses to characterise the sequences in terms of spatio-temporal distribution of lineages (genotypes) and molecular determinants of AMR, and to infer transmission dynamics at global and regional levels. Genotype and AMR frequencies will be reported for samples that are considered representative of their respective local epidemiological settings. Phylogenomic work will inform the improvement of existing genotyping frameworks such as Paratype, the accessibility of which will be enhanced using open-source Mykrobe and Pathogenwatch platforms.

RESULTS

Preliminary meta-analyses of publicly available published data have demonstrated a worrying AMR landscape including high levels of ciprofloxacin non-susceptibility observed in multiple genotypes circulating throughout South Asia and Southeast Asia. Heightened ciprofloxacin non-susceptibility mediated by the evolution of two mutations in the quinolone resistance determining region of gene *gyrA* is emerging in multiple genotypes from India and Pakistan, and co-resistance to both ciprofloxacin and azithromycin is emerging in genotypes 2.4.4 and 2.3.3 in Bangladesh. However, susceptibility to classical first-line drugs ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole appears to be widespread. Comparisons between locally collected genomes from within endemic settings and travel-associated genomes sequenced routinely by public health laboratories in high-income countries suggest that travel cases are a suitable means of sentinel surveillance for Paratyphi A genotypes (Pearson correlation 0.81,$p=2.14\times10^{-7}$) and AMR mutations (Pearson correlation 0.90,$p=6.1\times10^{-9}$) for pathogen populations circulating throughout Bangladesh, Cambodia, India, and Pakistan. Phylodynamic analyses are ongoing to elucidate the timeframes and frequencies of pathogen transmission between different settings.

CONCLUSIONS

This overview of the global distribution and spread of drug-resistant Paratyphi A will provide standardised, actionable data to inform public health policy, empirical treatment guidelines, and implementation of water, sanitation, and hygiene (WASH) interventions. These data will also inform the development of accessible software tools to facilitate future genomic epidemiology analyses without the need for high performance computing platforms or high-level bioinformatics expertise. We hope that this effort will encourage continued genomic data sharing for public health benefit.

Pan-Genome Clustering Reveals the Role of Prophage Elements in the Evolution and Adaptation of *Salmonella* Enteritidis

Jobin John Jacob, Christian Medical College, Vellore

Jobin John Jacob[1], Aravind V[1], Ramya I[1], Karthik G[1], Yesudoss M[1], Vasuki M[1], Jacob John[1], Kamini Walia[2], Balaji Veeraraghavan[1]

[1]Christian Medical College, Vellore, [2]Indian Council of Medical Research

BACKGROUND

Salmonella enterica serovar Enteritidis is a leading cause of bloodstream infections primarily in sub-Saharan African (sSA) countries. Although Typhoidal Salmonellosis has been well documented in South Asian countries, bloodstream infection (BSI) caused by non-typhoidal *Salmonella* serovars have received only less attention. In this study, the clinical

characteristics, phylogenetic placement, invasive potential and transmission dynamics of S. Enteritidis causing bloodstream infection (BSI) was analysed.

METHODS

A total of 101 S. Enteritidis clinical strains isolated from patients causing bloodstream infections (2012 – 2022) were accessed for collecting clinical data. Representative isolates of S. Enteritidis originating from other clinical samples (n=42) and livestock samples (n=17) were also included for comparative analysis. Study isolates were subjected to whole genome sequencing (WGS) using Illumina platform and population structure, invasive potential and transmission dynamics were studied by comparative genome analysis.

RESULTS

Clinical data of patients infected with S. Enteritidis suggests, infants and immunosuppressed are more susceptible to S. Enteritidis bloodstream infection. Phylogenetic analysis has clustered the isolates into four major lineages in which the majority of the study isolates from clinical samples were distributed in the newly emerging Asian cluster. Isolates distributed in the Asian cluster showed the second highest invasiveness index (median 0.221, SD= 0.013), following the West African cluster (median=0.253, SD=0.25). About 82% (n=14/17) of S. Enteritidis isolates sourced from poultry samples were clustered separately and not associated with the clinical isolates. Moreover, pan-genome clustering suggests the evolution of S. Enteritidis is largely driven by the acquisition of prophages.

DISCUSSION

Our data provide a contemporary insight into the dynamics of S. Enteritidis-associated BSI in India. Clinical characteristics, phylogenetic analysis, transmission dynamics, as well as the invasive potential suggest the continuing adaptation to this pathogen to cause extraintestinal infections.

Initial Immunogenicity and Safety Data From a First-In-Human Randomised Controlled Trial of an Invasive Non-Typhoidal *Salmonella* GMMA Vaccine: The SALVO Trial

Peter D Skidmore, Oxford Vaccine Group, NIHR Oxford Biomedical Research Centre, Department of Paediatrics, University of Oxford

Peter D Skidmore[1], Melanie Greenland[1], Kiarash Tanha[1], Brama Hanumunthadu[1], Tesfaye Demissie[1], Nelly Owino[1], Gareth Plested[1], Carla Ferreira Da Silva[1], Usman Nakakana[2], Daniele De Simone[2], Antonella Silvia Scire[2], Marta Benincasa[2], Chiara Crispino[2], Maria Grazia Aruta[2], Giulia Luna Cilio[3], Valentino Conti[2], Omar Rossi[2], Elizabeth A Clutterbuck[1], Rocio Canals[2], Maheshi N Ramasamy[1]

[1]Oxford Vaccine Group, NIHR Oxford Biomedical Research Centre, Department of Paediatrics, University of Oxford, [2]GSK Vaccines for Global Health (GVGH), Siena, 3GSK Biologicals SRL, Siena

BACKGROUND

Invasive non-typhoidal *Salmonella* (iNTS) disease is a global health concern, with an annual incidence of 51/100,000 people in sub-Saharan Africa. Young children and people living with human immunodeficiency virus are disproportionately affected. Over 90% of infections are caused by *Salmonella* enterica serovars Typhimurium and Enteritidis. An estimated case fatality rate of 15% and high rates of antimicrobial resistance make development of an effective vaccine a priority.

iNTS-GMMA is a bivalent vaccine based on Generalised Modules for Membrane Antigens (GMMA) technology and consists of outer membrane vesicles from genetically modified strains of S. Typhimurium and S. Enteritidis formulated with Alhydrogel.

METHODS

A first-in-human, phase 1, participant-observer blind, randomised clinical trial of the iNTS-GMMA vaccine was conducted at the University of Oxford, UK (ISRCTN51750695). Healthy adults aged 18-55 were randomised to receive placebo, low dose or full dose vaccine. Doses were administered intramuscularly at 0, 2 and 6 months, with participants followed up 6 months following third dose. The primary objective was safety and tolerability observed through recording of adverse events (AEs) and laboratory parameters. The secondary objective was determination of Immunoglobulin G (IgG) responses to serovar-specific O-antigen using enzyme-linked immunosorbent assays (ELISA). Exploratory analyses including serum bactericidal assays (SBA) were also performed. Blinded safety data for interim analysis were extracted on 7th September 2023. Immunogenicity data were available up to 28 days following second vaccination. All participants with available data were included in analyses. Follow-up is expected to complete in November 2023.

RESULTS

31 participants were randomised to receive placebo (n=12), low dose (n=4), or full dose (n=15) vaccine. The median age of participants was 27 years, 32% were female, and 87% were white. 24 participants received three doses of vaccine or placebo. Solicited AEs following each vaccination were mostly mild-to-moderate and transient. Two participants were not offered a third dose due to AEs (persistent neutropenia and a pronounced local reaction respectively). There were 59 unsolicited AEs, the majority (81%) of which had no relationship to the vaccine. No serious adverse events occurred.

IgG responses specific to S. Typhimurium O-antigen increased seven days following vaccination in the full dose group compared to baseline [day 7 geometric mean concentration (GMC) 187 EU/mL, 95% CI (64, 543)], baseline GMC 24 EU/mL, 95% CI (11, 54)]. At 28 days following first vaccination, full dose recipients demonstrated a higher IgG response [GMC 833 EU/mL, 95% CI (402, 1728)] compared to placebo recipients [GMC 41 EU/mL, 95% CI (18, 96)].

IgG responses following second dose were similar to those following first dose in the full dose group [GMC at 28 days post second dose 773 EU/mL, 95% CI (394, 1518)]. The same trends were observed in IgG responses against S. Enteritidis O-antigen.

SBA titres against S. Typhimurium 28 days following first vaccination increased for full dose recipients [IC50 geometric mean titres (GMT) 29989, 95% CI (18529, 48538)] compared to placebo [IC50 GMT 6694, 95% CI (2742, 16344)]. This pattern was also seen at 28 days following second vaccination [full dose IC50 GMT 27759, 95% CI (18224, 42281), and placebo IC50 GMT 6216, 95% CI (2798, 13807)]. Trends in SBA titres against S. Enteritidis were similar.

CONCLUSIONS

In this first-in-human trial, the iNTS-GMMA vaccine was well-tolerated at both low and full doses. The vaccine elicited antibodies against both targeted *Salmonella* serovars. Data regarding safety following third vaccination and antibody persistence to one year will be available in 2024, but this interim analysis supports further development of a promising vaccine.

Forecasting iNTS for the Global Burden of Disease Study

Jeffrey Stanaway, The Institute for Health Metrics and Evaluation, University of Washington

Jeffrey Stanaway

The Institute for Health Metrics and Evaluation, University of Washington

BACKGROUND

Between diarrhea, typhoid and paratyphoid fevers, and invasive non-typhoidal *salmonella* disease (iNTS), *Salmonella* infections were responsible for 290,000 deaths and 21.4 million DALYs globally in 2019. Given this large burden, a broad *Salmonella* vaccine could offer a cost-effective tool to improve public health; and, consequently, funders, scientists, and policy makers are exploring this idea. Fully understanding the potential future benefits, however, requires reliable forecasts of future burden. While the Global Burden of Disease (GBD) Future Health Scenarios project has produced robust forecasts of typhoid, paratyphoid, and diarrheal *salmonella* burden, the project's forecasting framework is less well suited to forecasting iNTS, given its complex historical trends and broader range of risk factors. This study builds on our work estimating iNTS burden for the GBD study, and the work of the Future Health Scenarios project, developing a bespoke framework to produce globally comprehensive forecasts of iNTS incidence, mortality, and burden, including 95% uncertainty intervals, for all GBD locations and demographic groups, for the years 2020 through 2100.

METHODS

We forecasted iNTS incidence using shape constrained additive models and data from the GBD study. We selected the final model from a collection of candidate models that varied in their predictive covariates and shape flexibility based on out-of-sample predictive performance in rolling basis cross-validation. The final model included fixed effects on HIV mortality, malaria mortality, water supply, sanitation, hygiene, socio-demographic index, age, and sex, with random effects on location. We used GBD estimates and Future Health Scenario estimates for past and future values of covariates, respectively. We then forecasted HIV attributable fractions, case fatality, mortality, and gap metrics including disability adjusted life-years (DALYs) following our approach for the GBD study. Our final outputs include estimates of iNTS incidence, mortality, and gap metrics, by country, age, sex, and year through 2100. Finally, we produced R code that allows users to develop iNTS forecasts from user-defined scenarios.

RESULTS

We estimate that global iNTS cases will decline 64.9% by the end of the century, from 568.9 (462.2 – 700.7) thousand cases in 2020 to 199.7 (121.4 – 310.8) thousand cases in 2100, and that age-standardized incidence rates will decline 56.4% from 8.10 (6.53 – 10.0) per 100,000 to 3.53 (2.23 – 5.55) per 100,000 in that same period. In the highest burden super-region, sub-Saharan Africa, we estimate an 81.9% decline in age-standardized incidence, with population grown effecting a more modest 63.5% decline in the absolute number of cases by the end of the century. Globally, estimates of case fatality decline from 14.0% in 2020 to 9.4% in 2100, and with declines in both incidence and case fatality, we estimate that iNTS deaths will decline by 76.4%, from 79.4 (46.5 – 127.3) thousand in 2020 to 18.8 (8.1 – 39.8) thousand in 2100.

DISCUSSION

To our knowledge, these are the first-ever globally comprehensive, purpose-built iNTS forecasts to 2100. Our estimates suggest steep declines in iNTS burden across all regions through the end of the century, though with regard to the absolute number of cases, declines in incidence rates will be partially offset by changes in the global population distribution: as we project continued population growth in sub-Saharan Africa combined with stagnant or declining population sizes elsewhere, we expect an increasing proportion of the global population will live in relatively higher burden locations. Our results should provide critical insights for funders and planners, and our scenario-based forecasting code should provide additional utility in evaluating multiple potential interventions.

Unmasking Typhoid Vaccine Hesitancy: A Study of Myths Surrounding TCV in Immunisation Programs within Refugee Communities in Southwestern Uganda

Muhumuza Umar, Africa Centers for Disease Control

Muhumuza Umar, Eleleta Surafel Abay

Africa Centers for Disease Control

BACKGROUND

The purpose of this research was to address Typhoid Conjugate Vaccine (TCV) hesitancy within refugee communities located in Southwestern Uganda. The objective was to investigate and mitigate the myths and misconceptions surrounding TCV, with the aim of improving vaccination rates and reducing the burden of typhoid fever within these vulnerable populations.

METHODS

This study, conducted over a period of six months, involved 500 participants within refugee settlements in Southwestern Uganda. We employed a mixed-methods research design, integrating quantitative and qualitative approaches. The study population consisted of both refugee community members and healthcare providers who met the inclusion criteria of residing within the selected refugee settlements. Data collection techniques included structured surveys, in-depth interviews, and focus group discussions.

RESULTS

The research yielded insightful findings. Prior to the intervention, only 40% of the surveyed population expressed willingness to receive the TCV. Concerns about the vaccine's safety, efficacy, and potential side effects were prominent, with 75% expressing such concerns. However, following targeted educational interventions, vaccine acceptance rates increased significantly to 80% ($p < 0.001$), demonstrating a substantial shift in attitudes.

CONCLUSIONS

These results hold significant implications for public health efforts within refugee communities in Southwestern Uganda. The statistically significant increase in vaccine acceptance rates underscores the effectiveness of tailored educational strategies. Moreover, the reduction in concerns related to vaccine safety and efficacy indicates the potential to address misconceptions effectively.

This research program highlights the critical role of addressing vaccine hesitancy in enhancing TCV adoption among refugee communities. The statistically significant change in attitudes and the substantial increase in vaccine acceptance rates demonstrate the tangible impact of targeted education. Such interventions not only contribute to mitigating typhoid within refugee settings but also offer a model for addressing vaccine hesitancy in other infectious disease contexts.

Bacterial Profile of Suspected Typhoid Intestinal Perforation Cases, Regional Hospital Centre, Maradi, Niger

Maman Laminou Sani, Regional Hospital Centre, Maradi

Maman Laminou Sani[1], Boubacar Moctar[1], Mohamadou Sidi Rahidou[1], Rouga Mohamed Moumoune[1], Dicko Daouda[1], Mohamed Boukari Abba[1], Abdoulaye Maman Bachir[2], Adakal Ousseini[3], Issaka Soumana[4]

[1]Regional Hospital Centre, Maradi, [2]Université Dan Dicko Dan Clodo De Maradi, [3]Université Dan Dicko Dan Clodo de Maradi, [4]Epicentre Maradi

INTRODUCTION

Typhoid fever remains a major health crisis in Niger. Due to delays in accessing healthcare, particularly in rural settings, patients may present with late-stage complications such as typhoid intestinal perforation (TIP). Although TIP has a pathognomonic surgical finding of an oval anti-mesenteric perforation, commonly in the distal ileum, blood culture confirmation, the gold standard in diagnosing typhoid, is rare. This study is the first in Niger to describe the bacterial profile of TIP, along with its antimicrobial resistance patterns.

METHODS

This study was conducted at the Regional Hospital Centre of Maradi (CHR Maradi), Niger. Between October–November 2022, we collected blood specimens from patients younger than 15 years of age who presented with suspected TIP and required surgery. Blood was sent to Epicentre for culture and sensitivity testing, using E-testing for quinolones and disc diffusion for all other antibiotics tested.

RESULTS

In total, 50 blood cultures were collected, 18 (36%) samples were positive for bacteria. Among the positive blood cultures, 8 (44%) were *Salmonella* Typhi (*S.* Typhi), 4 (22%) were *Escherichia coli* (*E. Coli*), and 3 (16%) were nontyphoidal *Salmonella*. Antimicrobial resistance testing showed *S.* Typhi isolates were resistant to ciprofloxacin, ampicillin, and cotrimoxazole. Additionally, all *S.* Typhi specimens remained sensitive to ceftriaxone and meropenem. All E. coli strains were resistant to ceftriaxone and piperacillin/tazobactam and pan-sensitive to carbapenems and amikacin.

CONCLUSION

In this study, 16% of suspected TIP patients had typhoid blood culture confirmation, consistent with the positive culture rates of 10–15% reported in the literature. The antimicrobial results represent a worrying trend in the development of antimicrobial resistance in the region and demonstrates typhoid quinolone resistance in Niger. These data should inform antibiotic choice for outpatient treatment of febrile illness in children, and support interventions such as improved water, hygiene, and sanitation and the introduction of the highly efficacious single dose typhoid conjugate vaccine — to prevent typhoid fever and its complications.

Impact of TCV Introduction on Ileal Perforations in Pakistan: A Comparative Analysis

Huma Syed Hussain, Aga Khan University

Huma Syed Hussain, Tahir Yousafzai, Farah Qamar

Aga Khan University Hospital

BACKGROUND

Ileal perforation, a complication of typhoid fever, has been noted in 0.8% to 39% of typhoid cases, majority in lower and middle-income countries. We aim to compare the incidence of typhoid related ileal perforation prior to and following the introduction of the typhoid conjugate vaccine (TCV) in Pakistan's Expanded Programme on Immunization (EPI).

METHODS

We gathered data on ileal perforation cases from two surveillance studies: the Surveillance of Enteric Fever in Asia Project (SEAP), which had enrollments three times per week from four Karachi tertiary hospitals between September 2016 and September 2019, and the "Impact assessment of the Typhoid conjugate vaccine following introduction in the Routine Immunization Program of Pakistan" (ITRIPP) study, which had daily enrollments from three Karachi tertiary care hospitals between March 2022 and August 2023. Trained research staff collected sociodemographic, clinical, and outcome data from medical records, along with available tissue samples for histopathology and blood cultures.

RESULTS

Ileal perforation cases enrolled pre-TCV were 242, and post-TCV were 374, with 10 cases having received TCV. Pre-TCV, 48% (117/242) of cases were aged <15 years, and 52% (125/242) were aged >15 years. Post-TCV, 25% (95/374) were <15 years, and 75% (279/374) were >15 years. Males were predominantly affected both pre-TCV 74.9% (180/242) and post-TCV 82% (308/374). In the pre-TCV study, among 86 patients, tissue cultures detected 3% XDR S. Typhi, and histopathology found ileal perforation with necrosis in 5%. Blood cultures in 76 cases revealed 11% (8/76) positive for XDR S. Typhi. The mortality rate was 7% (16/242). In the post-TCV study, out of 283 patients, histopathology identified ileal perforation with necrosis in 7% of cases. Among 336 cases that underwent blood cultures, 7% (25/336) tested positive for S. Typhi, with 2 cases indicating XDR infection. The overall mortality rate was 11% (40/374), with the majority 78% of deaths in the >15 years age group.

CONCLUSION

Post-TCV introduction, ileal perforations were primarily observed in individuals aged over 15 years, which is noteworthy given that TCV is administered to individuals under 15 years of age.

15:45–16:15 Coffee Break & Poster Viewing — FOYER

16:15–17:15 Forging a Path Forward: The Roadmap to Expand Solutions and Catalyze Change

KILIMANJARO BALLROOM

CLOSING PLENARY MODERATED BY:
Robert F. Breiman, Emory University
& Eunice Ubomba-Jaswa, Water Research Commission

In concluding this conference, our objective is to leave participants not only informed but also empowered to continue the vital work in the ongoing battle against typhoid and iNTS. Join us in the closing plenary, where we will embark on a compelling exploration of the pathways leading to impactful solutions. Speakers will share valuable insights into collaborative approaches, data-driven solutions, and global perspectives, all contributing to our collective mission. This session is crafted to inspire and equip attendees with the knowledge and tools essential for forging a lasting impact in the global fight against typhoid and iNTS, setting the course for a brighter and healthier future.

Charting a Comprehensive and Innovative Path to Fight Typhoid and Invasive Salmonelloses: The Importance of Multi-Sectorial Collaboration, Resource Mobilization, Health Systems Strengthening and Political Will
Robert Agyarko, African Risk Capacity

From Data to Action: Leveraging Existing Primary Healthcare Systems for Solutions
Samba Sow, Center for Vaccine Development

Accelerating the Fight Against Invasive *Salmonella* Diseases: Perspectives From WHO
Adwoa Benti-Enchill, World Health Organization

Looking Ahead — What Do We Need for Successful Enteric Fever Control?
Duncan Steele, Bill & Melinda Gates Foundation

Discussion

17:15–17:30 Closing Session

KILIMANJARO BALLROOM

Closing Remarks

Meeting Adjournment
Denise Garrett, Sabin Vaccine Institute,
& Anuradha Gupta, Sabin Vaccine Institute

SPEAKER & MODERATOR BIOS

DILIP ABRAHAM

Christian Medical College, Vellore

Dilip Abraham is a clinical microbiologist and has been working in The Wellcome Trust Research Laboratory since 2017. He completed his undergraduate degree in medicine from Govt. Medical College, Thiruvananthapuram and an M.D. in Medical Microbiology from Christian Medical College, Ludhiana. He also holds a Diploma in Tropical Medicine and Hygiene (DTM&H) from the Royal College of Physicians, London having completed the qualifying course in Global Health and Humanitarian Medicine (GHHM) by Medecins Sans Frontieres.

His current role is as an Associate Professor of Microbiology at the WTRL, Christian Medical College, Vellore, and has expertise in microbiology, bioinformatics, molecular diagnostic techniques, and genomic sequencing for infectious diseases. His research projects have included environmental and clinical surveillance of infectious diseases including *S.* Typhi, poliovirus, and helminth infections; development of molecular diagnostic assays for parasitic diseases and multi-pathogen detection; role of the environmental niches of *S.* Typhi as an endosymbiont within Acanthamoeba in the environment; and the evaluation of the impact of enteric infections and gut microbiota on oral vaccine efficacy and autoimmune diseases (e.g. Crohn's). He has collaborated with public health physicians at CMC Vellore to better understand household and environmental transmission of *S.* Typhi, and he is currently funded to standardize methods of and models of multi-pathogen detection from wastewater and perform environmental surveillance of *S.* Typhi during the Vellore Typhoid Impact Trial to assess changes in *S.* Typhi incidence over time and TCV impact.

Additionally, he works in the diagnostic parasitology laboratory at the Wellcome Trust Research Laboratory and is also involved in teaching undergraduate students in the medical school. He has also been engaged in optimizing molecular assays for the detection of Toxoplasma and Acanthamoeba in clinical samples.

KELVIN ABUGA

KEMRI-Wellcome Trust Research Programme

Kelvin Abuga is a PhD student at the KEMRI-Wellcome Trust and is funded by a Wellcome International Training fellowship. Kelvin has a background in immunology of infectious diseases. He is interested in understanding the interplay between anaemia/iron deficiency, immunity, and tropical infectious diseases. His doctoral work is on "the mechanisms underlying the relationship between severe anaemia and invasive bacterial infections in Kenyan children", and is supervised by Prof Sarah Atkinson, Dr. Manfred Nairz and Prof Calman MacLennan.

AMANI ADIDJA

World Health Organization Regional Office for Africa

Dr. Amani Adidja is a Senior public health physician, vaccinologist, and university lecturer/researcher with over 16 years of extensive experience. Currently serving as the Regional New Vaccines Introduction Medical Officer for WHO AFRO, she plays a vital role in driving new vaccine initiatives and combating vaccine preventable diseases across the 47 African member states.

In her capacity, Dr. Adidja is instrumental in norm and standard development, providing monitoring and evaluation guidance, and coordinating the introduction of new and underutilized vaccines, including Malaria Vaccines, TCV, and upcoming vaccines. Her distinguished career includes significant contributions during the COVID-19 pandemic, earning recognition and awards. She has also held leadership roles within the Government of Cameroon and in international non-governmental organizations (INGOs) in sub-Saharan Africa.

Academically accomplished, Dr. Adidja is a Fulbright Scholar and Mandela Washington Fellow. She holds degrees from Boston University, Virginia Commonwealth University, Georgia State University in the US, and the University di Siena in Italy. Her expertise is further demonstrated through numerous publications.

ROBERT DEGRAFT KWAME AGYARKO

African Risk Capacity

Robert deGraft Kwame Agyarko is a Global Health and International Development Expert with 25 years of experience. He joined the African Risk Capacity (ARC) in 2016 from the WHO/AFRO's Health Security and Emergencies. He is currently ARC's Lead Advisor for Disease Outbreaks and Epidemics; he has previously held other leadership roles in WHO-AFRO, GFATM, ALMA and UNICEF. Robert has provided strategic guidance and technical support to over 20 African countries in disease management and control of communicable diseases, such as Malaria and HIV/AIDS, and emerging and re-emerging infectious diseases.

In 2015 he served as the Coordinator of the Ghana Public Health Emergency Operations Centre and Technical Advisor to the Deputy Minister of Health. He holds two Master's degrees, one in Global Public Health from Queen Mary University of London, UK and another in Development Studies (Rural) from the University of Sussex, UK. He also undertook a certificate course in epidemiology and biostatistics at the Johns Hopkins Bloomberg School of Public Health.

Robert is a Chevening Scholar, an ex-Independent Study Fellow of the Institute of Development Studies (IDS, UK), an Aspen Senior New Voices Fellow, a member of the WHO Technical Advisory Group for Universal Health and Preparedness Review (UHPR) and a member of the Technical Review Committee for The Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM).

KRISTEN AIEMJOY

University of California Davis & Mahidol University Faculty of Tropical Medicine

Dr. Kristen Aiemjoy is an Assistant Professor of Epidemiology at the University of California Davis School of Medicine, and an adjunct assistant professor in the Department of immunology and Microbiology at Mahidol University in Bangkok, Thailand. Her research centers on measurement, surveillance, and diagnostics for infectious diseases with a focus on seroepidemiologic methods to understand the force of infection in populations.

ROCIO CANALS ALVAREZ

GSK Vaccines Institute for Global Health

Rocio Canals is the Project Leader for invasive nontyphoidal salmonellosis (iNTS) at GSK Vaccines Institute for Global Health (GVGH) in Siena (Italy) since October 2019. During this time, she has been leading preclinical studies and transition to clinical development of a GMMA-based candidate vaccine against iNTS, iNTS-GMMA, and a trivalent *Salmonella* candidate vaccine against iNTS and typhoid fever, iNTS-TCV. She has extensive expertise in the causative agents of iNTS after having spent the previous 6.5 years before joining GVGH at the University of Liverpool (UK) studying the molecular mechanisms involved in the pathogenesis of *Salmonella* strains causing iNTS in sub-Saharan Africa. Prior to that, she worked in a reference *Salmonella* laboratory in San Diego (USA) for five years, studying *Salmonella* enterica functional genomics of several serovars including Typhimurium, Enteritidis and Typhi. Before moving to the USA, she was post-doctoral fellow at the University of Naples Federico II (Italy), characterizing the chemical structure of cell surface polysaccharides from several bacterial species. She received her Ph.D. from the University of Barcelona (Spain) in 2007 after studying molecular mechanisms of bacterial virulence factors.

SOJUNG AN

International Vaccine Institute

SoJung An has been working for Vaccine Process Development section at International Vaccine Institute (IVI) in South Korea from 2005 to present. She received her PhD in 2012 in Bioengineering from Seoul National University, South Korea and worked as a visiting fellow from 2014 to 2016 in Dr. Patrick Duffy's lab (Lab of Malaria Immunology and Vaccinology) in National Institute of Allergy and Infectious Diseases (NIAID) of National Institute of Health USA.

She has worked on Vi-DT typhoid conjugate vaccine development and has played lead roles in the optimization of Vi-DT conjugation process and technology transfer to vaccine manufacturers. She has been also involving early-stage and process development of conjugate vaccine for pneumococcal conjugate vaccine, Hib PRP conjugate, iNTS conjugates, *Salmonella* paratyphi A OSP conjugate and bivalent typhoid-malaria conjugate vaccine. Recently, she received the Korean Health and Welfare Minister's Prize for her contributions to the vaccine development and technology transfer to vaccine manufacturers (SK bioscience, PT Biofarma, etc) of IVI's Vi-DT typhoid conjugate vaccine.

JASON ANDREWS

Stanford University School of Medicine

Jason Andrews is a physician and Associate Professor in the Division of Infectious Diseases and Geographic Medicine at Stanford.

ZAHIDA AZIZULLAH

Aga Khan University

Zahida Azizullah is currently a Research Specialist at the Aga Khan University Karachi, Pakistan at the Dept of Pathology & Laboratory Medicine. Beginning a career as a Laboratory technologist she joined Aga Khan University as Research Associate in 2012. With an experience of ten years in research, she has been part of various research studies which include the utility of the microcolony method for MDR TB patients in Karachi, a prospective prevalence study for Arboviruses in the Sindh region of Pakistan, a multicountry MDR TB project focusing on Bedaquiline drug resistance in the populations, COVID-19 variant detection study and evaluation studies for typhoid and dengue diseases using rapid diagnostic testing kits, and addressing the conflict of interest driving irrational prescribing of medicines in pluralistic health systems which is an interventional study in Pakistan. She has also co-authored several publications to her name. She holds a BSc (Hons), MSc in Microbiology and most recently completed her second Masters in Health Policy & Management from Aga Khan University.

RABAB BATOOL

Aga Khan University

Rabab is an esteemed epidemiologist and public health researcher, holds a faculty position at Aga Khan University Hospital in Pakistan. Currently a PhD candidate at Tampere University Finland, her research is at the forefront of crucial areas such as vaccine effectiveness, implementation strategies, and pediatric infectious diseases, with a particular focus on Typhoid Conjugate Vaccine impact assessment. Driven by an unwavering commitment, her goal is to make impactful contributions in the dynamic fields of vaccine-preventable diseases and AMR in LMICs.

OYENIYI STEPHEN BEJIDE

Chrisland University

Oyeniyi Stephen Bejide earned a B.Sc in Microbiology from University of Abuja, a Master's degree in Environmental Microbiology from University of Ibadan (both in Nigeria) and is a doctoral student of Pharmaceutical Microbiology from the same Institution. In addition, he has a host of other exposures to relevant courses and trainings spanning across the fields of clinical microbiology, public health and biotechnology. He is a member of some learned societies including BactiVac Network, African Society for Laboratory Medicine and American Society for Microbiology. He has volunteered for and led campaigns organized and supported by international organizations including the Royal Society of Biology, United Kingdom and World Health Organization such as the World Antimicrobial Awareness Week Campaign (2018 till date). He was a contributor to Nigeria's National Action Plan for Antimicrobial Resistance (2017-2022), an initiative of Nigeria Centre for Disease Control. He was a Fellow at the 21st International Vaccinology course of International Vaccine Institute (IVI), South Korea (2022). He has about five years experience as the biological scientist of Severe Typhoid in Africa Plus Project (Nigerian node) coordinated by IVI where he performed molecular biology operations, trained people on those operations and led a research subgroup. He is currently a lecturer at Chrisland University, Abeokuta, Nigeria where he teaches Microbiology, and coordinates research activities.

ADWOA BENTSI-ENCHILL

World Health Organization

Dr. Adwoa Bentsi-Enchill is a medical epidemiologist in the Department of Immunization, Vaccines and Biologicals of the World Health Organization, Geneva. Adwoa has over 25 years expertise in public health with a focus on vaccine preventable diseases. At WHO she has worked primarily on immunization safety and vaccines against typhoid and other invasive salmonelloses. She led the last revision of the global policy on typhoid vaccines (2017) including the first ever recommendations for typhoid conjugate vaccine use in endemic countries. She has had significant experience collaborating with key global stakeholders as well as providing technical support to several countries across WHO's six regions. Adwoa has an MBChB from the Kwame Nkrumah University of Science and Technology (Ghana) and an MSc (Epidemiology) from the University of Ottawa (Canada). Prior to joining WHO, Dr. Bentsi-Enchill worked as a physician in Ghana, and later as an epidemiologist in the Immunization Division of the Laboratory Centre for Disease Control, Health Canada (now Public Health Agency of Canada).

NAVNEET BICHHA

Indian Institute of Health Management Research

Dr. Navneet Bichha is a physician scientist from Nepal and currently a post graduate fellow in implementation research under the WHO/TDR with a wide range of experience in the field of clinical medicine, infectious disease surveillance and Phase 3 randomized control trials for vaccine and drug development in Nepal.

Dr. Navneet Bichha has served as an investigator for in conducting and strengthening capacity Phase 3 randomized clinical trial in Nepal for the typhoid conjugate vaccine, cholera vaccines and COVID-19 vaccines in Nepal for more than three years under the collaboration of international partners such as the International Vaccine Institute, South Korean Biosciences, Sanofi Pasteur and Glaxo Smith Kline.

Dr. Navneet has also been instrumental in the introduction and implementation of typhoid conjugate vaccine and COVID-19 vaccine in Nepal with the support of Ministry of Health and Population, Nepal.

His key interest lies in conducting clinical and implementation-based research and intervention focused on vaccine preventable disease, neglected tropical diseases and antimicrobial resistance.

JULIE BINES

University of Melbourne

Professor Julie Bines is Professor of Paediatrics at the University of Melbourne, a Paediatric Gastroenterologist at the Royal Children's Hospital Melbourne and leads the Enteric Disease Group at Murdoch Childrens Research Institute.

Julie has led the development of the human neonatal rotavirus vaccine, RV3-BB vaccine, aimed at preventing rotavirus disease from birth in infants worldwide, including the clinical trials of RV3-BB vaccine in Australia, New Zealand, Indonesia and Malawi. Julie is Director of the WHO Collaborative Centre for Child Health and the WHO Rotavirus Regional Reference Laboratory for the Western Pacific Region and is a member of the WHO Expert Advisory Committee for Vaccines to address AMR.

ROBERT F. BREIMAN

Emory University

Dr. Robert F. Breiman is Professor of Global Health, Environmental Health, and Infectious Diseases at Emory's Rollins School of Public Health and School of Medicine. Dr Breiman's primary areas of research have been related to addressing inequities with focus on child mortality, urbanization in impoverished settings, and a range of respiratory and enteric diseases, as well as a variety of emerging infectious diseases. In addition to his research, he is currently working on translating global health work to increase public awareness and engagement. He is PI of the CDC-funded project on SARS-CoV vaccine messaging, called COVID Vaccines Information Equity and Demand creation (COVIED) with partners at Emory, Johns Hopkins University, Morehouse School of Medicine, Georgia College--Rural Studies Institute, the National Association of Community Health Centers (NACHC), the Black Cross and Riwi. He is co-PI of the NIH-funded Centers for Research on Emerging Infectious Diseases in East and Central Africa (CREID-ECA) in collaboration with Washington State University, RTI, KEMRI and others. He is PI of a new grant funded by the Bill and Melinda Gates Foundation to support Typhoid Fever burden of disease studies and policies, working with WHO, IVI, Sabin Vaccine Institute, Christian Medical College in Vellore.

MEGAN E. CAREY

International AIDS Vaccine Initiative and London School of Hygiene & Tropical Medicine

Megan E. Carey, PhD, MSPH, is an infectious diseases epidemiologist and public health policy expert. Her primary research interests include the translation of epidemiological evidence to policy and the impact of vaccines on antimicrobial resistance (AMR).

Megan recently joined IAVI as an Associate Director, where she is leading the development of a new AMR strategy. Megan is also a Postdoctoral Policy Fellow at the London School of Hygiene & Tropical Medicine as part of the AMRnet project, which is focused on the development and application of genomic data visualization tools to inform public health action. Megan received a PhD from the University of Cambridge, where she focused on policy applications for *Salmonella* Typhi (*S.* Typhi) genomic data. Megan has also consulted for the World Health Organization, where she established the typhoid conjugate vaccine (TCV) research agenda, developed a framework for measuring the impact of vaccines on AMR, and presented an update on TCVs to SAGE. Megan also co-founded the Global Typhoid Genomics Consortium, which aims to aggregate, analyze, and visualize *S.* Typhi genomic data to

monitor the emergence and spread of AMR to inform public health interventions.

Previously, Megan worked at the Bill & Melinda Gates Foundation on the Enteric & Diarrheal Disease team, where she managed a large portfolio of grants focused on typhoid, rotavirus, and cholera control. Megan has a Master of Science in Public Health from the Johns Hopkins Bloomberg School of Public Health, specializing in Global Disease Epidemiology and Control and Vaccine Science and Policy. Megan studied Government at Harvard College, with a focus on International Relations and Economics.

SUPARNA CHAKRABORTY

National Institute of Cholera and Enteric Diseases

Suparna Chakraborty was born in Kolkata, India and spent her growing years in the city of joy. She completed her schooling in 2011 from Kolkata and B.Sc Microbiology from University of Calcutta in 2014. After that, she moved to the peaceful coastal city of Puducherry in India, where she studied at Pondicherry University and was awarded with the gold medal and the degree of M.Sc in Microbiology in 2016. Suparna stepped into research officially after joining the PhD program at National Institute of Cholera and Enteric Diseases (ICMR-NICED) with DST-INSPIRE fellowship. Currently she works with S. Typhi and S. Paratyphi A, etiological agent of typhoid and paratyphoid infection. Her study focuses on the adaptive immune responses after mucosal immunizations with *Salmonella* antigens. Simultaneous development of suitable animal model for understanding Paratyphoid infection is another of her research spectrum. She has published research article, review article and also a book chapter. She also applied for two patents. She has participated in several international conferences to present her research work and exchange pertinent scientific conceptual aspects. In addition to her academic pursuits, she is an avid reader who seeks solace in the lap of nature and finds pleasure in singing.

RICHELLE C. CHARLES

Massachusetts General Hospital-Harvard University

Richelle C. Charles, MD, FIDSA, is a physician-investigator funded by the National Institutes of Health and the Bill & Melinda Gates Foundation. Her research lab is part of multicenter collaborative efforts focused on broadening our understanding of host-pathogen and immune responses during human infection and vaccination, primarily focused on Vibrio cholerae (the cause of cholera) and *Salmonella* enterica serovar Typhi (the primary causes of enteric fever).

WILBUR CHEN

Center for Vaccine Development, University of Maryland School of Medicine

Dr. Wilbur Chen is an infectious disease physician-scientist and the Frank M. Calia, M.D. Endowed Professor of Medicine at the University of Maryland School of Medicine. He is Chief of the Adult Clinical Studies section within the Center for Vaccine Development and Global Health and Director of the UMB Travel Medicine Practice. His research is primarily focused on developing vaccines for enteric pathogens, infectious diseases chiefly of resource poor and economically disadvantaged countries and populations with poor access to clean water, hygiene, and sanitation.

To facilitate his research, Dr. Chen conducts human experimental challenge studies, closely monitored infections with well-characterized pathogens, to gain new insights into pathogenesis, the human immune response, or early efficacy of candidate vaccines or therapeutics. He is an active investigator within the NIAID-supported Vaccine and Treatment Evaluation Unit (VTEU) network, composed of 10 academic centers throughout the U.S. In the past 10 years he has been involved in the planning and conduct of challenge models which include: ETEC, cholera, *Shigella*, *Campylobacter*, norovirus, *Cryptosporidium*, and influenza. Dr. Chen personally holds FDA INDs for wild-type *V. cholerae* and enterotoxigenic *E. coli* (ETEC) challenge agents.

Dr. Chen serves on a number of advisory capacities, including as voting member of the CDC's Advisory Committee on Immunization Practices (ACIP), core member of NIAID's Data and Safety Monitoring Board, steering committee member of Defense Health Agency's Military Infectious Disease Research Program, and was a member of State of Maryland Governor Larry Hogan's COVID-19 Task Force.

MIKE CHISEMA

Malawi Ministry of Health

Dr. Mike Chisema has been with the Malawi Ministry of Health since 2006, where he is currently serving as Deputy Director of Preventive Health Services responsible for National Immunization Program-EPI Program Manager. Prior to this position, Dr. Chisema occupied the various positions at a district-level, which included posts like Assistant Environmental Health Officer for Blantyre District Council-Health Sector, District Medical Officer for Dedza District and Director of health and Social Services-Ntcheu District Council. Mike is also an accomplished operational researcher contributing to the pool of knowledge in workable health interventions and new innovations in health service deliveries.

BRÁULIO ROBERTO GONÇALVES MARINHO COUTO

Biobyte Sistemas Ltda

Bráulio Roberto Gonçalves Marinho Couto has a PhD in Bioinformatics, Computer Science MS Degree. Specialization in Statistics, Bachelor of Science in Chemical Engineering. He is Innovation Director of Biobyte Epidemiology Technology. His publication highlights: In Silico Modeling by Causal Inference for Identifying Biomarkers of Sepsis; Optimizing Empiric Antibiotic Therapy: A Probabilistic Approach; Prediction of Bloodstream Infection Events and Infections of the Lower Respiratory; Tract in ICU Patients: Expected and Unexpected Infections; Mathematical Modeling of COVID 19 Transmission by a k Phases SEIR Model; COVID 19 Normality Rate: Criteria for Optimal Time to Return to In Person Learning; Artificial Neural Networks to Predict Infection in the Surgical Site in Patients over 70 Years Old; Cobweb Chart for Infection Rates, Infectometer, and Outbreak Alert System: Real Time; Systems for Summarizing Nosocomial Data; A Predictive Model for the Prompt Identification of Suspected Sepsis Patients with High Death Risk; and Using Ozires, a Humanoid Robot, to Continuing Education of Healthcare Workers: A Pilot Study.

JOHN A. CRUMP

University of Otago

John Crump is Professor of Medicine, Pathology, and Global Health and Co-Director, Centre for International Health, University of Otago; Adjunct Professor of Medicine, Pathology, and Global Health at Duke University; and Guest Researcher, National Center for Emerging and Zoonotic Infectious Diseases, U.S. Centers for Disease Control and Prevention. He graduated from the University of Otago Medical School in 1993 and trained as both an internist in infectious diseases and as a pathologist in medical microbiology, training at Christchurch Hospital, New Zealand; the Royal Free Hospital, London; the Canberra Hospital, Australia; Duke University Medical Center; and with the U.S. Centers for Disease Control and Prevention. He is a Fellow of the Royal Australasian College of Physicians, a Fellow of the Royal College of Pathologists of Australasia, a Fellow of the Royal College of Physicians of the United Kingdom, and a diplomate of the London School of Hygiene & Tropical Medicine. He led a large research and service collaboration with Kilimanjaro Christian Medical Centre, Moshi, Tanzania, for 10 years. His main interests are in the prevention, diagnosis, and treatment of infectious diseases in low-resource areas, with particular focus on febrile illness; invasive bacterial diseases especially the salmonelloses; bacterial zoonoses; and enteric infections. He also works ethics issues in global health, including for global health training.

HELEN DALE

University of Liverpool

Helen is a Wellcome Clinical PhD Fellow at the University of Liverpool and the Malawi-Liverpool Wellcome Research Program. She is completing her Paediatric Doctor training at Sheffield Childrens Hospital. Her PhD focuses on the seroepidemiology and population sero-correlates of immunity to invasive non-typhoidal *Salmonella*, in children in endemic settings. Her work is based in Malawi and in collaboration with other sub-Saharan African sites.

ZOE ANNE DYSON

London School of Hygiene & Tropical Medicine

Dr. Zoe Anne Dyson is an Assistant Professor of Pathogen Genomics at the London School of Hygiene & Tropical Medicine and a co-coordinator and co-founder of the Global Typhoid Genomics Consortium. Zoe's research programme specialises in applying bioinformatic analysis techniques to whole genome sequencing data from typhoidal *Salmonella* to infer transmission dynamics and the evolution of antimicrobial resistance.

RACHES ELLA

Bharat Biotech

Dr. Ella is the Chief Development Officer at Bharat Biotech. He leads Bharat's Global Product Development division focused on discovery and clinical development for vaccines and therapeutics. Raches also oversees medical, safety, and regulatory support for the entire pipeline, and external science and innovation. He is a physician by training, with an M.S in clinical research at Emory University. Following his post-doctoral fellowship at Johns Hopkins, he completed his MBA at Harvard Business School.

NICHOLAS FEASEY

Liverpool School
of Tropical Medicine

Nicholas Feasey is an Infectious Diseases physician and clinical microbiologist, who has worked for the Liverpool School of Tropical Medicine since 2009 as a Professor of Microbiology and who was recently appointed Sir James Black Professor of Infection Medicine at the University of St Andrews. Until July, he was based at the Malawi Liverpool Wellcome Programme in Blantyre, Malawi. His research is focused on the surveillance and management of antimicrobial resistant bacterial infection, and taking a one health approach to exploring the transmission of enteric pathogens associated with invasive disease. His research group uses bacterial genomics, spatial statistics and transmission modelling in collaboration with Nick Thomson at the Wellcome Sanger Institute and Chris Jewell at the School of Mathematics and Statistics at the University of Lancaster.

FREDERICK FELL

University of Oxford

Frederick Fell is a data analyst and researcher on the Global Research on Antimicrobial Resistance (GRAM) project. Since he joined in 2019 he has worked on several systematic reviews and collected, processed and analysed data on different pathogens within the project. His primary focus has been to research antimicrobial resistance in invasive Non-typhoidal *Salmonella*.

Frederick had previously studied Mathematics at King's College London before completing a Master's degree on Mathematical Medicine and Biology at the University of Nottingham in 2017.

DENISE GARRETT

Sabin Vaccine Institute

Dr. Denise Garrett is the Vice President of Applied Epidemiology at the Sabin Vaccine Institute, where she leads a team dedicated to generating epidemiological evidence for informed vaccine decision-making, optimizing vaccine use, and enhancing the impact of immunization.

Denise brings extensive expertise in epidemiological operational research, program leadership and management, infectious disease control and prevention, and vaccine effectiveness studies. Before joining Sabin, she served as a medical epidemiologist at the U.S. Centers for Disease Control and Prevention (CDC) for over 23 years. During her tenure, Denise focused on international health and research, overseeing numerous multicenter studies in both high- and low-resource settings.

Dr. Garrett received her medical training, specializing in infectious diseases, and earned a master's degree in human biology from Brazil's Federal University of Minas Gerais. Additionally, she completed the Epidemic Intelligence Service (EIS) program at the CDC, where she received training in the practice of applied epidemiology.

MALICK GIBANI

Imperial College London

Malick Gibani is a Clinical Lecturer in Infectious Diseases at Imperial College London as well as a clinician specialising in infectious diseases and clinical microbiology. His research interests are centred around vaccinology, particularly in the application of controlled human infection models to accelerate vaccines for enteric diseases. Between 2014 and 2018 he undertook his DPhil at the University of Oxford, which focussed on the use of human challenge models to provide insights into enteric fever pathogenesis and immunity. Since 2018 he has worked at Imperial College London. He is the principle investigator of the Challenge NTS (CHANTS) study, which aims to develop the first controlled human infection model of *Salmonella* Typhimurium.

MELITA GORDON

University of Liverpool

Melita Gordon MA MD FRCP DTM&H is a gastroenterologist and clinical scientist, living in Blantyre, Malawi. She trained in internal medicine in Oxford, Zambia, and Belfast, and in Gastroenterology in Sheffield and Liverpool. She has researched invasive *Salmonella* disease in Malawi for 19 years, first as a Wellcome Trust Clinical Research Fellow, then during a UKCRC Senior Clinical Lectureship, and currently as Professor of Gastroenterology in the Institute of Infection and Global Health in the University of Liverpool. In 2011 she was awarded the British Society of Gastroenterology's Sir Francis Avery Jones Research Medal, and in 2012 the Shire SAGE first prize for Excellence in Gastroenterology. Her research encompasses clinical epidemiology and transmission modelling, clinical disease pathogenesis, host peripheral and mucosal cellular and molecular inflammatory response, bacterial phylogenomics. She is deputy director of a Wellcome Trust Clinical PhD Programme and academic lead of a University of Malawi and Liverpool joint PhD registration programme, both developing training young researchers working in low-income settings. She also leads a World Gastroenterology Organization International Training Centre for gastroenterology and GI endoscopy.

NICHOLAS GRASSLY

Imperial College London

Nicholas Grassly is a Professor in the Department for Infectious Disease Epidemiology, head of the Vaccine Epidemiology Research Group and associate director of the MRC Centre for Global Infectious Disease Analysis. He works on vaccine trials and disease surveillance. His research brings together epidemiological analysis and laboratory testing to identify optimal methods for disease prevention, focusing on pathogens in low- and middle-income countries such as polio, rotavirus and typhoid. He works with a network of collaborators at institutes worldwide, including in the UK, DRC, France, Ghana, India, Malawi, Pakistan and Zambia.

ANURADHA GUPTA

Sabin Vaccine Institute

Anuradha Gupta is the President of Global Immunization at the Sabin Vaccine Institute. A veteran public health leader, Ms. Gupta has in her previous roles spearheaded a host of successful global initiatives to improve the health of women and children and harness the full power of vaccines. Her work has created profound impact at a global scale, saving and improving millions of lives.

Prior to Sabin, Ms. Gupta spent several years at Gavi, The Vaccine Alliance, as its deputy CEO, where she pioneered the concept of zero-dose children — focusing on children who have not received even a single dose of the most basic vaccines. She also led efforts to roll out a new framework for a country-centric engagement immunization strategy with remarkable success.

Before her time at Gavi, Anuradha served as Mission Director of the National Health Mission of India, where she ran the largest public health program in the world and played a leading role in the country's efforts to eradicate polio, reduce maternal and child mortality, and revitalize primary health care.

Anuradha holds a Master of Business Administration from the University of Wollongong in Australia and received executive education from the John F. Kennedy School of Government at Harvard University, the Stanford Graduate School of Business and the Maxwell School of Citizenship and Public Affairs at Syracuse University.

(https://www.sabin.org/about/our-people/anuradha-gupta/)

HARSH VIVEK HARKARE

Swiss Tropical and Public Health Institute and University of Basel

Harsh is a scientific collaborator at the Swiss Tropical and Public Health Institute with a degree in Development Economics from the University of Göttingen. His research interests lie in disease modeling and cost-effectiveness of health interventions.

KRISTEN HEITZINGER

U.S. Centers for Disease Control and Prevention

Kristen Heitzinger, PhD, MPH, is an epidemiologist and global waterborne infections focus area lead of the Global WASH Team of the Division of Foodborne, Waterborne, and Environmental Diseases at US CDC. She has extensive experience in global disease surveillance, having served previously as the Epidemiology Branch Chief at US CDC's Mozambique office and as a consultant for WHO's Health Emergencies Programme. In her current role, Kristen works closely with national ministries of health and other partners to provide technical assistance for the conduct of typhoid fever, cholera, and other waterborne disease surveillance and outbreak response. She collaborates actively with colleagues in the Eastern Mediterranean region and globally to support typhoid fever surveillance capacity building, typhoid data use for decision-making, and other activities related to typhoid control, including prevention of drug-resistant typhoid fever.

YOGESH HOODA

Child Health Research Foundation

Yogesh is a Scientist and Lead, Molecular & Biochemistry laboratory at the Child Health Research Foundation, Dhaka, Bangladesh. Yogesh did his PhD in Biochemistry at the University Toronto where he identified the Slam family of proteins in Gram-negative bacteria. He then did his postdoctoral training on developing tools to study assembly of membrane proteins at the MRC Laboratory of Molecular Biology, Cambridge, UK. His lab investigates the evolutionary and spatial dynamics between *Salmonella* Typhi and its bacteriophages. Yogesh has made significant contributions in the analysis of whole genome sequences of *Salmonella* Typhi and Paratyphi A. In 2019, he identified the molecular basis of azithromycin resistance in typhoidal *Salmonella*. His interests include protein biogenesis, antimicrobial resistance, and genomic epidemiology. At the CAT conference, he will be discussing recent work in his lab on uncovering the role bacteriophage defense plays in the spread of drug-resistant *Salmonella* Typhi.

HUMA SYED HUSSAIN

Aga Khan University

Dr. Huma Syed Hussain, is a young physician from Karachi, Pakistan, and an alumnus of Ziauddin Medical College, where she earned her MBBS degree in 2021. After completing her degree, she began her professional journey as an intern at her home institute's hospital, gaining firsthand experience in local healthcare practices. In 2022, she expanded her horizons by gaining clinical experience in the United States, where she worked within a diverse and advanced healthcare system.

JUNAID IQBAL

Aga Khan University

Dr. Iqbal, who has undergone extensive local and international training in molecular and microbiology, possesses a wealth of expertise in the fields of molecular biology and bacterial cultures. He has actively participated in various projects related to vaccine seroefficacy and the large-scale whole-genome sequencing (WGS) of bacterial strains, specifically focusing on *Salmonella* Typhi. With professional experience spanning over 15 years, Dr. Iqbal is well-versed in multiple techniques and possesses the necessary skills required for this project. The combination of his proficiency in bacteriology, genomics, and molecular biology will greatly contribute to the successful execution of the proposed study. Moreover, his command over laboratory methodologies such as bacterial culturing, nucleic acid extraction, polymerase chain reaction (PCR), whole-genome sequencing, and bioinformatics analysis ensures the smooth and efficient completion of this project.

YASIR SHITU ISA

GSK Vaccines institute for Global Health

Yasir is a Medical Doctor from Nigeria and is currently the iNTS Project Physician at GSK Vaccines institute for Global Health (GVGH). He holds a Masters in Public Health from The University of Sheffield (UK) and MSc Advanced Biostatistics and Epidemiology from the École des Hautes Études en Santé Publique (EHESP) in Paris, France.

Before joining GVGH, Yasir worked as a Sub Investigator at the Medical Research Council (MRC) leading pneumococcal vaccine trials and Pneumonia Biomarkers study in The Gambia. He also practiced Medicine in his native Nigeria prior to working in the Gambia.

SHUBORNO ISLAM

Child Health Research Foundation

I'm Shuborno Islam, and with a passion for unraveling the mysteries of life, I embarked on a path of discovery that has defined my academic and professional pursuits. My educational journey began at the Department of Genetic Engineering and Biotechnology at East West University, where I studied biology and genetics. There, I realized my desire to make a tangible impact on public health, infectious diseases, and the environmental microbial community through the field of biotechnology.

After graduating in 2019, I joined Child Health Research Foundation in Bangladesh as a Microbiologist where I contributed to vital projects in viral infectious disease surveillance, particularly during the Covid-19 pandemic. My recent work involves the development of a Typhoid Surveillance Tool and the nationwide Typhi phage surveillance, which aimed to combat the spread of this infectious disease through vaccine implementation. At the same time, I'm continuing my studies at BRAC University, focusing on Biotechnology. I'm passionate about learning and pushing the boundaries of what we know in the field.

I have proudly contributed to the field, addressing crucial topics such as Covid-19 epidemiology, and SARS-CoV-2 variants and spread. Our team also studied Typhi Phage diversity, shedding light on the intricate interactions between bacteriophages and the Typhi bacterium and its genome.

My journey continues as I aspire to further scientific discoveries and innovations that can positively impact public health. The pursuit of knowledge and the quest for solutions remain at the core of my identity, driving me to explore the world of biotechnology and microbiology.

JOBIN JOHN JACOB

Christian Medical College, Vellore

Dr. Jobin John Jacob is a Post-doctoral Scientist specializing in leveraging genomics for tracking Enteric and Antimicrobial-resistant pathogens. Based in the Department of Clinical Microbiology, he employs advanced genomics, molecular biology, and microbiology techniques to investigate the evolution and dissemination of bacterial pathogens, including S. Typhi, S. Paratyphi A, and Non-typhoidal *Salmonella*. Dr. Jacob is also a member of Dr. Balaji Veeraraghavan's Antimicrobial Resistance (AMR) laboratory, where he specializes in genomic data analysis to identify robust molecular markers that provide valuable insights into bacterial pathogen evolution. Currently, his research involves analyzing extensive genomic datasets that shed light on the transmission patterns of *Salmonella* species and other enteric pathogens.

HYON JIN JEON

International Vaccine Institute

Hyon Jin Jeon is a PhD candidate and Project Manager in the Department of Medicine at the University of Cambridge, as well as a Senior Program Administrator at the Epidemiology, Public Health, and Impact (EPIC) unit of the International Vaccine Institute (IVI). With over 15 years of experience in managing multi-country research programs in resource limited settings, she brings valuable expertise to her role. Her research is focused on various areas including the epidemiology of vaccine-preventable diseases, the evaluation of vaccine effectiveness and impact, and the enhancement of access to safe and affordable vaccines in resource-limited settings. She has been actively engaged in extensive research related to multi-country typhoid and invasive non-typhoidal *Salmonella* (iNTS) in sub-Saharan Africa through the Severe Typhoid Fever in Africa Program (SETA) and the Typhoid Conjugate Vaccine Introduction in Africa (THECA) program.

SAMUEL KARIUKI

Kenya Medical Research Institute

Sam Kariuki (DVM, MSc, PhD) obtained his DVM from the University of Nairobi (1989), MSc in Pharmacology and Toxicology, University of Nairobi (1991), and a PhD in Tropical Medicine from the Liverpool School of Tropical Medicine (LSTM) in 1997. He was awarded Doctor of Science (Honoris causa) by the LSTM in December 2022. Currently he is Director, Drugs for Neglected Diseases Initiative (DNDi) East Africa Regional Office. Previously, he was Acting Director General at the Kenya Medical Research Institute (KEMRI) (2021-2023) and Director of Research and Development (2018-2022). He is Fellow, African Academy of Sciences and a Honorary Faculty Wellcome Sanger Institute, visiting Professor of Tropical Microbiology, Nuffield Department of Medicine, University of Oxford, and the Ohio State University One-Health Initiative. He is also a member of the American Society for Microbiology and Section Editor, Journal of Medical Microbiology.

Over the last 20 years his team has researched and published on epidemiology and genomics of Antimicrobial Resistance (AMR) and genomic surveillance of key enteric pathogens endemic in Kenya and the region. He has published over 200 papers in peer-reviewed journals and written 4 chapters in textbooks of Microbiology and Infectious Diseases, majoring in Genomics and Epidemiology. He is a member of the National Antimicrobial Stewardship Interagency Committee (NASIC) advising Ministry of Health on One Health approach in implementation of the National Action Plan to combat AMR, and a member of the WHO Strategic and Technical Advisory Group for Antimicrobial Resistance (STAG-AMR).

ABDUL MOMIN KAZI

Aga Khan University

Momin Kazi is an Assistant Professor (Research) at the Aga Khan University. He is a physician (M.B.B.S Dow Medical College, Pakistan), an epidemiologist (MSc. Vanderbilt University, USA), and is currently completing his PhD from the University of British Columbia, BC, Canada. His main research focus is mortality-related studies and surveillance systems. Over the last 15 years, he has focused on developing surveillance systems in Pakistan and implementing/evaluating health technology. Currently, he is involved in multiple research studies with the Department of Paediatrics, with a primary focus on maternal and child health using technology. His work also focuses on mobile-health-based behavioral interventions to improve vaccination coverage in Pakistan. He and his team's research in Pakistan encompasses community engagement, religious endorsements, and innovative surveillance methods, contributing significantly to understanding childhood mortality and the impact of COVID-19 in low-resource settings. He has published 60+ papers with an h-index of 24, emphasizing mortality studies and advocating for mobile-based interventions to enhance vaccination coverage in LMICs, focusing on crucial aspects of disease surveillance in resource-constrained settings. His papers have been published in leading journals, including the Lancet Infectious Diseases, Lancet Global Health, World Health Bulletin, and Journal of Medical Internet Research.

FARHANA KHANAM

icddr,b

Dr. Farhana Khanam, Associate Scientist, Infectious Disease Division, icddr,b, Dhaka, Bangladesh. Dr. Khanam's research emphasizes the basic and applied immunology of infectious diseases in addition to clinical trials of enteric vaccines, which are in Phase II to Phase IV of development. Her main work has been conducting disease burden studies in urban, high-risk populations on *Salmonella* Typhi/Paratyphi where she was able to demonstrate the high burden of typhoid fever in children and adults in urban slums in Dhaka city in the STRATAA consortium. She has also been co-leading the large Phase III Cluster Randomized Controlled Trial of typhoid conjugate vaccine under the TyVAC consortium, as well as several Phase II and non-inferiority trials of typhoid vaccines. She is also currently working on the Shigella burden study under the EFGH consortium. She has gained expertise in different laboratory assays and trained the laboratory staff on these techniques. She has been actively involved with other infectious diseases, including COVID-19 and oral cholera vaccine effectiveness studies using a test-negative design.

JEROME H. KIM

International Vaccine Institute

Jerome H. Kim, M.D., is the Director General of IVI and an international expert on the development and evaluation of vaccines.

Prior to IVI, he served as the Principal Deputy, US Military HIV Research Program and the Chief, Laboratory of Molecular Virology and Pathogenesis at the Walter Reed Army Institute of Research; and the US Army Program Manager for HIV vaccines. He led the Army's RV144 Phase III HIV vaccine trial that showed efficacy in the prevention of HIV-1.

Dr. Kim is an Adjunct Professor, Department of Medicine, Uniformed Services University of the Health Sciences, Bethesda, USA; Adjunct Professor, Graduate School of Public Health, Yonsei University, Republic of Korea; and an

Honorary Professor, University of Rwanda. He was named a Distinguished Visiting Professor, Seoul National University in 2022. He has authored over 350 publications.

Dr. Kim is a graduate of the University of Hawaii with high honors in History and highest honors in Biology, received his M.D. from the Yale University School of Medicine, and trained in Internal Medicine and Infectious Diseases at Duke University Medical Center.

Dr. Kim has received numerous awards: John Maher Award for Research Excellence, Uniformed Services University (2013); Department of the Army Research and Development Achievement Award for Technical Excellence (2013); Asia Pacific Vaccine Excellence Lifetime Achievement Award (2021); Medal of Honor for Civil Merit from the Government of the Republic of Korea (2022).

SUPRIYA KUMAR

Bill & Melinda Gates Foundation

Supriya Kumar is a Senior Program Officer in Global Health at the Bill & Melinda Gates Foundation, and leads the Environmental Surveillance portfolio. Prior to joining BMGF in 2017, she was a faculty member at the Graduate School of Public Health at the University of Pittsburgh. She collaborated with partners in India and at the CDC on household surveys to assess contact heterogeneities in rural Indian populations. She also used realistic, data-driven computational models of disease transmission to assess the impact of interventions to reduce respiratory infection inequalities in the US. At BMGF, Supriya draws on this experience to manage studies aimed at understanding the transmission of pathogens such as Campylobacter in children, and the incidence of typhoid in India.

MATTHEW LAURENS

University of Maryland School of Medicine

Dr. Matthew Laurens is a pediatric infectious disease specialist with a primary research interest in malaria, typhoid, and other tropical infectious diseases. He leads clinical trials that include controlled human infection and vaccine testing in resource limited settings, including studies of typhoid conjugate vaccines, malaria vaccines, and other clinical studies. He is Professor of Pediatrics at the University of Maryland School of Medicine and based at the university's Center for Vaccine Development and Global health where he directs the Fellowship Training Program in Pediatric Infectious Diseases.

RAMANAN LAXMINARAYAN

One Health Trust

Ramanan Laxminarayan is the founder and president of the One Health Trust, founded as the Center for Disease Dynamics, Economics & Policy (CDDEP). He is a senior research scholar at Princeton University. He is an affiliate professor at the University of Washington, senior associate at the Johns Hopkins Bloomberg School of Public Health, and a visiting professor at the University of Strathclyde in Scotland. Dr. Laxminarayan chairs the board of GARD-P, a global product development partnership created by the World Health Organization, that aims to develop and deliver new treatments for bacterial infections. He is founder and board chair at HealthCubed, which works to improve access to healthcare and diagnostics worldwide.

During the Obama Administration, Dr. Laxminarayan served on the U.S. President's Council of Advisors on Science and Technology's antimicrobial resistance working group and was appointed a voting member of the U.S. Presidential Advisory Council on Combating Antimicrobial Resistance. He is a series editor of the Disease Control Priorities for Developing Countries, 3rd edition.

In 2003-04, he served on the National Academy of Science/ Institute of Medicine Committee on the Economics of Antimalarial Drugs and subsequently helped create the Affordable Medicines Facility for malaria, a $450 million novel financing mechanism for antimalarials that reduced the cost of antimalarials worldwide. In 2012, Dr. Laxminarayan created the Immunization Technical Support Unit that supports the immunization program of the Ministry of Health and Family Welfare of the Government of India, which is credited with helping introduce four new vaccines and extending vaccination coverage to 3 million infants. As Vice President, Research and Policy at the Public Health Foundation of India between 2011 and 2015, he led the growth of a research division to over 700 technical and research staff.

Dr. Laxminarayan currently leads the largest Covid-19 epidemiology study in the world based on extensive contact tracing in India. The flagship paper from this study was published in Science in 2020.

JUNG-SEOK LEE

International Vaccine Institute

Jung-Seok Lee is the Head of the Policy and Economic Research (PER) Department at the International Vaccine Institute (IVI). Prior to joining IVI, he worked as a senior health economist at the University of Oxford, UK. His research interests lie in the economic and spatial perspectives of infectious diseases. Dr. Lee is particularly interested in linking applied economics and econometrics to geo-spatial analyses. His research aims at minimizing overall societal losses in many parts of the world including countries where healthcare resources are highly limited.

MYRON ("MIKE") M. LEVINE

University of Maryland School of Medicine

Myron ("Mike") M Levine, MD, DTPH, is Bessie & Simon Grollman Distinguished Professor and Associate Dean for Global Health, Vaccinology, and Infectious Diseases at University of Maryland School of Medicine. As Director of the Center for Vaccine Development (CVD) from 1974-2014, he made substantial contributions in basic vaccinology, bacterial pathogenesis, clinical research, field epidemiology, and public health. He consults for many organizations (WHO, NIH, National Academy of Medicine, Department of Defense) and advises multiple vaccine companies. A pediatrician, infectious diseases consultant, communicable disease epidemiologist, and vaccinologist, he has authored 732 scientific journal articles and 120 book chapters. Honors he has received include: Albert B. Sabin Gold Medal; American Society for Microbiology's Hilleman/Merck Award; Walter Reed Medal and Donald MacKay Medal from American Society of Tropical Medicine and Hygiene; "Grand Officer Rank" of National Order of Mali" for developing and distributing vaccines to children of Mali; American College of Physicians Award for Outstanding Work in Science as Related to Medicine; Maxwell Finland Award for Scientific Achievement from the National Foundation for Infectious Diseases. He is a member of National Academy of Medicine, USA and served as President of the American Epidemiological Society and the American Society of Tropical Medicine and Hygiene.

XINXUE LIU

Oxford Vaccine Group and the NIHR Oxford Biomedical Research Centre

Dr. Xinxue Liu obtained his medical degree in preventive medicine in 2005 and subsequently pursued a PhD in epidemiology and biostatistics. Dr. Liu currently holds the position of Associate Professor of Medical Statistics and Epidemiology at Oxford Vaccine Group, University of Oxford. In this role, he brings a wealth of experience in designing and analysing randomised controlled trials (RCTs) and observational studies.

As the lead of the Statistics and Epidemiology Group within the Oxford Vaccine Group, Dr. Liu oversees a team of 12 dedicated statisticians and epidemiologists. During the COVID-19 pandemic, Dr. Liu played an important role as the lead statistician and investigator in the development and execution of multiple COVID-19 vaccine policy trials. His work has yielded critical insights that have informed policymakers not only in the United Kingdom but also on the global stage. Dr. Liu's research interests span both clinical and methodological domains.

CALMAN A. MACLENNAN

Bill & Melinda Gates Foundation

Cal MacLennan is the Senior Program Officer for Bacterial Vaccines in the Enteric and Diarrheal Diseases team, Global Health, at the Bill & Melinda Gates Foundation, and is lead for the Shigella portfolio and *Salmonella* vaccines product development.

A clinician scientist by training, following his medical degree and DPhil from the University of Oxford, and during specialist training in clinical immunology, he spent time in Malawi and Kenya investigating immunity to invasive *Salmonella* disease. He continued this work as a senior clinical fellow at the University of Birmingham leading to key findings on the important role of antibody in protective immunity against invasive nontyphoidal *Salmonella*. From 2010, Cal MacLennan was Head of the Exploratory Programme at the Novartis Vaccines Institute for Global Health, Italy, developing vaccines against *Salmonella*, Shigella and meningococcus. The Vi-CRM_{197} typhoid conjugate vaccines that he was involved in inventing is now a licensed and WHO-prequalified vaccine manufactured by Biological E, India.

He returned to the University of Oxford, in 2015 to the Jenner Institute, before moving to the Bill & Melinda Gates Foundation in 2017. His work at the Jenner Institute focuses on gonorrhoea vaccine development. He is a

Jenner Investigator and group leader, Professor of Vaccine Immunology and Director of the MRC/GCRF BactiVac Bacterial Vaccinology Network at the University of Birmingham and a consultant immunologist.

AMIRA MAHBOOB

World Health Organization Regional Office for the Eastern Mediterranean

Amira is an Egyptian medical doctor and researcher with a master's degree in Public Health (MPH) majoring in Environmental Health and currently, she is a PhD candidate. She works as an assistant lecturer of public health at the High Institute of Public Health, Alexandria University. She believes that being an assistant lecturer of public health gives her the privilege to teach and guide eager young researchers and that's why she always seeks the latest advancements in science to be able to feed their brain's hunger for knowledge. Amira has thorough knowledge about the typhoid situation in the Eastern Mediterranean Region that was acquired from her fellowship at EMRO/ WHO program in Cairo. She was allocated during her fellowship program to the Health Emergency Department/ Infectious Hazard Prevention and Preparedness Unit for six months and that's when she successfully managed to conduct this research "Effectiveness of Typhoid Conjugate Vaccine (TCV): A systematic review."

JONATHAN MANDOLO

Malawi Liverpool Wellcome Programme

Jonathan Mandolo is an offsite Clinical Sciences PhD student at Liverpool School of Tropical Medicine (LSTM) based in Malawi under Infection and Immunity research group at Malawi Liverpool Wellcome Programme. He is working on developing/validating multiplexing serology technique which can be used to assess magnitude of pathogen transmission, vaccine coverage and their effectiveness for different Vaccine Preventable Pathogens of public health interest including Typhoidal *Salmonella*, Cholera, Rotavirus and SARS COV-2. Jonathan holds Bachelor of Science in medical laboratory sciences (honours) and Master of Science in Bioinformatics obtained at the university of Malawi in 2014 and 2021, respectively. Jonathan has published over 16 scientific papers in peer-reviewed journals and has given a number of presentations at local and international scientific conferences. His long-term plan is to become clinical research leader focusing on global health challenges to inform policy.

INACIO MANDOMANDO

Centro de Investigação em Saúde de Manhiça

Inacio Mandomando pursued his PhD in Medical Microbiology (2009) at the University of Barcelona (Spain); currently holding a position of Research Scientist at CISM (Mozambique) and Coordinator of Bacterial, Viral and Neglected Tropical Disease with interest in infectious disease and public health. He has been leading several studies conducted at CISM, and currently is a site Principal Investigator of the: i) Child Health and Mortality Prevention Surveillance (CHAMPS); ii) Towards the interruption of transmission of Soil;Transmitted Helminths: Project Clinical research development of a fixed-dose co-formulation of ivermectin and albendazole; and iii) Age-descending, randomized, placebo-controlled Phase 2 trial in three sites in sub-Saharan Africa to assess the safety and immunogenicity of a parenteral Trivalent *Salmonella* (*S.* Enteritidis/*S.* Typhimurium/*S.* Typhi Vi) Conjugate Vaccine (TSCV) versus placebo.

TAPFUMANEI MASHE

Ministry of Health and Child Care Zimbabwe/ World Health Organization

Dr. Tapfumanei Mashe is the AMR Project Coordinator in Zimbabwe, coordinating AMR activities for the government and the quadripartite. His research focus is on antimicrobial resistance and molecular epidemiology of infectious pathogens. He is the leader of the One Health AMR Secretariat in Zimbabwe and a member of the General Council for the Institute of Tropical Medicine in Belgium.

NAINA MCCANN

Oxford Vaccine Group

Naina McCann works at the Oxford Vaccine Group as a Clinical Research Fellow where she is currently undertaking her DPhil evaluating an oral live attenuated *Salmonella* Paratyphi A vaccine candidate using a human challenge model of paratyphoid infection. Her research is particularly focusing on investigating the mucosal immune response to paratyphoid vaccination and infection. She is an Infectious Diseases and General Medicine clinician by background.

JAMES E. MEIRING

University of Sheffield

I am an Academic Clinical Lecturer and Infectious disease physician at the University of Sheffield, UK, having completed my PhD at the University of Oxford based at the Malawi-Liverpool Wellcome Trust Programme in Blantyre, Malawi. I have experience in population based typhoid burden studies and typhoid vaccine trials through the STRATAA programme, TyVAC trials and Oxford human challenge studies. I have an interest in understanding and investigating the wider impact of vaccination at a population level, with particular focus on antimicrobial resistance and antibiotic usage.

ANNA MINTA

World Health Organization

Dr. Anna Minta is a pediatric infectious disease physician and epidemiologist who is currently a Surveillance Officer in the Vaccine-Preventable Diseases Surveillance and Risk Assessment Team at WHO-Headquarters. Her role is to strengthen surveillance, particularly for typhoid, measles, rubella, and other VPDs, and to collate, analyze, interpret, and disseminate surveillance data at the global level for use in policy decisions. Dr. Minta was previously at the U.S. Centers for Disease Control and Prevention where she provided technical assistance to several Anglophone and Francophone countries in sub-Saharan Africa, the Caribbean, and South-East Asia regarding infectious disease surveillance, hepatitis B and other VPD serosurveys, clinical trials, operational research, and programmatic activities, with a focus on eliminating vaccine preventable diseases, malaria, HIV, and TB among children.

ROUDEN ESAU MKISI

PATH

Mr. Rouden Esau Mkisi is a Senior Program Officer and Vaccine Technical lead for PATH–Malawi. Mr. Mkisi has two decades of experience in new vaccine introductions. Prior to joining PATH, Mr. Mkisi worked for John Snow Inc. on the Maternal and Child Health Project and as Regional EPI Officer for the Ministry of Health's northern region. He has a master's degree in public health from the University of Malawi College of Medicine, a degree in Health Science Education from Mzuzu University, and a Diploma in Environmental Health obtained from Malawi College of Health Sciences.

Mr. Mkisi has supported several new vaccine introductions including malaria vaccine, measles rubella, HPV, and TCV. While working as EPI Officer for the northern zone he helped to plan, coordinate, and monitor routine EPI and disease surveillance activities. He consolidated monthly EPI performance reports and provided oversight to districts for necessary improvements. He supported districts with various disease outbreak investigations, including those related to EPI disease conditions. Most recently, Mr. Mkisi provided technical support to the Ministry of Health to introduce TCV through an integrated campaign that included MR, bOPV, and Vitamin A supplementation. Mr. Mkisi is serving as co-investigator on a study to evaluate the cost of TCV-MR integrated campaigns and the subsequent transition to TCV in routine delivery in Malawi.

EMMANUEL MUGISHA

PATH

Dr. Emmanuel Mugisha leads PATH's Typhoid Vaccine Acceleration Consortium (TyVAC) and serves as a Senior Technical Advisor on Immunizations. In this role, he leverages decades of leadership experience and expertise to increase uptake of typhoid conjugate vaccines as part of an integrated approach to typhoid prevention and control.

Dr. Mugisha is a champion for vaccines as a tool for disease prevention, specializing in vaccine clinical trials, new vaccine introduction, and implementation, monitoring, and evaluation. He is a supporter of data-driven, bottom-up solutions to strengthen health systems in low- and middle-income countries.

He has nearly 30 years of public health and management experience, and his work has spanned the African and Asian regions.

MICHAEL MURAYA MUGO

Kenya Medical Research Institute

I am a Senior Medical Laboratory Analyst, working with Kenya Medical Research Institute at the Center for Microbiology Research, with a decade of experience in microbiology and parasitology research. My research interest entails the epidemiology of enteric pathogens, the role of the environment in the spreading of enteric pathogens, and the exploration of other alternatives to antibiotics in treating and controlling drug-resistant enteric bacteria (i.e., use of phages for therapy and biocontrol).

I am a principal investigator in two studies: Identification of bacteriophages that can treat MDR non-typhoidal *Salmonella* infections and Development of phage cocktail; a biocontrol for *V. cholerae*. Currently, I am also working as a lab analyst in: Multidrug-resistant invasive non-typhoidal *Salmonella* disease in children: The role of carriage in humans and environmental contamination in an endemic setting in Kenya (MISSIoN) and Cholera Prevention, Preparedness, and Control in Kenya through Hotspot Mapping, Genotyping, Exposure Assessment, and WASH + Oral Cholera Vaccine Interventions.

Academic and Professional Qualifications include Masters in Medical Laboratory Science (Microbiology choice) ongoing and BSc Medical Laboratory Science.

SIRA JAM MUNIRA

Child Health Research Foundation

Dr. Sira Jam Munira is a medical doctor with a robust research background in epidemiology and highly motivated to advance her career in disease prevention and health promotion. After completing her Master's, she embarked on her professional journey with the esteemed Child Health Research Foundation in Bangladesh.

During her five-year tenure, Dr. Munira acquired extensive expertise by collaborating on projects involving patient-centered hospitals and population-based surveillance. Her research efforts primarily centered around assessing the burden of infectious diseases, including but not limited to Typhoid, Paratyphoid, Pneumococcus, Dengue, and Respiratory Syncytial Virus, focusing on serosurveillance, antimicrobial resistance patterns, rapid diagnostics, and cost-effective modeling. Notable projects coordinated by her at CHRF include "Surveillance of enteric fever in Southeast Asia," "Sero-epidemiology and environmental surveillance," "Typhoid Conjugate Vaccine cost-effectiveness analysis," and "Rapid diagnostics using finger stick capillary blood." She has also participated in various international conferences, where she presented her research findings through oral and poster presentations. Her invaluable contributions to these projects have been recognized through co-authorship of articles published in reputable scientific journals. To further enhance her proficiency, she has been actively involved in numerous training programs, primarily focused on scientific writing and statistical analysis.

Her several years of dedicated research experience in vaccine-preventable infectious diseases exemplify her ability to independently manage projects, develop pragmatic research plans, collaborate effectively within multidisciplinary teams, and take a leadership role in achieving objectives. Dr. Munira is committed to leveraging her knowledge, skills, and potential in the realm of infectious disease research to their fullest extent.

SHIVA RAM NAGA

Dhulikhel Hospital

Shiva Ram Naga is a researcher specializing in tropical infectious diseases. His extensive experience spans multiple outbreak surveillance initiatives and communicable disease research. Shiva has been dedicated to fever surveillance, demonstrating his commitment to this critical area of study. Currently serving as a project coordinator at Dhulikhel Hospital, Shiva leads a multi-site, multi-country enteric fever surveillance program. His primary research interests revolve around antimicrobial resistance in pathogenic bacteria, reflecting his commitment to addressing crucial healthcare challenges.

USMAN NAKAKANA

GSK Vaccines Institute of Global Health

As a Senior Clinical Development expert, with specialist training in clinical pharmaceutical development, vaccinology, paediatrcis and paediatric infectious diseases. Dr. Nakakana is a specialist in the design and implementation of clinical development plans, with a broad knowledge and overview of early phase clinical trials and phase 3 trials for vaccines and anti-infectives. He trained as a vaccinologist at the Global programme in Vaccinology at the University of Siena and has wide-ranging experience in clinical trials, implementation research, public health interventions, patient care and clinical and epidemiologic research. In his role as senior project physician lead, he coordinates a team developing vaccines against infectious diseases of public health interest designing clinical trials, protocol development and broad medical and safety oversight of clinical trials through all phases of development. As a former Investigator, he led clinical trials in malaria and other infectious diseases. He is also broadly skilled in geospatial disease modelling, epidemiology of infectious and non-infectious diseases, regulatory affairs, medical affairs, manufacturing and product lifestyle management systems. He is also involved in advocacy, and actively pursuing partnerships to facilitate local research. His passion is to help develop life-saving interventions for children in resource constrained contexts and globally!

PROSCOVIA NALUYIMA

Makerere University Walter Reed Project

I am a laboratory scientist with a Bachelor's degree in Biomedical Laboratory Technology from Makerere University, a Master of Science degree in Biomedical Science from the University of Ulster, Northern Ireland, UK, and a doctorate in Medical Science, specializing in Immunology from Karolinska Institutet of Sweden. I have 20 years of experience in medical research with the Makerere University Walter Reed Project, Uganda, where I oversee laboratories that evaluate the health of patients, and the safety and immunogenicity of biological products for the prevention or therapy of infectious and non-infectious diseases. I lead the Laboratory Correlates and Immunology working group of the multi-country, multi-site BRILLIANT consortium that is conducting HIV vaccine research and development in sub-Saharan Africa. I lead efforts to develop capacity of laboratory personnel to conduct clinical research during filovirus outbreaks, and conduct research in sepsis. Furthermore, I am a member of the National Task Force, of the Uganda Public Health Emergency Operations Center of the Ministry of Health, that organizes the national response to public health emergencies. In the global health security sphere, I am involved in efforts to raise awareness of biosafety and biosecurity, particularly as regards the Biological Weapons Convention. I have been involved in efforts to enhance the participation of women in peace and security processes in Africa. I am a member of the Global

Health Security Agenda consortium steering committee and a member of the Signature Initiative to Mitigate Biological Threats in Africa (SIMBA) Sub-Working Group 4 (Non-Proliferation).

LATIF NDEKETA

Malawi-Liverpool Wellcome Trust Research Program

I am a Medical Doctor and Vaccine Epidemiologist based at Malawi-Liverpool Wellcome Trust (MLW) in Blantyre. I am passionate about reduction of morbidity and mortality of vaccine preventable diseases in low-income settings through novel surveillance methods for vaccine programmes. At MLW, I am the duty lead for the Infectious Disease Epidemiology group and as part of this role I am involved in several vaccine evaluation projects such as TCV and COVID-19 vaccines. I am the local PI for the RTS,S malaria vaccine phase IV study. I am a member of several national technical advisory and regulatory committees on vaccines in Malawi.

I am also an MRC funded clinical PhD candidate in Vaccinology and Immunology at University of Liverpool. My project is looking to improve population impact evaluations of new vaccine introductions to more accurately measure vaccine-attributable effects and differentiate these from other concurrent public health interventions.

KATHLEEN NEUZIL

University of Maryland School of Medicine

Dr. Kathleen Neuzil, Myron M. Levine Professor in Vaccinology, directs the Center for Vaccine Development and Global Health at the University of Maryland School of Medicine. An internationally recognized vaccinologist, her work has spanned dozens of low-resource countries with multiple vaccines, including influenza, rotavirus, human papillomavirus, Japanese encephalitis, typhoid conjugate, and COVID-19 vaccines. Dr. Neuzil directs TyVAC, the Typhoid Vaccine Acceleration Consortium, with the goal to accelerate the introduction of typhoid conjugate vaccines into low-resource countries. She is a member of the World Health Organization Strategic Advisory Group of Experts on Immunization, and the National Academy of Medicine.

OSWARD NYIRENDA

Blantyre Malaria Project

Osward Nyirenda is a Malawian clinician and public health researcher. He holds Diploma in Clinical Medicine; BSc Degree in Public Health and he is Master of Public Health candidate at Kamuzu University of Health Sciences formerly College of Medicine in Malawi.

Osward has been involved in a research work studying the immunogenicity and safety of a novel typhoid conjugate vaccine in African children at Blantyre Malaria Project a center of clinical research excellence affiliated with the Kamuzu University of Health Sciences (KUHES), Maryland (UMB), and Michigan State (MSU). He has clinical and research interest in infectious diseases with a special emphasis on vaccine preventable diseases in sub-Saharan Africa. He is currently working as a Research Coordinator for the Blantyre Malaria Project.

IRUKA N. OKEKE

University of Ibadan

Iruka N. Okeke is Professor of Pharmaceutical Microbiology and of Medical Microbiology and Parasitology at the University of Ibadan, Nigeria. She is a Fellow of the Nigerian and African Academies of Science and a Calestous Juma Science Leadership Fellow. Iruka's research group uses microbiology, genetic and genomic methods to investigate the mechanisms bacteria use to colonize humans, cause disease and gain drug resistance. She also studies laboratory practice in Africa and her group contributes to antimicrobial resistance surveillance in Nigeria.

Iruka received B.Pharm., M.Sc. and Ph.D. degrees from Obafemi Awolowo University (formerly University of Ife), Nigeria, post-doctoral training at the University of Maryland, USA and Uppsala Universitet, Sweden She is author/ co-author of several scientific articles and chapters as well as the books *Divining Without Seeds: The Case for Strengthening Laboratory Medicine in Africa* (Cornell Univ Press) and *Genetics: Genes, Genomes and Evolution* (Oxford Univ Press). A teacher scholar, Iruka has mentored over a hundred research students, the majority of whom continue to work in science and health. She is the 2023 recipient of the UK Microbiology Society's Peter Wildy Award and was recently selected for the 2024 American Society for Microbiology Moselio Schaechter Award.

IOANA DIANA OLARU

London School of Hygiene & Tropical Medicine

Ioana Diana Olaru is an infectious diseases physician and epidemiologist with a special interest in improving diagnostics and in antimicrobial resistance in low-resource settings. Ioana coordinated a large study on causes of febrile illnesses in Harare, Zimbabwe which was then experiencing a severe typhoid fever outbreak. This work was done while Ioana was working at the London School of Hygiene & Tropical Medicine and was part of a multisite study on febrile illnesses (FIEBRE).

ALPHONSE OUEDRAOGO

Groupe de Recherche Action en Santé

My name is Dr. Alphonse Ouedraogo. I trained as a Medical Doctor at the University of Ouagadougou in 2002. The following year, I joined the Centre National de Recherche et de Formation sur le Paludisme (CNRFP), a leading research institution within the Ministry of Health, Burkina Faso, due to my passion for research. I have been working there for 17 years. In 2013, I obtained a PhD degree in Epidemiology from the University "La Sapienza" in Rome, Italy. After serving as a clinical investigator for CNRFP from 2003 to 2010, I assumed the role of Head of New Drugs and Vaccine Development Department from 2014 to 2018. Subsequently, I held the position of Senior Scientist until May 2021. Presently, I serve as the Senior Scientist and Scientific Director at Groupe de Recherche Action en Santé (GRAS), a health research institute established in 2008 in Burkina Faso.

Over the past two decades, I have led several clinical studies and implementation research activities related to infectious diseases, including typhoid. These studies have yielded more than 60 scientific publications reviewed by peers.

Additionally, I was an integral member of the team that conducted co-administration trials of TCV with routine immunization at 9 and 15 months in Burkina Faso. These findings provide support for the introduction of TCV in sub-Saharan Africa. They represent the first co-administration data for measles-rubella and yellow fever vaccines at 9 months, as well as for meningococcal type A and measles-rubella vaccines at 15-23 months.

MICHAEL O. OWUSU

Kwame Nkrumah University of Science and Technology

Dr. Michael Owusu is a Clinical Microbiologist and a Senior Lecturer at the Department of Medical Diagnostics, Kwame Nkrumah University of Science and Technology (KNUST). He holds master's degree in Applied Statistics and PhD in Clinical Microbiology from KNUST and the Institute of Virology, University of Bonn Medical Centre, Germany.

Prior to his appointment at the University, he had worked as Biomedical Scientist at the Microbiology Department of the Komfo Anokye Teaching Hospital for 10 years, where he engaged in the use of classical microbiological techniques for identification of microbiological agents. Dr. Owusu did

his Post-doctoral fellowship training was in the discovery of epidemic prone infectious agents in wildlife and other animal host. He is a fellow of the African Programme for Advanced Epidemiology training (APARET), European and Clinical Trials Partnership (EDCTP) and the African Research Excellence Fund (AREF). He is a leader and an administrator with passion in mentoring young scientists in academics and non-academic circles. His research interest is in the area of viral zoonosis, epidemiology of microbial pathogens of public health significance, environmental surveillance of microbial agents and molecular evolution of viral and bacterial organisms. He is currently collaborating with scientists from Imperial College to conduct surveillance of viral and bacterial agents in environmental water sources in Ghana. Dr. Owusu has published over 70 papers in peer-reviewed journals and contributed to 4 book chapters. He is also a member of the Board of Reviewers of the American Society of Microbiology and College of Experts of AREF.

CHRISTOPHER PARRY

Liverpool School of Tropical Medicine

Christopher Parry is a Senior Lecturer in Tropical Medicine at the Liverpool School of Tropical Medicine and Honorary Consultant at Alder Hey Children's Hospital in Liverpool, UK. He is the Programme Director for the Professional Diploma in Tropical Medicine and Hygiene (DTMH) and Clinical Director of the Clinical Diagnostic Parasitology Laboratory at LSTM. He has previously held positions in Oxford University and Nagasaki University. He has a research interest the management of severe bacterial infections in LMIC with a focus on typhoid fever. He is a co-investigator in the ACT-South Asia trial of antimicrobial treatment for suspected typhoid fever which is in progress in Bangladesh, Nepal and Pakistan.

PRIYANKA PATEL

Malawi Liverpool Wellcome Trust

Dr. Priyanka Patel is a study clinician and master's student at Malawi Liverpool Wellcome Trust. She is working on several typhoid studies. She was the lead clinician for a phase 3 vaccine trial of 28,000 children (from which she has published as the first author in a NEJM paper), and has taken a leading role as a study clinician in the phase 4 Impact surveillance study in a population of 150,000 in Blantyre, including a census, health utilisation survey and ongoing blood culture passive surveillance at 4 sites, which is part of the Typhoid Vaccine Acceleration Consortium (TyVAC). TyVAC is funded by the Bill & Melinda Gates Foundation. In addition, she is the sub-investigator in the team commencing the phase 2a study of the triple valent typhoid and iNTS vaccine in Africa, funded by the Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) at Boston University and sponsored by GlaxoSmithKline Biologicals S.A. (GSK) Vaccines Institute for Global Health (GVGH). She thus has unparalleled hands-on experience in clinical trials from phase 2a to phase 4. She is passionate about finding new ways to keep people safe from diseases that can be prevented by vaccines, especially in places with limited resources. Alongside this, she is also pursuing an online MSc in Clinical Trials at the University of London.

VIRGINIA PITZER

Yale School of Public Health

Virginia Pitzer, Sc.D., is an Associate Professor in the Department of Epidemiology of Microbial Diseases at Yale School of Public Health. She received her Sc.D. in Epidemiology from Harvard School of Public Health, and was a postdoctoral fellow at Princeton University and Fogarty International Center/National Institutes of Health prior to joining the Yale faculty in 2012. Her research focuses on mathematical modeling of the transmission dynamics of infectious diseases, including rotavirus, typhoid fever, and RSV. She studies how interventions such as vaccination, improved treatment of cases, and improvements in sanitation affect disease transmission at the population level. She is currently a member of the World Health Organization's Immunization and Vaccine-related Implementation Research Advisory Committee (WHO IVIR-AC).

ANDREW J. POLLARD

University of Oxford

Sir Andrew is Director of the Oxford Vaccine Group at the University of Oxford and an honorary consultant paediatrician (infectious disease and immunology) at Oxford Children's Hospital. He received a knighthood in the Queen's Birthday Honours in 2021 for services to Public Health and the Order of Medical Merit from the Federal Republic of Brazil in 2022.

His research includes the design, development and clinical evaluation of vaccines including those for typhoid, meningococcus, *Haemophilus influenzae* type b, pneumococcus, plague, pertussis, influenza, rabies, coronavirus and Ebola. His work on pneumococcal and meningococcal vaccines has been used in global public health policy. His studies on typhoid both using the human challenge model and in field sites supported the WHO prequalification of a new typhoid conjugate vaccine and WHO recommendations for its use in countries with a high burden of disease with more than 50 million vaccinated since 2021. He was the chief investigator for the clinical

trials of the Oxford-AstraZeneca vaccine in 2020 in 24,000 participants in UK, South Africa and Brazil, which led to authorisation of the vaccine for use in more than 180 countries with over 3.5 billion doses distributed and award of the Copley Medal by the Royal Society in 2022. He has supervised 50 PhD students and his publications includes over 700 manuscripts. He chairs the UK Department of Health and Social Care's Joint Committee on Vaccination and Immunisation, was a member of WHO's Strategic Advisory Group of Experts (2016-2022).

FIRDAUSI QADRI

icddr,b

Dr. Firdausi Qadri, Senior Director, Infectious Disease Division and Head, Mucosal Immunology and Vaccinology Unit, at icddr,b, Dhaka, Bangladesh. She is also the founder and leads to Institute for Developing Science and Health Initiatives (ideSHi). Her work includes basic and applied immunology of infectious diseases but also clinical and large field-based studies on enteric vaccines. Dr. Qadri has been elected a fellow and member of many societies including ASM, AAM, TWAS, IDSA, BAS, INSA, and NITAGE, and serves on advisory boards including the ISDB science, biotechnology, and innovation board. Recently, her research focuses very much on Covid-19 infections and vaccinations. Dr. Qadri has more than 550 publications in a peer-reviewed journal of high impact (Web of Science). Dr. Qadri has been honored with this prestigious award due to her magnificent contribution to infectious disease control, immunology, vaccine development, and clinical trial. Such as the Gold medal in Biological Sciences from the Bangladesh Academy of Science, Moselio Schaechter Award by the American Society for Microbiology (ASM), Christophe & Rodolphe Mérieux Foundation Prize, French Academy of Sciences, Prof. C.N.R. Rao Prize from TWAS. She is a laureate of the 2020 L'Oréal-UNESCO For Women in Science Award for her contribution to understanding and preventing infectious diseases affecting children in developing countries, and promoting early diagnosis and vaccination with global health impact. Dr. Qadri won the Ramon Magsaysay Award 2021, known as Asia's Nobel Prize.

FARAH QAMAR

Aga Khan University

Professor Qamar is a clinical researcher with over 15 years of experience. Her most notable achievements include spearheading the outbreak investigation of XDR typhoid in Hyderabad, Pakistan, and introducing the newly approved Typhoid conjugate vaccine (TCV) into the national immunization program. Her work has been translated into global policy. She has served on multiple national and international advisory boards, Professor Farah's expertise in clinical research has significantly impacted infectious diseases and global health policies. With nearly 100 publications and active participation in global health initiatives, she has earned the Presidential Medal of Excellence, highlighting her significant contributions to public health.

SAQIB QAZI

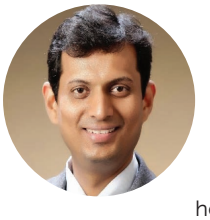
Aga Khan University

Dr. Qazi is a constant Paediatric Surgeon and currently working as Assistant Professor of Paediatric Surgery at Aga Khan University, Karachi, Pakistan. Dr. Qazi did their MBBS from remote city of Larkana, Pakistan and Post Graduation in Paediatric Surgery and are a Fellow of College of Physicians & Surgeons of Pakistan.

EILEEN QUINN

PATH

Eileen Quinn is the Deputy Director of Policy, Access, and Introduction at PATH's Center for Vaccine Innovation and Access. She has over thirty years of experience advancing issues at the intersection of science and public policy including public health, climate change, energy, and biotechnology. Prior to joining PATH in 2006, she spent six years as Deputy Director of the Alliance for Healthy Homes and ten years as Communications Director for the Union of Concerned Scientists. Previously, she was a producer for seven years at C-SPAN, producing the call-in talk shows and coverage of Congress and election campaigns.



SUSHANT SAHASTRABUDDHE

International Vaccine Institute

Sushant Sahastrabuddhe has a total of 20 years work experience in public health and vaccine development projects in multiple countries; 18 years' experience in vaccinology with a certificate in vaccine science and policy and 13 years' experience in vaccine lifecycle management with a focus on vaccine development, policy, and programs. Skills range from clinical medicine to clinical research, epidemiology, biostatistics, surveillance, program management, and fund raising.

He is currently leading a team of around 40 scientists (clinical, regulatory and operational) and administrators to implement vaccine development programs across different parts of the world. The clinical group is leading studies in Cholera, Typhoid, HPV, Chikungunya, COVID-19, HEV, among other pathogens. The grants include development of a novel typhoid conjugate vaccine at IVI (~$29M), Chikungunya vaccine ($24M), and COVID vaccine ($45M) and have teams working in various areas of vaccine development (process development, clinical immunology, clinical development, biostatistics, clinical operations, and quality management) working with him.

He has been involved in more than 5 phase I clinical trials, 5 phase II clinical trials and multiple phase III clinical trials for various vaccines.

He joined the staff of the International Vaccine Institute in Seoul Korea and in 2021, he worked as Associate Director General, Typhoid Program. Since 2023, he's acting Deputy Director General of CARE(Clinical-Assessment-Regulatory-Evaluation) unit.

MAMAN LAMINOU SANI

Regional Hospital Centre, Maradi

Maman Laminou Sani completed their medicine degree at the University of Maiduguri in Nigeria from 1998 to 2006, then general surgery from 2008 to 2015(diplôme d'étude spécialisé en chirurgie générale en 2015 a l'université Abdoulmoumouni de Niamey). He is working for the government attached to the Ministry of Health.

His initial post was Agadez on the 8 regions of Niger from 2015 to 2020. He was chief surgeon from 2016 to 2020. Now he is in Maradi.

YAKOUBOU SANOUSSI

Hopital de la SIM Galmi, Niger

Yakoubou Sanoussi is the Director of SIM Galmi Hospital. Before being named Director in June 2022 he was chief of surgery and director of a General Surgery training program and was responsible for all surgical patients, training African residents and assisting junior faculty. He was also member of the hospital leadership team. He was board member of SIM Niger as well as the Danja hospital fistula Board.

Yakoubou is a general surgeon member of the Pan African Academy of Christian surgeons, the West African College of surgeon and the East-Central-And Southern African College of Surgeon.

JYOTSHNA SAPKOTA

FIND

Dr. Jyotshna Sapkota, MBBS, MD in Clinical Microbiology, holds the position of project manager at FIND. In addition to her role at FIND, she is an Associate Professor at Nepal Medical College, Nepal. Jyotshna has significant contribution to the field of diagnostic research, particularly in the evaluation of tests for typhoid and other febrile illnesses.

JESSICA SEIDMAN

Sabin Vaccine Institute

Jessica Seidman is an epidemiologist with nearly 20 years of experience in global health research. She has worked on several multi-disciplinary, multi-national collaborative research studies with an emphasis on vaccine preventable diseases and maternal and child health. At Sabin, Jessica has worked on improving methods to measure enteric fever disease burden and a clinical trial evaluation of fractional booster doses of COVID-19 vaccines. Prior to joining Sabin, Jessica spent 12 years working in the Division of International Epidemiology and Population Studies, Fogarty International Center, US National Institutes of Health where she managed the data coordinating center for an eight-country study of child malnutrition, enteric disease, growth and development. Jessica has a strong commitment to growing and strengthening in-country capacity for data management and data analysis and has organized several training workshops to provide hands-on learning experiences to researchers from low and middle income countries.

MILA SHAKYA

Patan Academy of Health Sciences

Dr. Mila Shakya's research interests are infectious diseases and vaccine-preventable diseases. She is currently involved in studies on the efficacy of the typhoid conjugate vaccine TyVAC (Assessing the Impact of a Vi-Polysaccharide Conjugate Vaccine in Preventing Typhoid Infection Among Nepalese Children — A Phase III Trial) and TyVOID (Assessing the Medium-Term Impact of a Vi-Polysaccharide Conjugate Vaccine in Preventing Typhoid Infections Among Nepali Children) Nepal.

Dr. Mila Shakya's research interests are infectious diseases and vaccine-preventable diseases.

SHRIJANA SHRESTHA

Patan Academy of Health Sciences

Professor Shrijana Shrestha is a Paediatrician currently working as Professor of Paediatrics at Patan Academy of Health Sciences (PAHS), Nepal. She has been practicing Paediatrics for more than 2 decades at Patan Hospital which is a teaching hospital of PAHS and has trained and supervised many medical students, postgraduate residents and junior faculties. She has completed two successive tenures as the Dean School of Medicine, PAHS (2014-2022) during which she contributed to designing and implementing an innovative undergraduate medical curriculum and started the competency-based postgraduate residency program.

Prof. Shrestha has worked as the principal investigator (PI)/co-investigator in several collaborative Research projects with University of Oxford on vaccine-preventable diseases in children. Some of her important projects are: Pneumococcal vaccine (PCV) schedule studies (2015-2016; 2019); PCV impact assessment study (2014-2021); Efficacy of typhoid conjugate vaccine in Nepal: phase 3, randomised, controlled trial (TyVAC; 2017-2020); Assessing the medium-term impact of a Vi-Polysaccharide Conjugate Vaccine in preventing typhoid infections among Nepali children (TyVOID; ongoing), Optimisation of DPT containing vaccine in Infant Immunization schedule (OPTIMMS, ongoing). These research projects are mainly focused on generating local data on disease burden, vaccine schedules, vaccine efficacy and impact which help in policy decisions on new vaccines and schedules.

PETER SKIDMORE

Oxford Vaccine Group

Peter is a Clinical Research Fellow in Adult Vaccinology with the Oxford Vaccine Group, based within the Centre for Clinical Vaccinology and Tropical Medicine at the University of Oxford. He is currently a co-investigator on phase I clinical trials of vaccines for enteric pathogens, including invasive non-typhoidal *Salmonella* and *Shigella*.

CHRISTOPHER SMITH

Imperial College London

Christopher Smith is a specialty trainee in Infectious Diseases and General Internal Medicine in Liverpool, UK. He qualified MBChB (Hons) from the University of Aberdeen before completing Academic Foundation Training in Manchester and Core Training in Liverpool. Following completion of the Diploma in Tropical Medicine at LSTM, he spent a year as a research intern in the *Salmonella* and Enteric Disease group at the Malawi-Liverpool-Wellcome Trust Programme, investigating the economic burden of Typhoid fever.

SAMBA SOW

Center for Vaccine Development-Mali

Pr Samba Sow is a distinguished figure in public health, renowned for his impactful leadership as a former Minister of Health and currently as the Director General of CVD MALI.

His career in public health began with roles in local health departments, where he focused on disease prevention, health promotion, and addressing healthcare disparities. Pr Sows' dedication and innovative approaches have earned him worldwide recognition such as winning the Roux prize in 2017, propelling him to more significant roles in regional and international health administration. Pr Sow serves as a WHO Special Envoy for Covid-19 in West Africa, board member of the CEPI, a member of WHO's Independent Advisory and Oversight Commitee and was recently elected to the US National Academy of Medicine.

As Minister of Health, he has led reforms in healthcare policy, primary health care, and accessibility to healthcare for hard-to-reach populations.

Prof Sow also has conducted many research programs on maternal health and pandemics such as Ebola and Covid. His emphasis on building communities trust through effective communication significantly aided public health response during the Covid-19 pandemic in Mali. He also established Mali's first blood culture surveillance system for children <5 yrs.

Pr Sow has been an advocate for health equity, with a dedication to healthier communities. His tireless efforts in shaping health policies and improving healthcare infrastructure have left a lasting impact on the field of public health amongst Malian Communities. He remains an influential voice providing guidance and expertise to organizations and public health professionals.

SUSHMITA SRIDHAR

Universidad Peruana Cayetano Heredia and University of New Mexico

Dr. Sushmita Sridhar is a Fogarty Global Health postdoctoral fellow at the University of New Mexico based at the Universidad Peruana Cayetano Heredia in Lima, Peru. She completed her PhD in microbial phenotyping and genomics at the University of Cambridge and the Wellcome Sanger Institute, where she became interested in antimicrobial resistance and using genomics and higher-throughput screening methods for pathogen surveillance, particularly in low-resource settings. She recently finished a postdoctoral fellowship at Massachusetts General Hospital using genomic approaches to characterize multidrug resistant Klebsiella pneumoniae and E. coli from diverse global settings. Sushmita is increasingly interested in improving efforts for pathogen surveillance as well as developing capacity for genomics in lower-resource settings. Her current work is focused on pathogen and antimicrobial resistance gene surveillance of urban wastewater in Peru, as a proxy for community-level burden of disease and drug resistance. One of the research goals for this project is to determine the burden of non-typhoidal and typhoidal *Salmonella*, if detectable, in these samples.

JEFF STANAWAY

University of Washington

Jeff Stanaway, PhD, MPH, is an Associate Professor of Health Metrics Sciences and Global Health at the Institute for Health Metrics and Evaluation (IHME) at the University of Washington. He has been part of the research team for the landmark Global Burden of Disease since 2013. In this role, he models morbidity and mortality from enteric diseases and environmental risk factors. His research focuses on macro-epidemiology with a special interest in understanding connections between the physical environment and the spatiotemporal distribution of disease and how these connections may inform interventions, surveillance, and research.

DUNCAN STEELE

Bill & Melinda Gates Foundation

Duncan Steele, PhD, is a South African trained microbiologist with experience in diarrhoeal diseases and clinical studies. He leads a team focused on developing safe, effective and affordable vaccines for the major diarrheal and enteric pathogens including rotavirus, cholera, *Shigella* and enteric fever. This encompasses products from early pre-clinical data through to policy decisions and country-led introductions. The vaccine strategies and priorities are driven by evidence generated in large epidemiological studies supported by EDGE.

Previously, Duncan was a Technical Advisor at PATH, working with the Rotavirus Vaccine Program (funded by Gavi) and with the Advancing Rotavirus Vaccines program and Enteric Vaccines Initiatives (both funded by the Gates Foundation). Earlier, at the Initiative for Vaccine Research, Department of Immunization, Vaccines and Biologicals, World Health Organization, Duncan was responsible for the diarrheal disease vaccines portfolio, coordinating a global strategic agenda for disease burden and vaccine research for the major diarrheal and enteric diseases. In this role, he coordinated and facilitated vaccine clinical trials in Africa and Asia and coordinated regional surveillance networks in Africa, the Middle East, and Eastern Europe in collaboration with the WHO Regional Offices, ministries of health, PATH, and CDC.

Formerly, Dr. Steele was Director of the SA MRC Diarrhoeal Pathogens Research Unit at the Medical University of Southern Africa, South Africa, where he developed a program of research activities with local and international collaboration and funding that expanded into other parts of Africa. He established a vaccine clinical trial site in the Madibeng District, South Africa which conducted several international studies undertaking the clinical evaluation of rotavirus vaccines, live attenuated influenza vaccines and other childhood vaccines. Dr. Steele is the author of more than 350 scientific publications on vaccine research, development, evaluation, and diarrheal diseases.

ANELEY GETAHUN STROBEL

Peter Doherty Institute for Infection and Immunity, University of Melbourne

Aneley is a research project manager on antimicrobial Resistance at the Peter Doherty Institute for Infection and Immunity in Melbourne. She is an accomplished public health physician with a career spanning 25 years in Africa, Asia and the Pacific.

Aneley's research interests are mainly in communicable diseases and antimicrobial resistance. She actively works to establish collaborative networks, fostering partnerships among organizations and experts in the realm of epidemiology and public health to improve population health.

Aneley holds a PhD form the Peter Doherty Institute at the University of Melbourne, a Master degree in clinical tropical medicine from the Mahidol University in Thailand and a Medical Doctorate from Addis Ababa University in Ethiopia.

MARCELO SZTEIN

University of Maryland School of Medicine

Dr. Sztein is Professor of Pediatrics, Medicine and Microbiology and Immunology at the University of Maryland (UMB). Dr. Sztein is also Associate Director for Basic and Translational Research, Leader of the Immunology Group, and Chief of the Cellular Immunology Section at the prestigious Center for Vaccine Development and Global Health (CVD) and Director of the Flow Cytometry and Mass Cytometry Core Facility at UMB.

Dr. Sztein is an accomplished investigator in immunology of infectious diseases. To date he has published 250 papers in peer-reviewed journals and written 35 invited chapters. In 2002 he established the Immunology Group at the CVD, to centralize and expand interdisciplinary efforts in translational research to accelerate vaccine development. Over the past 3 decades he has directly mentored over 30 postdoctoral fellows, medical fellows, graduate students and visiting scientists from the U.S. and overseas. Moreover, he has extensive experience in managing large multidisciplinary teams of investigators as part of NIH contracts and U19 grants and served as Senior Immunologist and other leadership positions in Vaccine Testing Evaluation Units (VTEU)- and Collaborative Influenza Vaccine Innovation Centers (CIVICs)-sponsored studies since 1990.

Dr. Sztein's research focuses on understanding the mechanisms underlying the generation of the innate and adaptive immune responses to infectious organisms and vaccines in humans and animal models and host-pathogen interactions. He has studied children, young adults and the elderly following exposure to wild-type organisms and/or immunization against, among others, *Salmonella* Typhi, *Shigella*, Enterotoxigenic *E. coli*, *V. cholerae*, hepatitis B, *P. falciparum*, influenza, *F. tularensis* and Ebola.

KUDZAI PATIENCE TAKARINDA

National Microbiology Reference Laboratory Zimbabwe

Kudzai is a highly skilled Medical Laboratory Scientist and Epidemiologist, with a Master of Public Health degree from the University of Zimbabwe. She brings with her a wealth of experience spread between research, teaching, and multidisciplinary diagnostic laboratories. She is a collaborative researcher and surveillance expert on antimicrobial resistance of microorganisms, including clinical and environmental surveillance of *Salmonella* and molecular epidemiology. She is a passionate advocate for emergency management, epidemic preparedness and response, disease surveillance, and health systems strengthening. Kudzai is the author of several scientific publications and has presented her work at various international conferences. She is a dedicated and caring individual who is committed to making a positive impact on the world. Currently, Kudzai is based at the National Microbiology Reference Laboratory, Zimbabwe.

DIPESH TAMRAKAR

Dhulikel Hospital-Kathmandu University Hospital

Dr. Dipesh Tamrakar an assistant professor in the department of community medicine at Kathmandu University School of Medical Science. He is also an adjunct faculty for infectious diseases epidemiology in the department of public health and community programs. He is leading the multi-site multi-country surveillance of enteric fever in Asia project in Nepal which tries to characterize the burden and antimicrobial resistance of enteric fever as well as study the effectiveness of recently introduced typhoid vaccination. He is also leading a phase III clinical trial of adjuvant recombinant SARS-CoV-2 Protein subunit Vaccine and oral cholera vaccine. He is also working as an Infectious disease expert in the Rapid Response Team of Dhulikhel Hospital Kathmandu University Hospital and Kathmandu University.

ARIF MOHAMMAD TANMOY

Child Health Research Foundation

Arif Mohammad Tanmoy is currently working as an Associate Scientist at the Child Health Research Foundation (CHRF) in Dhaka, Bangladesh. In this capacity, he leads the CHRF genomics team, operating under the guidance of Professor Samir Saha and Dr. Senjuti Saha. His contributions have been instrumental in establishing a sequencing facility at CHRF and enhancing genome analysis pipelines. As a vital member of the bioinformatics team, he played a pivotal role in designing the genotyping system for *Salmonella* Paratyphi A and wrote the Paratype script.

Arif has successfully submitted his Ph.D. thesis at the Erasmus University Medical Center in Rotterdam, the Netherlands and is currently awaiting his defense. He was awarded the "ARTS" Ph.D. scholarship from IRD, France, in support of his doctoral research. His Ph.D. thesis is focused on investigating the population structure and antimicrobial resistance (AMR) of *Salmonella* Typhi in Bangladesh. Notably, he conducted and published the first large-scale genomic study of *Salmonella* Typhi from Bangladesh. Furthermore, he made significant contributions to another recent typhoid genomic epidemiology study in South Asia, published in 2022.

Arif earned his Master's degree from the Department of Biochemistry and Molecular Biology at the University of Dhaka, Bangladesh. To date, he has authored 20 publications in peer-reviewed journals and presented many conference abstracts.

NADA TAQI

World Health Organization

Dr. Nada is a Yemeni physician, who specialises in public health, and health management, planning and policy from the University of Leeds.

She has more than 10 years of experience in Vaccine Preventable Disease (VPDs) prevention and control, with long experience working in Pakistan as an international VPDs technical officer, where she worked in the establishment and expansion of typhoid sentinel site surveillance after the introduction of TCV in routine immunization. She supported decision-makers in further understanding the country's typhoid epidemiology, evaluating the impact of TCV introduction, and estimating the proportion of Extensive Drug Resistance (XDR) typhoid among cases.

She also has solid experience in Polio eradication, measles elimination and cholera control, working in both, developmental and emergency settings.

THARANI PRIYA THIRUMOORTHY

Christian Medical College, Vellore

Tharani Priya Thirumoorthy, a doctoral student working under the supervision of Prof. Balaji Veeraraghavan in the Department of Clinical Microbiology, Christian Medical College, Vellore, India. She is interested in exploring and understanding the mechanisms of antimicrobial resistance, disease transmission dynamics, and bacterial evolution in *Salmonella* Typhi. In 2022, she was awarded a prestigious travel grant for the 16th Asian Conference on Diarrheal Diseases and Nutrition (ASCODD), Kolkata India. Currently, her research work focuses on genomic epidemiology, plasmids involved in transferring resistant determinants, and monitoring the transmission dynamics of *Salmonella* Typhi in community settings and outbreaks.

CATHERINE TROMAN

Imperial College London

Catherine Troman is a Senior research technician within the Vaccine Epidemiology Research group at Imperial College London. She contributes to projects on direct detection of poliovirus in stool and wastewater samples, and also projects involving wastewater surveillance and detection of *Salmonella* Typhi. Both of these methods include targeted PCR and sequencing of the products using Oxford nanopore sequencing technology.

EUNICE UBOMBA-JASWA

Water Research Commission

Dr. Eunice Ubomba-Jaswa holds a PhD in Microbiology from the Royal College of Surgeons in Ireland (RCSI) and an MSc in Medical Microbiology from the London School of Hygiene & Tropical Medicine (LSHTM), UK. Her areas of expertise lie in microbiological water quality and how it ultimately affects human and ecosystem health. Dr. Ubomba-Jaswa is currently a Research Manager: Water Resources Quality at the Water Research Commission (WRC) in South Africa where she manages a portfolio of projects that deal with the thematic areas of source water pollution and protection (including both microbial and chemical emerging contaminants), water-related human health and WASH activities. She also supervises both PhD and MSc students registered in a number of universities in South Africa. She

has co-authored over 30 publications which involve water research as well as popular articles which address a variety of topical science issues regarding water, the environment and health. She also sits on a number of editorial boards, technical committees and working groups involved in water, health and environmental issues.

MUHUMUZA UMAR

Africa Centers for Disease Control

Dr. Muhumuza Umar is a dedicated researcher, medical doctor and public health practitioner with a strong commitment to extending comprehensive healthcare to improve health outcomes for marginalized populations. With frontline experience combating epidemics, pandemics and infectious diseases, he leads pandemic preparedness efforts and founded the "Hope for Refugees" advocacy group, championing increased health services for refugee communities. Driven by his role in Africa's CDC "Bingwa" initiative, he boosts COVID-19 vaccinations and addresses vaccine hesitancy. As a team lead in the East African Community Youth Ambassadors' division of health and environment, he focuses on fostering positive climate sensitive health behavior change. Dr. Muhumuza envisions promoting health equity for marginalized communities and empowering young refugee women to advocate for their health. His vision includes influencing policy through research, establishing mobile clinics, and creating a user-friendly health app for enhanced access.

KIRSTEN VANNICE

Bill & Melinda Gates Foundation

Kirsten Vannice, PhD, MHS, joined the Bill & Melinda Gates Foundation in 2020 as a Senior Program Officer in the Enterics, Diagnostics, Genomics & Epidemiology program, primarily supporting the *Salmonella*, Shigella, and Hepatitis E vaccine and surveillance portfolios. Her career has spanned both domestic and international health, focusing on communicable disease surveillance, outbreak response, and vaccine development, evaluation, and policy. Prior to joining the Foundation, Kirsten was an Epidemic Intelligence Service Officer with the U.S. Centers for Disease Control and Prevention, hosted by Public Health–Seattle & King County. Previously, as a Scientist with the World Health Organization's Initiative for Vaccine Research, Kirsten led and supported global vaccine research and policy development for several vaccines against mosquito-borne diseases, including dengue, Zika, malaria, Yellow fever, and Japanese encephalitis. She has been deployed internationally and domestically to support local Ebola and COVID-19 responses. She was also a Fellow at the U.S. Department of Health and Human Services, National Vaccine Program Office and Research Assistant with the Rockefeller University. Kirsten received her PhD and MHS degrees from the Johns Hopkins Bloomberg School of Public Health, Department of International Health, Global Disease Epidemiology and Control.

ALUMITA VUAKANISAKEA

Ty-Five Project, International Vaccine Institute

Dr. Vuakanisakea is a medical doctor currently leading the Typhoid in Fiji–Vaccination and Elimination (Ty–FIVE) project in the Northern Division, Fiji, which covers a population of 139,803. Her areas of interest and passion are Public Health and Primary Health Care, particularly in the prevention and control of Communicable Diseases and improving population health outcomes. She has worked for fifteen years in a mixture of urban and rural settings in Fiji as a Primary Health Care and Public Health Physician and hospital manager.

CELESTINE WAIRIMU

Kenya Medical Research Institute

Celestine Wairimu is a research scientist at the *Salmonella* AMR Surveillance Unit in Centre for Microbiology Research, Kenya Medical Research Institute. She holds an MSc in Medical Microbiology from Jomo Kenyatta University of Agriculture and Technology. Over the past seven years, she has actively participated in conducting research on antimicrobial resistance and the epidemiology of enteric pathogens, including *Salmonella*, Vibrio cholerae, and Shigella. She has co-authored seven publications in peer-reviewed journals. Currently, she is focused on studies investigating the role of carriage in the transmission of multidrug-resistant *Salmonella*. Her research interests include the gut microbiome, genomics, bioinformatics, Enterobacterales, and antimicrobial resistance.

JO WALKER

Yale School of Public Health

Jo Walker (they/them) is an epidemiologist and doctoral candidate in Virginia Pitzer's research group at the Yale School of Public Health, where they apply quantitative tools to improve the surveillance and control of typhoid fever. Before arriving at Yale, Jo worked on influenza and COVID-19 modeling at the Centers for Disease Control and Prevention in Atlanta, their hometown. Their research interests with a background in mathematical modeling, transmission dynamics, and vaccine research When Jo is not building models or writing their dissertation, they enjoy cooking, playing basketball, and exploring new places.

TAHIR YOUSAFZAI

Aga Khan University

Dr. Tahir Yousafzai is an infectious diseases epidemiologist, holding a PhD in clinical epidemiology with a focus on disease surveillance from the prestigious Kirby Institute at the University of New South Wales in Australia. Presently, he serves as an Assistant Professor of Research at the Department of Paediatrics and Child Health at the Aga Khan University in Karachi, Pakistan. Additionally, he holds the position of Adjunct Senior Lecturer at the School of Population Health, UNSW Australia. His research interests encompass a wide spectrum, including the surveillance of vaccine-preventable diseases among children, monitoring viral hepatitis, including the utilization of population-wide linked data, and assessing the impact of newly introduced pediatric vaccines and vaccine acceptance.

RAPHAËL ZELLWEGER

International Vaccine Institute

Raphaël Zellweger is a Senior Research Scientist in the Unit of Epidemiology, Public Health and Impact (EPIC). He leads the department of Immunoepidemiology, where he oversees projects at the interface of immunology and epidemiology ranging from pre-clinical development to disease surveillance and vaccine roll-out. Prior to joining IVI, Raphaël has worked in vaccine immunology, infectious disease epidemiology and antimicrobial resistance in academic settings.

Raphaël has a PhD in immunology from ETH-Zürich (Switzerland) and performed his post-doctoral research on dengue virus at the La Jolla Institute near San Diego (California, USA). Subsequently, he undertook training in epidemiology and public health (MPH) at the London School of Hygiene & Tropical Medicine (UK), from which he also holds a postgraduate diploma in infectious diseases.

YIYUAN ZHANG

Oxford Vaccine Group and National Institute for Health and Care Research Oxford Biomedical Research Centre

Yiyuan obtained her master and PhD degree in Statistics from the University of Warwick and bachelor degree in Accounting and Finance from Xiamen University. She joined the Oxford Vaccine Group Department of Paediatrics in 2022 as a medical statistician. She has been involved in studies of typhoid vaccine and Nipah virus vaccine.

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75	**Nakakana, Usman Nasir**	Safety and Immune Response of a Trivalent Vaccine Against iNTS and Typhoid Fever in European and African Adults: A Phase 1/2a Observer-Blind Multi-Country Study
76	**Naseer, Omera**	Antimicrobial Resistance in Blood Culture Isolates of *Salmonella* Typhi and Paratyphi Received from Laboratories Across Pakistan From January to December 2021
77	**Niang, El Hadji Aly**	An Outbred Mouse Model of Invasive *Salmonella* for Study of Pathogenesis and Development of Vaccines
78	**Nnadi, Nnaemeka**	Characterization, and Comparative Genomic Analysis of Two Lytic Bacteriophages Infecting *Salmonella Typhi*
79	**Nnani, Yvonne**	Mama Put Joints Increases the Causes and Spread of Typhoid Fever to People of Aba Town in Abia State of Nigeria
80	**Odeyemi, Jesutofunmi**	Genomic Characterization of *Salmonella* Strains Isolated From Household Water in Municipal Ibadan, Oyo State, Nigeria
81	**Odityo, Georgina**	Factors associated with Nontyphoidal Salmonella Infection in Children Below 5 Years in an Urban Informal Settlement in Nairobi, Kenya
82	**Ofiri, Pascal**	Burukutu as a Major Cause Factor and Spread of Salmonella Typhi in Wukari Town of Taraba State, Nigeria
83	**Ofiri, Pascal**	Homemade Water Filter and Boiling to Reduce the Level of Typhoid Fever and Other Water-Borne Diseases in the Wukari Area of Taraba State in Nigeria
84	**Ofiri, Pascal**	Widal Test as a Typhoid Fever Diagnostic Test in Most Health Facilities at Onitsha Town of Anambra State, Nigeria has Led to Ciprofloxacin Misuse and Resistance
85	**Ogunleye, Veronica O**	Slow-growing Salmonella Enterica Typhi Mistaken for *Salmonella* Gallinarum in Ibadan, Nigeria
86	**Ongayi, Duncan**	Salmonella Surveillance Cases at Nyahera Sub County Hospital, Kisumu County, Kenya
87	**Paganotti Vicentine, Margarete**	Development of a Live Attenuated Vaccine against Salmonella Paratyphoid A Using a Human Challenge Model

1. The Current Epidemiological Trend of Typhoid Fever in Kenya: A Case Study of Three Referral Hospitals in Nairobi, Kenya

Melanie Abongo

Aga khan University/NEST360/KNH

INTRODUCTION

Typhoid is still an emerging Global public health burden with increased intensity in low income countries. In 2022, there were reported cases of up to 101,400 cases and 1,205 deaths, with 66% being children aged less than 15 years. There is an estimate of 822 cases per 100,000 in the general populations, children of ages 2 to 4 years of age have even a higher prevalence of 2,243 cases per 100,000. Recent data shows an increase in multi-drug resistant typhoid and most locally available drugs including ampicillin, chloramphenicol, tetracycline, streptomycin and co-trimoxazole. This creates the need for more expensive and rarely available treatment options.

Nairobi City, the capital of Kenya is one of the high endemic key areas in Kenya as it houses three major slums in the city i.e. Kibera, Kayole and Kariobangi slums. The burden of infection is largely due to its low hygiene standards, lack of water and latrines and poor housing facilities. Over the years this condition has not changed, however the population has developed multi drug resistance to the locally available antibiotics, and demand for a scale-up in the management of the disease. With the ongoing scientific advancement, the looming introduction of a typhoid fever vaccine could make a great impact to the country and other low income countries. This study aims to assess the current trend of typhoid fever in this population and current management strategies in anticipation of the roll-out of the vaccine.

OBJECTIVES

This study aims to assess the current epidemiological trends of typhoid fever in Kenya, The secondary objectives of this study are; 1) to describe the prevalence of typhoid fever in the population; 2) to assess the mortality rates as a result of typhoid in the population, and 3) to describe the current treatment options for typhoid fever in Kenya.

STUDY SETTING

The study will focus on the four national government referral hospitals bordering the slums in Nairobi City i.e. Kenyattta National Hospital, Mama Margaret Pediatric Referral Hospital, Mbagathi Hospital and Mama Lucy Referral Hospital.

METHODS

This is a retrospective longitudinal study using the hospital's archived data for five years, this will be retrieved from 1st June 2018 to 1st June 2023 to reveal the longitudinal trends of reported typhoid fever.

RESULTS AND CONCLUSIONS

This study will inform on the most current epidemiological trend of typhoid fever in the region: the impact of the disease on the population and mortality and epidemiology of the disease and the emerging issues on the disease and overlying factors and also illuminate the treatment strategies that are being implemented and the impact of this on the population. The study findings inform on the disease burden and the need for expedited typhoid fever vaccine to the population.

2. Antimicrobial Resistance in *Salmonella* typhi From Febrile Patients in Ibadan, South-West Nigeria

Ini Adebiyi[1], Veronica Ogunleye[1], Oluseyi Elaturoti[1], Moyosore Davies[1], Jesutofunmi Odeyemi[1], Oluwaseun Alaran[1], Adegoke Adeoye[1], Ifiok Udofia[1], Janet Ogundairo[1], Victoria Nwachukwu[1], Halimah Babalola[1], Olayemi Olagbenro[1], Chinasa Agbakwe[1], Oluwafemi Popoola[1], T revor Toy[2], Ondari Mogeni[2], Mohamadou Siribie[2], Aderemi Kehinde[1], Florian Marks[2], Iruka Okeke[1]

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BACKGROUND

Typhoid fever causes considerable morbidity and mortality in Nigeria and other endemic countries. Understanding antimicrobial susceptibility patterns of *Salmonella* Typhi, and resistance trends over time, informs empiric antimicrobial treatment. Use of antimicrobials before presenting at healthcare facilities may reduce pathogen recovery and select for drug resistance. We compared antimicrobial susceptibility patterns of *Salmonella* Typhi isolates recovered in Ibadan from 2017-2020 to those recovered between 2021 and 2023.

METHODS

Consenting febrile patients were recruited at University College Hospital, Our Lady of Apostles Catholic Hospital, Adeoyo Maternity Teaching Hospital, and Kola Daisi Foundation Primary Health Care Centre, Ibadan, between February 2017 and May 2020 and between June 2021 and May 2023. Blood samples were collected and cultured using BACTEC FX40 and patients were interviewed to collect information on antimicrobial use. Pathogens from positive blood cultures were identified using Analytical Profile Index (BioMerieux). Antimicrobial susceptibility testing of pathogens was by Kirby-Bauer method according to the Clinical and Laboratory Standards Institute protocol.

RESULTS

Between February 2017 and May 2020, 4,237 patients were blood cultured, yielding 602 pathogens (14%) and 65 *Salmonella* Typhi isolates. From June, 2021 to May, 2023, 148 pathogens were isolated from 2636 blood cultures (5.6%), of which 34 were *Salmonella* Typhi.

Isolates from 2017-2020 and those from 2021-2023 showed similar resistant rates for ampicillin, trimethoprim-sulfamethoxazole and ciprofloxacin. However, resistance increased from 11% to 38.7%, 16% to 36.4% and 6% to 18.2% for chloramphenicol, amoxicillin-clavulanic acid and ceftriaxone, respectively. Four isolates were resistant to azithromycin. Multidrug-resistance increased from 5/48 (10%) to 12/34(35.3%) between 2017-2019 and 2021-2023. Between 2021 and 2023, 349 recruited patients reported taking antibiotics pre-recruitment, most commonly amoxicillin 89(25.5%) and cefuroxime 62(17.8%) and including 8(2.3%) that had taken azithromycin. Pathogens were recovered from 28 (8.0%) pretreated patients, including 8 *Salmonella* Typhi.

CONCLUSION

Typhoid remains common in Ibadan but recovery rates have declined in recent years, potentially because antimicrobial pre-treatment is common. Of additional concern is the rising rate of resistance to antimicrobials. Advocacy for preventive measures against typhoid, such as conjugate vaccines and improved water and sanitation, as well as improvements in antimicrobial stewardship are urgently needed in Nigeria.

3. Antimicrobial Resistance Pattern of *Salmonella typhi* in Low and Middle-Income Countries: A Systematic Review

Miracle Adesina, Oluwadarasimi Asaolu, Isaac Olufadewa, Ruth Oladele

Slum and Rural Health Initiative

BACKGROUND

Typhoid, commonly associated with *Salmonella enterica* serovar Typhi (*Salmonella* typhi) is a highly pathogenic enteric disease that causes over 100,000 deaths globally, with low- and middle-income disproportionately affected. The effects of *Salmonella typhi* antimicrobial resistance are more pronounced in low and middle-income countries, given its multi-drug resistance abilities (resistance to first-line antibiotics; chloramphenicol, ampicillin, and trimethoprim-sulfamethoxazole (co-trimoxazole), and newer drugs such as the fluoroquinolones and cephalosporins). However, the trend has yet to be understood, systematically analyzed and reported. This study aims to summarize the trends of antimicrobial resistance of *Salmonella typhi* in low and middle-income countries.

METHOD

A comprehensive search was conducted on MEDLINE and Embase for original papers reporting *Salmonella* typhi antimicrobial resistance in low- and middle-income countries where data was collected between year 2000 till date (2023). The study was conducted in line with the Preferred Reporting Item for Systematic Review and Meta-Analyses Guideline. Studies that reported phenotypic resistance only, risk factors for AMR acquisition, did not test sensitivities to antimicrobials of interest, review papers, etc were excluded. Relevant data such as the year of data collection, name of the first author, year of publication, study setting, duration of the study, total number of isolates, and number of resistant strains to different antibiotics such as ciprofloxacin, chloramphenicol, ampicillin, nalidixic acid, and co-trimoxazle were extracted.

RESULTS

Of the 137 studies that met the eligibility criteria, 76.6% (105) were conducted in Asian countries and 23.4% (32) in Africa. In total, 22,839 individual *Salmonella typhi* isolates were recorded of which 20,779 were seen in Asia and 2,060 isolates from Africa. In Asia, *Salmonella typhi* showed the highest resistance to ciprofloxacin (13,018) and the lowest resistance to cephalosporins (1,936) while in Africa, the highest resistance was towards Ampicillin (1,469) and lowest resistance to cephalosporins (110).

CONCLUSIONS

Resistance to *Salmonella typhi* in low and middle-income countries is a growing threat that needs urgent attention. Resistance posed by this organism to newer drugs (fluoroquinolones and cephalosporins) is an alarming issue and is a major cause of failure in treatment. Health educators and policymakers need to create public health programmes and policies to mitigate this urgent.

4. Social Media Information on the Prevention and Control of Typhoid Fever in Africa: A Qualitative Analysis of Tiktok and Youtube-Based Videos

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Slum and Rural Health Initiative

INTRODUCTION

According to the World Health Organization, typhoid affects approximately 9 million people globally. It is endemic in many low-middle-income countries with high mortality rates. Social media platforms such as TikTok and YouTube have become popular sources of health information for many people, but the quality and accuracy of these videos are often questionable. Therefore, this study aimed to assess the quality and content of typhoid fever educational videos on TikTok and Youtube.

METHOD

We conducted a comprehensive search on TikTok and YouTube for videos related to typhoid fever using the keywords such as "typhoid fever", "typhoid fever prevention and control", etc. We included only English-language videos uploaded between 2015 and 2023. We extracted

metadata on the video such as the upload date, country of origin, number of views, likes, and comments. We then evaluated the video quality using the Medical Quality Video Evaluation Tool (MQ-VET), which measures the accuracy, comprehensiveness, and presentation of health information in videos.

RESULT

We identified 24 eligible videos (8 from TikTok and 16 from YouTube). Most videos (87.5%) addressed topics on the etiology, symptoms, prevention, control, myths of typhoid fever, while others (12.5%) provided information about the typhoid fever vaccine. More videos (54.2%) were from Nigeria, and most (33.3%) were uploaded in 2022. Tiktok videos had more views, likes and comments than the YouTube videos. The mean MQ-VET score for the videos was 52.55 ± 12.90, indicating moderate quality.

CONCLUSION

Our study revealed that the quality and content of typhoid fever educational videos on TikTok and YouTube were suboptimal and inconsistent with current evidence and guidelines. There is a need for health professionals to collaborate with social media influencers to produce and disseminate high-quality and reliable health information on typhoid fever.

5. Investigating Chromosomal Integration and the Complexity of Atypical Antimicrobial Resistance in Drug-Resistant *Salmonella* Typhi

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Aga Khan University

BACKGROUND

Extensive drug-resistant (XDR) *Salmonella* Typhi (*S.* Typhi) carrying *Inc*Y plasmid poses a growing public health concern due to resistance against first-line drugs, quinolones, and third-generation cephalosporins. The limited treatment options demand a deep understanding of the genomic characteristics and diverse antimicrobial-resistant (AMR) patterns. These strains exhibit resistance through plasmid or chromosomal integration. From various typhoid surveillance studies, an atypical AMR pattern was observed in *S.* Typhi clinical strains showing resistance to ceftriaxone and quinolones but was sensitive to chloramphenicol and co-trimoxazole. This study investigates the diverse AMR patterns and the genotypic-phenotypic profiles of *S.* Typhi isolates, including those exhibiting atypical antimicrobial susceptibility.

METHODS

Fifteen isolates were selected from typhoid surveillance studies in Pakistan based on resistance patterns. Six isolates were XDR strains, and nine exhibited atypical resistance patterns. The isolates underwent sequencing using the Illumina MiSeq platform, and in silico analysis was performed to identify their genomic characteristics.

RESULTS

Genomic analysis revealed that all isolates belonged to the H58 sub-lineage 4.3.1.1 lineage and harbor resistance to ceftriaxone. Among them, nine were also resistant to ciprofloxacin but susceptible to co-trimoxazole, chloramphenicol or both. In-silico analysis confirmed the XDR phenotype of six isolates with MLST distribution of ST-01 (n=2), ST-102 (n=3), and one predicted as a novel ST. Atypical AMR strains exhibited various geno-phenotypic profiles, with 4/9 isolates confirmed as XDR with ST-102, 4/9 isolates susceptible to both chloramphenicol and co-trimoxazole with ST-102, and 1 isolate sensitive only to co-trimoxazole with ST-1. A degenerative *Inc*Y plasmid was identified in three XDR and three atypical-resistant isolates. Surprisingly, three isolates harboring the blaCTX-M-15 gene showed no plasmid presence, indicating chromosomal integration. Hence, we identified several novel chromosomal integrations with the ESBL region and composite multidrug resistance transposon at different positions with the loss of a plasmid in 02 XDR and 04 atypical resistance isolates.

CONCLUSION

Genomic profiling provided valuable insights into the resistance patterns and genomic characteristics of *S.* Typhi, including ESBL region integration, and partial presence, absence, or loss of *Inc*Y plasmids. The sensitivity of ESBL-producing strains to cotrimoxazole and chloramphenicol emphasises the need for enhanced surveillance and genomic investigations for the effective management of enteric fever.

6. Clinicians Unsatisfied with Current *Salmonella* Diagnostics in Ghana

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BACKGROUND

Salmonella belongs to a group of gastrointestinal pathogens that cause a wide spectrum of diseases from self-limiting gastroenteritis to invasive disease with huge disease burden particularly in Sub-Saharan Africa.

There are concerns about over-reliance on the Widal test in diagnosing Enteric fever and less attention has been given to invasive non-typhoidal salmonellosis (iNTS) diagnostics. This survey therefore sought to explore clinicians' awareness of Non-typhoidal *Salmonella* (NTS) disease and practices towards *Salmonella* diagnostics in Ghana.

METHODOLOGY

The study was a cross-sectional study among medical doctors in the Ashanti Region of Ghana from January-April 2023.

A calculated sample size of 235 was randomly selected from a pool of doctors' profile in the region. Data collection was done using easy-to-answer questionnaire administered via google forms and the Epicollect 5 app targeting the selected doctors. The questionnaire solicited practices towards *Salmonella*-related disease diagnosis and employed the Customer Satisfaction (CSAT) score and Net Promoter Score (NPS) to assess prescribers' satisfaction of these methods in their facilities. Data were imported from MS Excel 2019 into IBM SPSS Version 27 for statistical analyses.

RESULTS

Of the 235 respondents, majority 193 (82.13%) had less than 5% of daily suspected cases of *Salmonella*-related illness. A total of 62 (26.38%) employed non-culture-based method whiles another 34 (14.47%) relied solely on the Widal test in all *Salmonella* diagnoses. Antigen-based Rapid Diagnostic Test (RDT) would have been preferred by 52 (22.13%) if there was one. Majority 204 (86.80%) were either not sure or had never made a diagnosis of NTS. The Widal test is used by 34 (14.47%) of the clinicians in diagnosing NTS whiles another 74 (31.49%) were not sure the Widal test is not indicated for NTS diagnostics. More than half 124(52.77%) of the doctors gave a low CSAT score of current *Salmonella* diagnostic methods at their facility with NPS score of -65.52%. Majority 228(97.02%) called for either new reliable or improvement of existing *Salmonella* diagnostics.

CONCLUSION

This survey is not exhaustive but provides preliminary data of clinicians' practices and concerns about *Salmonella* diagnostics in Ghana which may be a wake-up call for further studies.

7. Mapping Typhoid Fever in Bangladesh Using Environmental Surveillance

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Child Health Research Foundation

BACKGROUND

Typhoid fever, caused by the bacterium *Salmonella* Typhi, remains a significant global public health concern, particularly in many countries in South Asia and Africa. This systemic infection primarily affects the gastrointestinal tract and is commonly transmitted through contaminated food or water. Two groups from Bangladesh and Nepal have conducted successful pilot studies demonstrating that the detection of phages specific to *Salmonella* Typhi (Typhi-phages) in sewage water may serve as an indicator of the presence of typhoid fever in the area. Consequently, surveillance of Typhi-phages may be developed as a rapid, low-cost tool to address the challenges associated with blood culture-dependent typhoid fever surveillance. As part of the ongoing efforts to combat typhoid fever, the Government of Bangladesh is considering the incorporation of the Typhoid Conjugate Vaccine (TCV) into the Expanded Program on Immunization in Bangladesh. We initiated a nationwide study expanding on the utilization of Typhi-phages as environmental surveillance tool to track typhoid hot spots in Bangladesh for prioritization during TCV introduction and subsequently monitoring vaccine impact.

METHODS

In this study, 50 sewage water samples are collected from the largest city of all 64 districts in Bangladesh twice a year, starting from February 2023. Sampling points were plotted on a customized map using My Maps tools, followed by site visits aided by Google Earth. 12 ml water is aseptically collected from designated points and transported to the laboratory within 48 hours, and exact geolocation is captured using a GPS tracker. In the laboratory, the samples are filtered through a 0.22 µm filter, enriched by incubation with *Salmonella* Typhi Ty2 cells, and spotted on a lawn of *Salmonella* Typhi Ty2 cells to identify phage plaques. Field and lab-generated data are managed, monitored and evaluated using Epicollect 5 and Power BI tools.

RESULTS

In the first collection window, between March and May 2023, we collected and tested 2,603 sewage water samples from 64 districts. Of them, 366 samples were positive for Typhi-phages. Average phage positivity was 14.1%, with maximum positivity of 46% in the Narayanganj district, a dense-populated and rapidly growing city; Phage positivity was >20% in 16 districts, between 10 and 19% in 18 districts and <10% in 18 districts (1%~9%). No typhi-phages were detected in 12 districts.

CONCLUSION

This study enables the identification of typhoid hotspots nationwide and can aid in targeted interventions. The evidence generated from this study will serve as baseline data for vaccine introduction, and continued Typhi-phage surveillance can help monitor vaccine impact in the post-TCV era.

8. Managing Clinical Trials in Ghana: Opportunities, Threats and Approaches, the Case of TyVEGHA Study

Patricia Amoah Yirenkyi[1], Michael Nti Ababio[2], John Kojo Menlah[3], Michael Owusu-Ansah[2], Ellis Owusu-Dabo[2]

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BACKGROUND

Clinical trials in Africa are notoriously underrepresented. Clinical trials have been conducted successfully on the African continent in countries such as Egypt and South Africa. In recent years, Ghana has made considerable strides in conducting clinical trials. However, the conduct of trials brings a plethora of opportunities, threats, and risks.

The participation of African countries in clinical trials, while highly constrained by their associated costs, is equally drawn back by their management. This study investigates the potential, opportunities, constraints, and processes in conducting and managing clinical trials in under-resourced settings like Ghana. The findings of this study are expected to identify the potential opportunities that can be leveraged to increase participation in clinical trials.

METHODS

This study will investigate the experiences of the management of the cluster-randomized, controlled Phase IV trial to assess the effectiveness of the Typbar® typhoid conjugate vaccine (TCV) in preventing typhoid infection in children in Asante Akim, Ghana (TyVEGHA) as a case study. We shall sample some management personnel, laboratory, data, and field for the purposes of conducting an in-depth interview to know their experiences.

RESULTS

The study is expected to identify the potential for an increase in clinical trials, the vast number of qualified researchers and supporting staff in the country to implement clinical trials, and the availability of institutional support; an opportunity is the growing credibility of Ghanaian researchers and institutions among funders. Identify how financing constraints clinical trials and existing community, institutional and socio-cultural challenges in managing clinical trials.

CONCLUSIONS

Thus, understanding the proper conduct of clinical trials will help mitigate existing threats, opportunities, and challenges that would yield the desired outcome, propelling Africa to the next level of clinical trials while developing local capacities to promote international collaborations.

9. *Salmonella* Combination Vaccine Research and Development (R&D): Do We Have the Funding and Pipeline Needed to Get a Successful Product?

Alex Asamoah Ankomah, Amelia Hynen, Vipul Chowdhary, Cécile Ventola, Hinjal Bhatia, Lindsay Keir

Policy Cures Research

BACKGROUND

Africa has the highest incidence of invasive nontyphoidal *Salmonella* disease (iNTS) while paratyphoid A causes over 25% of enteric fever in Asia. Alongside this burden, *Salmonella* remains a threat due to antimicrobial resistance, diagnostic challenges, and no approved vaccine for iNTS nor paratyphoid fever. An effective combination vaccine strategy against the leading four serovars is urgently needed for control. This study provides a comprehensive analysis of global R&D funding for *Salmonella* combination vaccines with an emphasis on iNTS, and contextualises this with the pipeline to inform research priorities and investment decisions that would facilitate vaccine approval for paratyphoid fever and iNTS.

METHODOLOGY

Investment data was collected from funders, intermediaries, and product developers from 2008-2021 via Policy Cures Research's G-FINDER survey. Active pipeline candidates were identified from major pipeline data sources including clinical trial databases and publicly available portfolios from 2015–2022. The Portfolio-to-Impact(P2I) tool was used to estimate likely product launches from the 2022 pipeline. Data was analysed by sub-disease type, R&D stage, and funder, using Microsoft Excel.

RESULTS

Global R&D funding totalled $93m from 2008-2021. From 2013's high of $9.6m, funding fell by $5.2m(-54%) in 2016 and then rose steadily to reach $11m in 2021, thanks to Wellcome ($4.0m, 37%). However, the US National Institutes of Health represented the largest funder with $30m from 2008-2021. In 2021, preclinical R&D investments dominated($3.7m, 35%). For iNTS, only $3.9m was invested in 2021, a rise from 2020(up $1.8m, +81%). Like previous years, the European Commission provided most funds in 2021 for a bivalent iNTS-GMMA vaccine($1.6m, 41%). Five new combinations have entered clinical development since 2019 including one bivalent iNTS vaccine. A candidate launch based on a simple vaccine archetype is expected by 2032.

CONCLUSION

There is promising progress with increased R&D investment and the expanding clinical pipeline. However, R&D is dominated by three funders leaving the landscape vulnerable to even small shifts in funding priorities. Increased and sustained investments from a more diversified funder base are needed. Streamlining R&D efforts by defining the preferred characteristics for a combination vaccine and prioritizing candidates with broad geographical use is crucial to achieve a successful launch.

10. A Method to Stratify Vaccine Impact By Wealth Quintile and Subnational Region: the Case of Typhoid Fever Micro-Array Patch Vaccines

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BACKGROUND & AIMS OF THE STUDY

Stakeholders are increasingly interested in the impact and economic evaluations of vaccines that help in addressing disparities and crafting regionally-tailored policies. In order to explore how extant data on transmission, the distribution of risk factors, and poverty could allow for sub-national policies of vaccine prevention, we adapted a transmission model of typhoid. We then apply it to a cost-effectiveness model in India of a novel vaccine presentation, a micro-array patch, which could drive greater benefits through improved vaccination coverage in the lower wealth quintiles.

METHODS & RESULTS

We stratified the transmission model by age and wealth quintiles, linked to a typhoid outcomes probability tree model, we examine the economic value of introducing TCV-MAPs into routine immunization programs of the 36 states and union territories of India. Because injectable TCVs are expected to be introduced in India by 2026, we first use the model to project the expected typhoid transmission levels by the time TCV-MAPs are deployed in 2032. The primary metric of cost-effectiveness is the incremental cost-effectiveness ratio or the cost of each disability-adjusted life year averted. We find that the greater the wealth-related disparity in coverage of the measles-containing vaccine (a proxy for TCV as measles-containing vaccine is administered at the same time as TCV) the greater the likelihood that TCV-MAPs will be cost-effective. In states with a narrower difference in coverage across wealth quintiles, the additional coverage gains to lower wealth quintiles from TCV-MAPs would have a limited impact on typhoid disease burden overall, even when the province has a greater share of its population in the lower wealth quintiles.

IMPLICATIONS

In India, the key drivers of cost-effectiveness are vaccine coverage, followed by access to improved water and sanitation, and disparities among wealth quintiles. Disparity in vaccine coverage among the wealthiest and poorest quintiles within a state was found to be a key determinant of the cost-effectiveness of MAPs. Where greater disparity was consistent with greater cost-effectiveness for TCV-MAPs.

11. Emergence of a Novel Resistance Island Showing Resistance to 4th Generation Cephalosporin and Fluroquinolone in *Salmonella enterica* Typhi Isolated From Pakistan

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BACKGROUND

Typhoid fever is endemic in South-East Asian and African countries with a significantly high incidence and mortality rate. A case of Typhoid fever reported at a tertiary care hospital in Rawalpindi showed resistance to cefepime (4th generation cephalosporin) and several fluroquinolone antibiotics including moxifloxacin. A comprehensive analysis was carried out to understand the underlying molecular basis of the increased resistance to the higher generation antibiotics. Antimicrobial susceptibility assays revealed the isolate to be extensively drug-resistant. Molecular analysis and, whole genome sequencing and annotation revealed the presence of a putative novel resistance island. The resistance island harbored various resistance genes (including *bla*CTX-M15, *bla*TEM-1, and qnrS1), insertion elements and mobile element proteins. An ESBL producing *S.* Typhi harboring a novel resistance island and lacking a discrete MDR plasmid calls for an elaborate surveillance of *S.* Typhi in endemic regions. This would enable physicians to determine the appropriate empirical therapy for Typhoid fever in order to thwart the increasing antimicrobial resistance.

12. Adopting the Test, Treat and Track Malaria Strategy for Managing Typhoid Fever in Kintampo, Ghana: A Nested Health Facility Survey

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BACKGROUND

Diagnosing Typhoid Fever (TF) in rural areas is often based on symptoms and occasionally the use of widal test usually after negative malaria test outcomes thereby resulting in either over or under diagnosis. This does not only affect the true burden of TF but also affect its management especially in the midst of antibiotics abuse and resistance. The purpose of this study was to analyze health facility data to enhance accurate clinical profiling of TF burden by exposure and serve as basis for appropriate management of TF based on the Test, Treat and Track (3Ts) strategy of malaria management and estimate TF and malaria coinfection in a malaria endemic area.

METHODS

Secondary data was extracted from both laboratory and patient records of all suspected TF cases for the period 6th March, 2023 to 15th June, 2023 following the adoption of the 3Ts strategy of malaria management for managing TF in a community clinic which has a daily average outpatient attendance of 100 patients. Every suspected case of TF is tested first for exposure (acute-IGM reactive, chronic-IGG reactive and acute on chronic-IGG/IGM-reactive) using an antibody IGM/IGG test cassette. Diagnosis of TF is only made and reported if a patient is exposed after which treatment is given. Malaria is tested through either rapid diagnostic test or microscopy.

RESULTS

A total of 1570 patients were tested out of which females were 70.8% (n=1112) and males 29.2% (n=458) with a mean age of 32 years. Acute, chronic and acute on chronic exposures represented 19.9% (n=312), 0.3% (n=5) and 3.4% (n=53) respectively of those tested. Exposure amongst females was 21.9% (n=243), 0.3% (n=3) and 4.0% (n=44) whilst that amongst males was 15.1% (n=69), 0.4% (n=2) and 2.0% (n=9) for acute, chronic and acute on chronic exposures respectively. Acute, chronic and acute on chronic exposures in children ≤5 years was low accounting for 4.8% (n=15), 0.0% (n=0) and 3.8% (n=2) respectively as compared to adults ≥18 which accounted for 84.0% (n=262), 20.0% (n=1), 92.5% (n=49) respectively. Malaria coinfection with acute, chronic and acute on chronic exposures was 20.2% (n=20), 0.0% (n=0) and 3.0% (n=3) for respectively. All exposed patients were treated with appropriate antibiotics.

CONCLUSIONS

Exposure to TF was high amongst females and adults. Approximately a quarter of exposed patients had malaria coinfection. Treatment and reporting of TF was limited to only exposure after testing. Adopting the 3Ts strategy of malaria management for the control of TF can be valuable in profiling its burden and appropriate management in rural and malaria endemic areas.

13. The Rapid Emergence of *Salmonella* Typhi with decreased Ciprofloxacin Susceptibility Following an Increase in Ciprofloxacin Prescriptions in Blantyre, Malawi

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BACKGROUND

Ciprofloxacin is the first-line drug for treating typhoid fever in many high burden countries in Africa, but the emergence of non-susceptibility poses a grave challenge to public health programmes. Through enhanced surveillance as part of vaccine evaluation, we set out to investigate the occurrence and determinants of ciprofloxacin non-susceptibility in Blantyre, Malawi.

METHODS

We performed systematic typhoid fever and antibiotic prescription surveillance in two health centres in Blantyre, Malawi between 01/10/2016 and 31/10/2019, as part of the STRATAA and TyVAC studies. Blood culture isolates from study participants underwent i) pefloxacin screening and ciprofloxacin E-tests to identify ciprofloxacin non-susceptibility and ii) whole genome sequencing (WGS) to identify drug resistance mutations and phylogenetic relationships between non-susceptible and sensitive isolates. We constructed logistic regression models to investigate associations between ciprofloxacin prescription rates and the proportion of *S.* Typhi isolates with Quinolone Resistance Determining Region (QRDR) mutations in the following month.

RESULTS

We carried out 11,295 blood cultures and microbiologically confirmed 239 cases of typhoid fever, with isolates from 193 participants sequenced (mean age of participants with sequenced genomes 12.8 years, 47% male). Between October 2016 and August 2019 2.3% (n=4/175) of WGS-confirmed typhoid fever cases were caused by *S.* Typhi with QRDR mutations, compared with 33.3% (n=6/18) in September and October 2019. Nine of the ten *S.* Typhi with QRDR mutations had a decreased ciprofloxacin susceptibility phenotype. Every additional prescription of

ciprofloxacin given to study participants in the preceding month was associated with a 4.2% increase in the relative risk of isolating *S.* Typhi with a QRDR mutation (95% CI, 1.8-7.0%, p=0.0008). Phylogenetic analysis showed that *S.* Typhi isolates with QRDR mutations in September/October 2019 belonged to two distinct sub-clades encoding two different QRDR mutations and were closely related (difference of 0-6 SNPs) to susceptible *S.* Typhi endemic to Blantyre.

CONCLUSIONS

We have shown a close temporal association between empiric antimicrobial usage with an increase of fluoroquinolone non-susceptibility in *S.* Typhi, with two sub-clades responsible for the increase. Decreasing ciprofloxacin usage by improving typhoid diagnostics could help to limit the emergence of resistance. ongoing surveillance following the county-level introduction of typhoid conjugate vaccines is essential to determine not just the impact of TCV on disease incidence but also antimicrobial usage and AMR trends.

14. A Comparison of the Microbiome of Typhoid Patients and Healthy Controls From Malawi and Bangladesh

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BACKGROUND

Typhoid fever, caused by *Salmonella enterica* subsp. *enterica* serovar Typhi, causes over 100,000 deaths per year, primarily in Asia and Africa. Recent sero-survey data from high burden areas has shown that as many as 8 in 100 people are exposed to *S.* Typhi per year, although most of these exposures do not result in symptomatic disease. As the site of entry of *S.* Typhi is the gastrointestinal tract, we hypothesise that gut microbiome characteristics could modify the outcome of *S.* Typhi exposures in endemic regions.

METHODS

We carried out Illumina shotgun metagenomic sequencing from the stool of three groups of participants from Dhaka, Bangladesh, Blantyre, Malawi and Kathmandu, Nepal. The three groups were acute typhoid fever patients, healthy controls who were household contacts of the typhoid fever patients, and people with a high Vi-antibody titre, as a proxy for *S.* Typhi carriage. We sequenced samples from 103 typhoid fever cases, 110 carriers and 97 healthy controls across the three sites. We carried out taxonomic profiling using Metaphlan4 and identified taxa associated with participant groups using linear models within Maaslin2. Functional gene profiling was carried out using GutSmash and BiG-MAP, and comparisons between groups with Maaslin2. Co-variables for both analyses included age, sex, prior antibiotic usage, and sequencing run.

RESULTS

Five species were significantly associated with healthy controls, and one species with typhoid disease, in both Malawi and Bangladesh. Data from Nepal produced no significant associations with participant type. The species associated with health included *Prevotella copri, Haemophilus parainfluenzae*, and *Romboutsia timonensis*. Healthy controls had more functional groups associated with anaerobic fermentation and short chain fatty acid (SCFA) production than typhoid cases in both Malawi and Bangladesh.

CONCLUSIONS

Our findings support the hypothesis that the gut microbiome plays a role in typhoid fever susceptibility in high burden regions. This could be driven by high levels of SCFA producers preventing *S.* Typhi infection. Furthermore, prior work has shown that P. *copri* induces Th-17 mucosal inflammatory response which is vital in the control of invasive *Salmonella* infections, and H. *parainfluenzae* induces gut mucosal (IFN-γ)+ CD4+ T cells, which are important in response to *Salmonella*.

15. Increased Recovery of Beta Lactam-Resistant Invasive Non-Typhoidal *Salmonella* in Ibadan, Nigeria Between 2017 and 2022

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BACKGROUND

Invasive non-typhoidal *Salmonella* are less prevalent than *Salmonella* Typhi in Ibadan, Nigeria but are a significant cause of invasive salmonellosis. This study aimed to assess the recovery trend of invasive non-typhoidal *Salmonella* from blood culture, and antimicrobial susceptibility pattern of isolates in Ibadan, Nigeria.

METHODS

Febrile patients were recruited for salmonellosis surveillance in University College Hospital, Adeoyo Maternity Teaching Hospital, Our Lady of Apostles Catholic Hospital and Kola Daisi Foundation Primary Healthcare Centre from 2017 to 2022 (including during the COVID-19 pandemic). Blood was cultured using the BACTEC FX40 system, isolates were identified using the Analytical Profile Index and antimicrobial susceptibility was performed by disc diffusion method based on Clinical Laboratory Standard Institute Protocols. Unsupervised antibiotic use among patients before and from the start of the COVID-19 pandemic was assessed.

RESULTS

There was a steady increase in non-typhoidal *Salmonella* from blood culture that was only interrupted by a reduction in enrollments earlier in the COVID-19 pandemic. A total of 3(1.83%), 8(7.2%), 14(11.6%), 5(5.9%) and 9 (12.2%) invasive non-typhoidal *Salmonella* isolates were recovered from positive blood cultures in 2017, 2018, 2019, 2020-21 and 2022 respectively. Overall resistance rates to ampicillin, amoxicillin-clavulanate and cefuroxime were 28 (82.3%), 13 (37.1%) and 7 (23.3%) respectively. Compared to other antimicrobial classes, beta-lactam resistance rates increased over the study period. Second generation cephalosporin (cefuroxime) resistance rose steadily from 40% in 2017-18 to 100% in 2021-22, and third generation cephalosporin resistance (ceftriaxone), while remaining low overall, appeared at referral facilities in 2019. No resistance to ceftazidime or ertapenem was recorded. There was a progressive increase in reported antibiotic use from 109 (11.4%) in 2017, to 147 (11.5%) in 2018 to 241 (14.5%) in 2019; then 303 (14.5%) in 2020-21, to 187 (14.8%) in 2022.

CONCLUSION

Recovery of invasive non-typhoidal *Salmonella* and their resistance to beta lactam antibiotics, often used to manage these infections, increased steadily from 2017 to 2022 in Ibadan. This shift in pathogen recovery and beta-lactam resistance is paralleled by increasing evidence of patient self-treatment. Routine surveillance is essential to track resistance trends and inform empirical treatment of invasive salmonellosis in Nigeria.

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16. Efficacy of Maternal Immunization with a Nontyphoidal *Salmonella* Conjugate Vaccine and its Impact on Vaccine-Induced Immunity and Protection in Infant Mice

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BACKGROUND

Invasive non-typhoidal *Salmonella* (iNTS) disease, predominantly caused by serovars Enteritidis and Typhimurium, is a significant public health issue in sub-Saharan Africa with high disease burden in children <5 years old. No vaccines are currently approved for human use. We developed NTS glycoconjugate vaccines consisting of the core and O-polysaccharide (COPS) covalently linked to the type I flagellin protein (FliC) from the homologous serovar. We previously established the immunogenicity and efficacy of the COPS:FliC conjugates in mice and rabbits. For other pediatric vaccines, maternal antibodies can decrease vaccine responsiveness in newborns, possibly enhancing their susceptibility to infection later in life. The present study, therefore, uses the mouse model to investigate the protective efficacy of maternal immunization with *S.* Typhimurium COPS:FliC and addresses whether maternal antibodies influence COPS:FliC immunogenicity and efficacy in early life.

METHODS

Seven-week-old female CD-1 mice were immunized intramuscularly three times (two week intervals) with *S.* Typhimurium COPS:FliC (2.5 µg polysaccharide/dose). Control mice were similarly immunized with PBS or left naïve. Serum was collected two weeks after the third dose. The mice were mated, giving birth to offspring that were either immune (born to COPS:FliC-vaccinated mice) or naïve (born to PBS-immunized or naïve mice). In one experiment, serum was collected from 2-week-old naïve and immune pups that were then challenged intraperitoneally with 8 x 10^2 CFU (~LD_{100} for 2-week-old mice) of *S.* Typhimurium D65 (blood isolate from Mali). In another experiment, naïve and immune pups were immunized intramuscularly with three doses of *S.* Typhimurium COPS:FliC (2.5 µg polysaccharide/dose) or PBS at 2, 4, and 6 weeks of age. A subset of immune pups was left unimmunized to track maternal antibody decay. Serum was collected two days before each dose and two months after the third dose. Nine weeks after the final immunization (when maternal anti-COPS IgG had waned to near background levels), mice were challenged intraperitoneally with 3.5 x 10^5 CFU (~LD_{100} for adult mice) of *S.* Typhimurium D65. In all cases, serum was screened for COPS:FliC-induced IgG by ELISA, and geometric mean titers (GMTs) were calculated.

RESULTS

Maternal COPS:FliC-induced IgG were detectable in 2-week-old infants, and maternal-infant antibody levels were well-correlated (Spearman's $r \geq 0.64$, $P \leq 0.05$). Immune offspring born to COPS:FliC-vaccinated dams were robustly protected from challenge with *S.* Typhimurium D65 relative to naïve controls (efficacy=91-100%, $P<0.0001$). When naïve pups were immunized with COPS:FliC, two doses were required for full seroconversion to anti-COPS IgG, and a third dose boosted titers in all mice. By contrast, immune offspring demonstrated high levels of maternal antibodies prior to vaccination that declined over six weeks but remained elevated over the naïve group for the first month of life ($P<0.0001$). After two vaccine doses, the anti-COPS IgG GMT in the immune group was lower than that of vaccinated naïve offspring at this time point ($P<0.0001$). Three immunizations with COPS:FliC successfully boosted

COPS-specific IgG levels in immune mice to a level comparable to the naive pups (P=0.91). Finally, COPS:FliC vaccination of both naïve and immune offspring provided full protection against challenge compared to PBS-immunized controls (vaccine efficacy=100%, P<0.0001). The unvaccinated immune mice with decaying maternal antibodies showed limited protection (efficacy=27.8%, P=0.26).

CONCLUSIONS

Our results highlight a protective role for anti-COPS:FliC antibodies in controlling NTS infection during early life. They suggest a possible blunting effect of maternal antibodies on COPS:FliC responsiveness that is diminished when adequate doses of vaccine are administered. Importantly, COPS:FliC vaccine efficacy is not compromised by maternal antibodies. These data have translational implications in that maintaining an adequate level of protective anti-*Salmonella* antibodies, either through pediatric or maternal COPS:FliC vaccination (or both), may reduce iNTS disease in infants in sub-Saharan Africa.

17. Hospital Based Surveillance of Enteric Fever in Secondary and Tertiary Care Hospitals and Antimicrobial Susceptibility of *Salmonella* in Chandigarh, North India

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BACKGROUND

Enteric fever is responsible for 26 million fever cases and about 1,00,000 deaths globally. World Health Organization has recommended use of typhoid vaccines in endemic countries. Burden estimates of enteric fever is required to take policy decisions on the introduction of typhoid vaccine in India. This study was planned to estimate the contribution of severe enteric fever among the patients admitted with all febrile illness at secondary and tertiary care hospitals in Chandigarh (urban area), India and antimicrobial resistance among the isolates of *S.* Typhi and *S.* Paratyphi.

METHODOLOGY

A facility-based surveillance system was set up at secondary care hospitals (Civil hospital Sector-45, Government Multi-speciality Hospital, Sector 16) and tertiary care hospital (Government Medical College and Hospital, Sector 32) to enrol patients above six months of age hospitalized with fever from a defined catchment population (residents of Sector 45 and Sector 52) for a period of 2 years (October 2021 to September 2023). Blood samples (3-5 ml in children and 10 ml in adults) were collected, and tested using Bactec® system to identify culture-confirmed typhoid fever. The *Salmonella* positive samples were tested for antimicrobial susceptibility using disc diffusion method. Proportion of enteric fever out of all febrile illness admitted in the study hospital were calculated. The results are reported for the data collected in one and a half year *i.e* October 2021-March 2023.

RESULTS

Out of 20433 patients screened 1459 (7.14%) were eligible to participate in the study (52.78% males). A total of 429 (29.4%) participants were less than 15 years of age. Blood for culture was collected in 1436 (98.4%) participants. *Salmonella* was detected in 57 (4%) blood samples (*S.* Typhi: 31, 2.15% and *S.* Paratyphi: 26, 1.8%). Pediatric age group (<15 years) was more affected (6.5%) as compare to patients with age more than 15 years (2.8%). Proportion of cases were more (10%) in winter season (December-February). *Salmonella* isolates were found to be 100% susceptible to ampicillin, azithromycin, ceftriaxone and cotrimoxazole and least susceptible to ciprofloxacin (28%).

CONCLUSION

The results indicated high admission rate of enteric fever in Chandigarh. High resistance to ciprofloxacin was observed.

18. Development of Live Attenuated Non-Transmissible (LANT) *Salmonella* Typhimurium vaccines

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BACKGROUND

Invasive non-typhoidal *Salmonella* (iNTS) disease, commonly caused by *Salmonella enterica* serovar Typhimurium, is a significant cause of morbidity and mortality in infants and toddlers in sub-Saharan Africa. Previous live NTS vaccine candidates haven't progressed due to prolonged shedding in stool. We have developed **l**ive **a**ttenuated **n**on-**t**ransmissible (LANT) *S.* Typhimurium vaccines with improved safety and reduced shedding, and hence low potential for transmission.

METHODS

We genetically modified the genome of *S.* Typhimurium D65 Δ*guaBA* which is an attenuated strain that requires exogenous guanine for growth. We replaced the wild-type promoter of the gene that encodes single-stranded DNA binding protein (*ssb*), with the P_{BAD}-arabinose inducible promoter using lambda red recombination. We also deleted the Δ*araC* Δ*araBAD* locus to prevent intracellular catabolism of imported arabinose. The resulting recombinant LANT strains were referred to as D65 Δ*guaBA* P_{BAD}-ssb and D65 Δ*guaBA* Δ*araC* Δ*araBAD* P_{BAD}-*ssb*. Live attenuated vaccine CVD 1931 (Δ*guaBA* Δ*clpX*) was used as a comparator within

individual experiments. We determined the persistence, immunogenicity, and protective efficacy of our *S.* Typhimurium LANT candidate vaccines in six-to-eight-week-old BALB/c mice (n=15 mice/group).

RESULTS

Following peroral immunization of mice, we observed that LANT vaccine strain D65 Δ*guaBA* P_{BAD}-*ssb* was shed in stool for 2.00 ± 0 days (mean ± [SD]) which was significantly less than the conventional live attenuated vaccine CVD 1931 (7.53 ± 6.90 days; $P \leq 0.05$, Student's *t*-test). In contrast, D65 Δ*guaBA* Δ*araC* Δ*araBAD* P_{BAD}-*ssb* was shed for 7.86 ± 3.90 days but this was still significantly less than CVD 1931 (13.60 ± 1.05 days; $P \leq 0.0001$). Both LANT vaccines elicited robust serum IgG and fecal IgA antibodies against core O-polysaccharide (COPS). VE of D65 Δ*guaBA* P_{BAD}-*ssb* and D65Δ*guaBA* Δ*araC* Δ*araBAD* P_{BAD}-*ssb* in male mice was 69% ($P \leq 0.001$; two-tailed Fisher's exact test) and 85% ($P \leq 0.001$), respectively, whereas in female mice VE was 85% ($P \leq 0.001$) and 79% ($P \leq 0.001$), respectively.

CONCLUSIONS

We have developed two live attenuated non-transmissible iNTS vaccine candidates that exhibit reduced shedding in stool but maintain immunogenicity and clinical efficacy in mice. We propose to progress these candidates into clinical trials as potential live oral vaccines to prevent iNTS disease in humans.

19. Clinical Profile and Anti Microbial Resistance in Young Children with Typhoid Bacteremia: A Single Centre Experience From A Teaching Hospital Of North India

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BACKGROUND

Typhoid fever has been reported from all parts of the world. With the improvement in the sanitation and standard of living,the disease is uncommon in the developed countries. However,in the developing countries it is still one of the the major infectious diseases.Lack of antibiotic stewardship has also led to an increase in the antimicrobial resistance .A large proportion of young children particularly those below 2 years age remain unprotected because no vaccine is available for them .So this study looked at the clinical profile and antimicrobial resistence in this group of children.

METHODS

This prospective study was conducted at Dayanand Medical College and Hospital, a private tertiary care hospital in Ludhiana,Punjab,India over a 3 year period from March 2020 to February 2023. The study was approved by the institutional review board. Cases were diagnosed as typhoid fever if patients presented with fever (temperature>38C) for at least 3 days and their blood culture yielded S. typhi .Case records were analyzed for clinical data, laboratory parameters, treatment and follow up details.

RESULTS

During the study period total of 9159 children were admitted in pediatrics department,out of which 959 were diagnosed as cases of typhoid fever(on clinical grounds and lab parameters) and out of these typhoid cases 211 were blood culture positive.Out of these 211 cases ,35(16.6%) were in children less than 2 years.Male to female ratio was 1.7:1.Maximum number of cases (43%) were seen during the months of July,August and September. All the patients (100%) had fever at presentation,followed by diarrhea(48.5%),vomiting(31.4%).On examination anemia was present in 31 (88.5%),hepatomegaly (48.5%),splenomegaly (25.7%).Maximum patients (80%) had defervescence within first 7 days of starting antibiotics. On laboratory investigations ALT was raised in 30 (85.7%) cases,LDH (31.4%),Serology i.e. widal test(TO titres more than 160) was reactive in 6 (17.1%) cases.Out of total 35 cases *salmonella* typhi was seen in 31(88.5%) and paratyphi in 4(11.5%) cases.Out of total 35 *salmonella* isolates all (100%) were resistant to naldixic acid,10(28.5%) were resistant to aminoglycosides,2 (5.7%) to fluroquinolones and 9 (25.7%) to both.All patients were unimmunized against typhoid vaccine.29 out of 35 patients were being bottle fed

CONCLUSIONS

This study showed that one of the significant risk factors associated with occurrence of typhoid fever was the continued use of bottle feeding and non vaccination against Typhoid fever.All the *salmonella* typhi isolates were resistant to naldixic acid and aminoglycosides.Now that conjugate typhoid vaccine is available ,the inclusion of this vaccine in the national immunization schedule will go a long way in decreasing the disease burden in this age group.

20. Surveillance of Typhoid Fever in the Peri-urban Area of Burkina Faso: Case of the Nongr Massom Health District

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BACKGROUND

Typhoid fever is an infectious disease caused by *Salmonella typhi*. It is endemic in many developing countries, including Burkina Faso. Leading to complications such as intestinal

perforation, haemorrhage, and sepsis, it represents a major burden for healthcare systems in Africa, which are already under pressure due to the high prevalence of many infectious diseases. Since 2014, a typhoid fever surveillance program has been implemented to estimate its incidence and guide decision-makers in the introduction of a vaccine in Burkina Faso. The aim of this study was to estimate the incidence of typhoid in an urban health district and characterize antimicrobial resistance using data from the Severe Typhoid in Africa (SETA) program.

METHODS

A surveillance in one hospital and one health center has been conducted in the Nongr Massom health district from 2016 to 2019. Eligible patients were those with fever ≥37.5°C axillary or 38°C tympanic, or those who reported history of fever for three consecutive days in the seven days preceding their visit to the health center, and who lived in Nioko 2 or Polesgo. These two peri-urban informal settlements are all part of the area covered by the Ouagadougou Health and Demographic Surveillance System. These are areas with spontaneous, anarchic settlements lacking basic sanitary facilities, running water and electricity, and with promiscuous households favoring the spread of germs. To estimate the incidence of the disease at population level, we applied a Bayesian statistical mixture model.

RESULTS

Of the 4472 participants recruited over 43 months, blood cultures were performed in 4399 (98%). The median age of participants was 10 years (3-25 IQR). Female patients were more represented (56%). Sixteen percent of blood cultures were positive, including 2% with potentially pathogenic germs. The adjusted overall *Salmonella* Typhi incidence per 100,000 person-years of observation (PYO) was 1189 (95% CI, 490-2,940). The highest adjusted incidence rate was observed in the 5-14 age group, with an incidence of 2,493 per 100,000 person-years (95% CI, 546-8,333). In addition, 70% of isolates tested were insensitive to cotrimoxazole and 45% to chloramphenicole.

CONCLUSION

Based on the results of this study, it is important to strengthen strategies for the rapid prevention of typhoid fever. One way of doing this is to introduce the typhoid fever conjugate vaccine into the National Immunization Program, in conjunction with the intensification of WASH (water, sanitation and hygiene) programs, which can also significantly reduce the spread of the disease in urban informal settlements.

21. Effectiveness of iNTS Vaccination in Sub-Saharan Africa

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BACKGROUND

Invasive non-Typhoidal *Salmonella* (iNTS) is one of the leading causes of bloodstream infections especially among children in sub-Saharan Africa (sSA). iNTS disease may be difficult to diagnose, particularly in areas where malaria is endemic, and difficult to treat partly because of the emergence of antibiotic resistance. iNTS disease has been globally associated to 87,100 [53,800-131,000] deaths due to bloodstream infection, with an average Case Fatality Rate of about 15% and age mortality of 1,2 years (Marchello et al. JID, 2021 and the Lancet ID, 2022; Ikuta et al. the Lancet 2022). The Burden of iNTS Disease is estimated in 4.26 million (2.38-7.38) DALYs.

METHODS

We developed an age- and comorbidity- structured model for the transmission of iNTS in sSA. Our model uses a susceptible-infected-recovered framework (Keeling and Rohani, Princeton University Press, 2011), where the population is divided in compartments depending on their age and health status, and transitions between compartments over time. We simulated the transmission dynamic for each country separately, using country-specific population pyramids, comorbidity data and vaccine coverage rates. The impact of the iNTS vaccine introduction has been projected for 49 sSA countries in two scenarios: a status quo and a vaccination scenario using a catch-up campaign followed by a routine campaign. Vaccine efficacy between 85% and 95% has been simulated.

RESULTS

Under the status quo scenario cumulated number of cases estimate in sSA from 2021 to 2038 is 9,733,000. The model shows that 10-year Routine + Catch-Up campaigns between 2028 and 2038 could prevent between 2,605,000 and 2,981,000 cases, when vaccine efficacy is between 85% and 95%. Without any intervention annual number of cases in children below 5 years will grow to an estimate cumulative 9.7 million cases by 2038. The introduction of a 85% (or 95%) effective vaccine in 2028 would prevent 2.6 (or 2.9) million new infections. Our model estimates a reduction of iNTS cases between 41.7% and 47.8% among children below 5 years in all sSA. Assuming a CFR of 15% vaccination would avert between 391,000 and 447,000 deaths over 10 years, reducing BoD by 34,187,000-39,117,000 DALYs for all sSA.

CONCLUSIONS

We evaluated the iNTS disease diffusion in sSA, by country and age class and considering endemic comorbidities. Calculations made with our model highlighted that the iNTS transmission among children below 5 years of age will be increasing over the next 20 years without any health intervention. Significantly, comorbidities are showed to have a great impact on the diffusion of iNTS. Our analyses indicated that vaccination of children below 5 years of age could effectively and efficiently reduce iNTS burden in sSA, providing consistent benefits for the population at risk.

In addition, we have identified the combination of immunization strategies needed to reduce as early as possible the burden of the disease, reducing permanently its incidence.

Our results clearly indicate the importance of evaluating the vaccination impact at the country level, and may be used in helping set priorities for vaccine need, demand and development.

Overall, our findings lead to the conclusion that until safer sources of water and sanitization are not widespread, vaccination against iNTS appears to be a highly beneficial and cost-effective medical measure, possibly to be prioritized as a primary health intervention.

22. Burden of Enteric Fever and Antibiotic Sensitivity in Nepalese Children Prior to Typhoid Vaccine in National Immunization Programme

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INTRODUCTION

Enteric fever is still prevalent with major public health problem in developing and under developed countries. Case fatality rate without treatment is 10-30% and with appropriate treatment is only 1-4%. Gold standard for diagnosis is isolation of *Salmonella* enterica from blood or bone marrow. The rate of gaining resistance to antibiotics is skyrocketing evidenced with emergence of multidrug resistance S. typhi in late 1980s and extensively drug resistant S. typhi in recent days. Azithromycin resistant S. typhi has been isolated from Nepal. Government of Nepal has introduced typhoid conjugate vaccine (TCV) into routine immunization program since April 2022.

METHODS

This study was retrospective descriptive where six-years blood culture records were included and the drug sensitivity pattern were reviewed. The desired variables were encrypted and descriptive analysis made via statistical software SPSS version 20.

RESULTS

The culture positivity rate was 2.8% (1778 positive case among 62,643 samples sent for blood culture) and 7.6% (n=136) among the culture positive cases were *Salmonella* species. *Salmonella* typhi (121; 88.9%) was the most frequently isolated species, followed by *Salmonella* paratyphi A (13; 9.5%) and *Salmonella* paratyphi B (2;1.4%). Children with age 5-10 years was the most affected age group for infection with *Salmonella*, 50.0% (n=68). Most of the cases were isolated during spring season 39.7% (n=54) followed by Summer 26.4% (n= 36). Boys were slightly more affected 56.6 % (n=77) compared to girls 43.4 % (n= 59). Nalidixic acid is resistant in 89.9% *Salmonella* typhi; followed by ciprofloxacin (31.8%), ofloxacin (18.2%), ampicillin (9.6%), azithromycin (8.4%), chloramphenicol (8.2%), cotrimoxazole (5.4%), cefixime (4%), ceftriaxone (2.5%) and cefotaxime (0.0%). Cefixime, ceftriaxone, cefotaxime are 100% sensitive to *Salmonella* paratyphi, followed by cotrimoxazole (92.9%), ofloxacin (81.8%), chloramphenicol (75%), azithromycin (66.7%), ampicillin (60%), ciprofloxacin (50%) and Nalidixic acid (23.1%).

CONCLUSION

The number of *Salmonella* species culture isolatation are declining every year. Fluoroquinolones category second line typhoid drugs have more resistance than first line. However, 3rd generation cephalosporins are promising in killing *Salmonella*. Azithromycin resistant species are also abundant.

23. Emergence of Carbapenem and Azithromycin Resistant XDR *Salmonella* Typhi in Pakistan: A Case Report

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BACKGROUND

This abstract presents a case report describing the emergence of carbapenem-resistant extensively drug-resistant (XDR) *Salmonella* Typhi in a pediatric patient from Pakistan. The study highlights the challenges associated with treating this multidrug-resistant strain and emphasizes the need for effective management strategies. The case involves a seven-year-old female with Down's syndrome

and congenital heart disease who presented with recurring episodes of enteric fever. Previous treatment regimens involving macrolides and carbapenems failed to fully eradicate the infection. The patient was admitted to a government hospital, where blood cultures revealed the presence of XDR S. Typhi, resistant to multiple antibiotics except for azithromycin and meropenem. The initial treatment involved intravenous meropenem and oral azithromycin. However, a subsequent relapse occurred, and the patient was referred to a private hospital for further management. Repeat blood cultures once again showed the presence of S. Typhi but resistant to ampicillin, third-generation cephalosporins, fluoroquinolones, chloramphenicol, cotrimoxazole, azithromycin, and meropenem and sensitive to colistin only.

METHODS

Blood cultures were taken and initially identified using API 20E (bioMérieux) as well as the Vitek MS (bioMérieux). Antibiotic susceptibility (AST) was initially performed via the disc diffusion Kirby-Bauer method and MIC testing for further performed for meropenem, azithromycin and colistin. Cultures were referred to the reference laboratory where two morphologically distinct strains were sequenced, and AST was further confirmed with Microbroth dilution methods (Sensitive, Thermofisher).

RESULTS

During the relapse, blood cultures confirmed the presence of carbapenem-resistant XDR S. Typhi. The patient was treated with intravenous meropenem and colistin for 11 days, which resulted in a positive clinical response. The patient's symptoms improved, and she was discharged from the hospital. Molecular characterization and genome sequencing of the isolated strains revealed hetero-resistant profiles, both with the acquisition of carbapenemase-producing genes and additional antimicrobial resistance determinants including the IncN plasmid. The colony morphology the variant 2 strain containing additional resistance determinants was smaller, indicating a potential fitness cost. Long-read sequencing is currently being conducted to gain insights into the acquisition of the heteroresistance in these strains.

CONCLUSIONS

This case report highlights the emergence of carbapenem-resistant XDR *Salmonella* Typhi in Pakistan, emphasizing the challenges associated with treating this highly resistant strain. The study underscores the importance of surveillance, appropriate antibiotic stewardship, and infection control measures to prevent the further spread of pan-resistant strains. Future research is needed to better understand the resistance mechanisms and develop effective strategies for outbreak control.

24. The Relationship Between Gut Health, Malaria and Enteric Non-Typhoidal *Salmonella* Infection Events

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BACKGROUND

Non-Typhoidal *Salmonella* (NTS) in African children presents as 3 distinct syndromes: asymptomatic enteric NTS exposure (eNTS); diarrhoeal illness (dNTS); or invasive bloodstream disease (iNTS), the most devastatingly severe of these 3 phenotypes. Enteric NTS infections can thus lead to either diarrhoeal or invasive disease. eNTS exposure events are common in Malawi and represent a common primary exposure leading to protective immunity. In Sub-Saharan Africa, individuals with malaria, anaemia, Human Immunodeficiency Virus (HIV), malnutrition, or sickle cell disease are particularly at risk of iNTS. Although the mechanisms by which these risk factors increase an individual's susceptibility to iNTS remain unclear, it is hypothesized that this may be mediated by the effects of these risk factors, particularly malaria, on gut health.

AIM

Explore the relationship between eNTS exposure, malaria, malnutrition, and gut health.

METHODS

We randomly recruited 1000 children aged 0-5 years from a community-based census, resident in a rural area of high malaria prevalence in Malawi from whom stool, and serum samples were collected. Data on risk factors, socioeconomic status, water, and sanitation were collected via rapid diagnostic tests (malaria, sickle cell disease, HemoCue), anthropometry, and electronic reporting. Stool samples were processed for NTS culture and pan-*Salmonella* polymerase chain reaction (ttr). Gut health was assessed through the Micronutrient and Environmental Enteric Dysfunction Assessment Tool (MEEDAT), and stool myeloperoxidase (MPO).

RESULTS

To date, MPO stool ELISAs have been performed on 908 stool samples. Intestinal inflammation (MPO concentration >2000ng/mL) was present in 2.09% (n=19). Severe acute malnutrition/wasting was present in 1% (n=9) by weight-for-height z-scores (<-3SD) and 3% (n=27) by mid-upper arm circumference (<12.5cm). Chronic malnutrition/stunting was present in 12.5% (n=114) by height-for-age

z-scores (<-3SD). MEEDAT and MPO data correlations, inclusive of data on other risk factors will be presented after subsequent analysis.

CONCLUSION

Understanding the association between malaria and impaired gut health could suggest mechanisms for the role of malaria in enabling eNTS exposure events and/or invasive disease. An improved understanding of the impact of malaria on gut health would be essential for informing iNTS disease control measures, either by preventing initial eNTS colonization or preventing those colonizations from becoming iNTS cases through the identification of nutritional or malaria interventions, including informing oral or parenteral vaccine development.

25. Qualitative Study to Explore the Enablers and Barriers of Blood-Draw for Research From a Typhoid Vaccine Clinical Trial Conducted in Lalitpur, Nepal

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Blood sample collection is a common practice in clinical studies, including randomized controlled trials (RCTs). However, there is sparse research on perception on clinical studies involving blood sample collection from sick participants for research purposes. Understanding perspectives on blood collection within and outside clinical studies is crucial to develop participant-centered research and appropriate engagement strategies for upcoming trials.

We designed a qualitative study with an aim to explore the perceptions on blood collection and identify the enablers and barriers for blood-draw from sick individuals for research purposes. Between May 2022 and June 2023, we conducted 41 in-depth interviews (IDIs) with the parents/guardians of the children who were vaccinated in the typhoid vaccine trial alongside the parents/guardians of non-vaccinated children and adults. These participants visited passive surveillance clinic established for an ongoing cohort study following the typhoid vaccine trial. Alongside, five IDIs with the medical officers and nurses involved in the blood-draw process for the study were also conducted.

Participants who had prior experience of blood collection and familiarity with the typhoid vaccine trial were amenable to give blood sample for research. Those with an understanding that blood examination help identify infections were likely to agree for blood-draw for research purposes as well. Trust in research medical professionals and belief in the benefits of research influenced participants' willingness for blood-draw for research. The parents who refused consent for blood draw from their sick children narrated dizziness and physical weakness in children after blood collection. The participants who declined blood-draw were more likely to not know its purpose for research. Fear of pain during the blood collection and the misconception that "too much" blood was being taken were also the reasons for denial.

To facilitate research involving blood collection, it is crucial to improve communication between medical professionals and participants, ensuring that the purpose of blood collection for research is clearly explained and that their concerns are identified and alleviated during the informed consent process. Community engagement efforts could help inform the public about the purpose of blood-draw in research and address misconceptions with the active involvement of medical professionals.

26. Clinical and Epidemiological Characterization, *Salmonella* Exposure, and Sero-Incidence of iNTS in a Large Community-Based Cohort in Malawi (SAiNTS-Malawi Study)

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BACKGROUND

Non-typhoidal *Salmonella* (NTS) are a major cause of paediatric bloodstream infections in sub-Saharan Africa. Understanding the seroepidemiology and correlates of protection (COP) for invasive NTS (iNTS) in relation to risk factors (malaria, anaemia, malnutrition) among children is needed to inform vaccine implementation.

OBJECTIVES

SAiNTS-Malawi aims to: 1) understand the epidemiology of enteric NTS and subsequent acquisition of immunity in children; estimate iNTS seroprevalence and seroincidence; 2) investigate and quantify the impacts of gut health, enteric *Salmonella* exposure, malaria exposure and geographic setting; identify a population COP and 3) understand antibody kinetics in disease and natural immunity.

METHODS

SAINTS is a prospective community cohort study collecting 3-monthly paired serology samples from children ages 0-5 years in Malawi, to measure age-stratified acquisition of lipopolysaccharide O-antigen immunoglobin G antibody

and serum bactericidal activity to the main serovars causing invasive NTS disease (*Salmonella* Typhimurium and Enteritidis). Children were selected from censused randomly selected households in Chikwawa, Malawi, with heterogenous malaria burden. Data on risk factors, socioeconomic status, water and sanitation, were collected via rapid diagnostic tests (RDT), anthropometry, and electronic reporting. Stool samples were processed for *Salmonella* culture and pan-*Salmonella* PCR (TTR-primer). Acute cases of iNTS disease were followed longitudinally.

RESULTS

2,428 children were enrolled. *Salmonella* stool culture positivity in healthy children was 5.3% (n=127) overall: S. Typhimurium 15.0% (19), S. Enteritidis 12.6% (16), S. Typhi 1.6% (2), *S.* species 70.9% (90), and showed a seasonal pattern. Age-stratified distribution of *salmonella* stool culture and PCR positivity showed a sigmoidal distribution, with low exposure in the first 6 month of life (2% culture and 5% PCR positive), exponentially increasing during the weaning period, plateauing after 24 months (10% culture and 20% PCR positive). Malaria RDT positivity at enrollment was 10.7% (261); 31.6% (218/690) in high and 3.0% (43/1444) in low malaria transmission areas. Severe-acute malnutrition was present in 1.3% (31) by weight-for-height z-scores (<-3 SD) and 3.3% (79) by mid-upper arm circumference <12.5cm.

CONCLUSIONS

We will assess NTS immunity and sero-incidence in relation to these epidemiological exposures and risks, to derive COP; identify windows of immune susceptibility; and inform vaccine implementation.

27. The Impact of the Community and Public Health Response to COVID-19 on Paediatric Typhoid Surveillance and Detection in Malawi

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BACKGROUND

Typhoid is an important cause of morbidity and mortality. Disease estimates depend on blood culture confirmation; however, this is dependent on health-seeking behaviour and access to health facilities with blood culture services. The COVID-19 pandemic has affected healthcare attendance, and may affect accurate estimates of typhoid burden.

METHODS

We investigated the impact of COVID-19 on patient attendance, blood culture surveillance and typhoid detection in Malawi, using segmented negative binomial regression, with both 'step' and 'slope' changes post-COVID (01 April 2020 31 May 2022) and spline terms to account for seasonal peaks. We utilised data from: 1. routine paediatric blood cultures collected at Queen Elizabeth Central Hospital (QECH), Blantyre, Malawi, and enhanced community surveillance within the Typhoid Vaccine Acceleration Consortium (TyVAC) phase 3 Typhoid Conjugate Vaccine clinical trial 2. Paediatric in- and out-patient (OP) healthcare attendance data from patient registers at QECH, and two community health centres 3. Malawi National censuses.

RESULTS

COVID-19 substantially impacted paediatric typhoid case detection rates in Blantyre, with an estimated fall of 59.9% (54.3 to 65.5), resulting in an estimated 329 (239 to 419) missed typhoid cases between 1st April 2020 and 31st May 2022. There was a concordant fall in paediatric blood culture collection rates of 56.9% (55.6 to 58.1), with a predicted 26,838 (25,437 to 28,239) being missed. Health facility attendances declined between 39.1% (37.9 to 40.2) and 70.1% (66.8 to 73.5). During the study period, healthcare attendance, blood culture collection, and typhoid detection did not recover to pre-COVID levels, except at Zingwangwa Health Centre.

CONCLUSION

Paediatric typhoid case detection fell substantially post-COVID, driven predominantly by reduced health facility attendance and did not recover within the study period. The proportion of febrile presentations and blood culture positivity did not change, suggesting a substantial burden of typhoid was being missed in the community, potentially leading to increased morbidity, mortality or typhoid transmission.

28. Costs of the TCV Integrated Campaign and Subsequent Routine Delivery in Malawi

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BACKGROUND

In May 2023, Malawi introduced TCV through a nationwide campaign, reaching more than 7 million children younger than 15 years old. The integrated campaign delivered typhoid conjugate vaccine (TCV), measles rubella vaccine, oral polio vaccine, and vitamin A supplementation. TCV is now available in the national immunization program and routinely given to children 9 months old. This study estimates the cost of TCV introduction and delivery through the

integrated campaign and follow-on routine immunization. Understanding the costs of TCV introduction and delivery in Malawi provides critical information to countries considering TCV introduction and will inform budget planning and sustained delivery in Malawi and neighboring countries. This study will provide important empirical evidence to local and international policymakers about the cost of TCV delivery programs and the related cost-drivers.

METHODS

The study will collect data through immunization staff interviews from 50 facilities involved in the campaign and routine immunization activities. Micro-costing methods will retrospectively collect data on resources used for the integrated campaign and for routine immunization delivery in Malawi. Secondary data will be collected on all campaign interventions and on additional vaccines in the national immunization program, to allocate shared cost for the campaign and routine delivery. Financial and economic costs will be evaluated from the provider perspective, with no tracking of the payor.

RESULTS (DATA COLLECTION ONGOING; PRELIMINARY RESULTS AVAILABLE BY DECEMBER 2023)

Results, when available, will report the total financial and economic costs of the campaign, the cost per intervention, and cost per dose of TCV delivered by main activity (e.g., service delivery, training), cost type (e.g., fuel, maintenance, human resources) and administrative level (national, district, health facility). For routine immunization, the study will report on the annual financial and economic costs, cost per dose, and by main activity, cost type, and administrative level.

CONCLUSION

Study results will complement existing data on integrated immunization campaign costs and costs to introduce and deliver TCV. Evidence can be use by policymakers in Malawi and countries in the region to inform decision-making and planning for TCV programs. It can also inform Gavi support for integrated (or single antigen) campaigns.

29. Genetic Adaptation of Nontyphoidal *Salmonella* in Humans, Animals and in the Environment-Anthroponotic Transmission?

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BACKGROUND

Nontyphoidal *Salmonella* causes more than 1.2 million annual deaths worldwide, the majority in resource-limited countries such as sub-Saharan Africa. Nontyphoidal *Salmonella* have also become increasingly resistant to antibiotics and are the most frequent cause of bacteraemia in sub-Saharan Africa. Recent data suggests that this typically livestock- associated pathogen has genetically developed and adapted to different hosts and environments, proposing anthroponotic transmission.

METHODS

Within this study, we collected *Salmonella* from humans (stool and blood), animals and the environment (dust and soil), in Tanzania and in Ghana. Strains were identified by biochemical methods and confirmed using the VITEK 2 System. Serotyping and antibiotic susceptibility testing was performed. Further, isolates were subjected to sequencing using a NextSeq 500 Illumina machine.

RESULTS

9,099 samples were collected. From these, 222 Nontyphoidal *Salmonella* were identified comprising 58 serovars. The highest level of resistance was in humans with fluroquinolone resistance on the increase and multidrug resistance highest in isolates from blood cultures (24%, n/N=11/46). Of the invasive strains, MLST analysis confirmed the serovars and sequence types S. Typhimurium (ST313/ST19) being most common followed by S. Enteritidis (ST11/ST1479) and S. Dublin (ST10). A sequence type overlap amongst humans and livestock or environmental strains was detected for ST19.

CONCLUSIONS

Our study demonstrates a broad serovar distribution of *Salmonella* from livestock and the environment not typically associated with human infections. The substantially high level of multidrug resistance and emerging fluoroquinolone resistance seen in the invasive Nontyphoidal *Salmonella* poses a challenge to current treatment strategies. Interestingly, we found ST19 more common in invasive human disease but also prevalent in samples from livestock compared to ST313, only seen in human samples. These findings are not in line with previous results, mainly from East Africa where ST313 was identified as the dominant sequence type in disseminated human disease, strongly indicating anthroponotic transmission of ST313 but not of ST19 in sub-Saharan Africa.

30. Gastroenteritis Outbreak Isolates of *Salmonella enterica* as High-Risk Agents for invasive Infections in Sickle-Cell Disease Patients in Senegal

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Salmonella enterica groups +2,600 serotypes some of which infecting humans and animals causing two types of diseases, gastroenteritis and invasive infection like

typhoid fever. Outbreaks of *Salmonella* gastroenteritis is very common in low-income countries (LIC), especially in sub-Saharan Africa (sSA). These outbreaks represent an important public health concern in a context of global increase of antimicrobial resistance and the presence of populations at high risk of invasive, life-threatening *Salmonella* infections. Recently, we added genomics as an additional analytic approach of outbreak isolates. We perform whole genome sequencing is performed on Illumina and/or Oxford Nanopore platforms. Genome assembly and downstream analyses including MLST, serotyping, detection of antimicrobial resistance and virulence genes are performed using in-house developed pipelines and freely available online bioinformatics tools. We identified serotype Enteritidis ST11 as a cause of three outbreaks that occurred in Senegal in 2019, 2021 and 2023. Interestingly, the outbreaks of 2019 and 2023 occurred in a densely populated, low-income suburb of Dakar and we found that their respective isolates were genetically very close suggesting a local circulation of these clones causing recurrent epidemics.

Among populations at risk of *Salmonella* infection are sickle-cell disease (SCD) patients. SCD is an inherited genetic disorder of hemoglobin whose prevalence is highest in sSA. Many complications associated with this neglected disease lead to frequent morbidity, high rates of premature mortality and ongoing disability. In Senegal, the estimated prevalence of S hemoglobin allele is ~10% and the incidence of severe sickle cell syndromes is 0.5% of births. Death from SCD complications occurs mostly in children under five years, adolescents and pregnant women. Bacterial infections are a major cause of morbidity and mortality in SCD patients, especially children. The most frequently reported infection in SCD individuals are pneumococcal pneumonia, meningitis and *Salmonella* osteomyelitis. These concerns are exacerbated by frequent emergence of multidrug resistant (MDR) clones of bacteria frequently involved in invasive infections, including sepsis, in SCD individuals.

In order to get an insight on the serotypes of *Salmonella* infecting SCD patients, we conducted a retrospective genomic analysis of 24 isolates recovered from SCD children admitted at the Children and Adolescent Sickle Cell Disease Outpatient Treatment Unit, Children hospital, Dakar, Senegal between 2010 and 2019. The isolates originated from pus (*n* = 12), blood (*n* = 4), urine (*n* = 4) CSF (*n* = 2) lung (*n* = 1) and peritoneal fluid (*n* = 1). WGS analysis revealed several serotypes including Enteritidis (*n* = 8), Typhimurium (*n* = 4), Grumpensis (*n* = 2), Chester (*n* = 2), Typhi, Give, Oranienburg, Nottingham, Colindale, Johannesburg, Lille and Virchow. When conducting a comparative genomic analysis of Enteritidis ST11 isolates from Senegal, we found a close genetic proximity between clones that caused gastroenteritis outbreaks and those isolated from invasive infection in SCD children. Additionally, one isolate of serotype Grumpensis was MDR and carried a large conjugative plasmid that contained several antimicrobial resistance genes, suggesting a potential for high dissemination of AMR genetic determinants. These results highlight the need of an active surveillance of *Salmonella* in SCD patients in sub-Saharan Africa where the incidence of SCD is high.

31. Quinolone Resistance Phenomena Among *Salmonella Enterica* Serovar Typhi and Paratyphi A in Nepal

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BACKGROUND

Increasing resistance to fluoroquinolones (FQ) among *Salmonella enterica* serovar Typhi and Paratyphi A remains worldwide clinical concern. Despite reports of changing resistance trends and alarming nalidixic acid (NA) resistance particularly in emerging *S.* Paratyphi A strains, molecular determinants for quinolone resistance among *Salmonella* isolates from Nepal are limited and mostly confined to *S.* Typhi.

METHODS

We tested antimicrobial disc susceptibility assay of *S. enterica* isolates (n=110) collected and archived under national antimicrobial resistance surveillance program in Nepal with a set of 19 antibiotics. For NA, ciprofloxacin and ofloxacin, minimum inhibitory concentration (MIC) was also determined. Based on the quinolone resistance phenomenon, 16 isolates were further investigated by PCR amplification and sequence analysis of quinolone resistance determining region (QRDR) of *gyrA, gyrB, parC* and *parE.*

RESULTS

We observed 10 different patterns of antibiotic resistance in our *S. enterica* isolates, with dominant NA resistance phenotype. Multiple resistance was observed among few *S.* Typhi isolates, while *S.* Paratyphi A isolates were mostly NA resistant. All of our NA resistant strains harbored mutation in QRDR in *gyrA* with or without *parC*, while no such alterations were seen in *gyrB* and *parE*. NA resistant *S.* Typhi with reduced susceptibility to ciprofloxacin (MICs 0.19µg/ml), and ofloxacin (MIC 0.25µg/ml) exhibited a single point mutation in *gyrA* (Ser83-Phe), while different mutations in *gyrA* (Asp87-Asn) along with *parC* (Ser80-Ile) were observed among ciprofloxacin resistant *S.* Typhi strains (MICs >8µg/ml). Though intermediately susceptible to ciprofloxacin (MICs 0.25-0.38µg/ml) and ofloxacin (MICs 1-1.5µg/ml), *S.* Paratyphi A isolates showed three substitutions: *gyrA* (Ser83-Phe, Gly133-Glu) and *parC* (Thr57-Ser). *parC* mutation in *S.* Paratyphi A was not reported previously from Nepal.

CONCLUSIONS

High level FQ resistance in *S.* Typhi is attributed to multiple mutations in both *gyrA* and *parC* in Nepal. In contrast, *S.* Paratyphi A paradoxically exhibited intermediate susceptibility towards FQ despite the presence of three QRDR mutations in Nepal. Whether all QRDR mutation do not lead to FQ resistance or some mutations possible play compensatory effect, needs further molecular confirmation and a continued AMR surveillance with molecular approach in necessary to address these issues

32. Genomic Analysis of *Salmonella* Kentucky ST198 Resistant to Ciprofloxacin and Cefotaxime Causing Acute Gastroenteritis Among Children in Kolkata, India

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BACKGROUND

Emergence of multi-drug resistant (MDR) non-typhoidal *Salmonellae* (NTS) poses significant burden in healthcare system, mostly affecting the developing countries. *S.* Kentucky has been reported earlier from European, North American, African and Asian countries from agricultural products, foods and various animal species (livestock, pets and wildlife), but is rarely documented from clinical samples. In this study, we have focused on genomic analysis of MDR *S.* Kentucky isolates from stool samples of children with acute gastroenteritis.

METHODS

Rectal swabs from children ≤ 5 years of age with acute gastroenteritis attending the OPD of Dr. B.C Roy Post Graduate Institute of Paediatric Sciences from 2017 to 2023 were collected and processed following standard microbiological protocols for NTS identification. The isolates were tested for antimicrobial susceptibility, AMR genes, plasmid profiles, and multi-locus sequence typing (MLST). Whole genome sequencing (WGS) (Illumina Novaseq 6000) was performed for four MDR *S.* Kentucky isolates from India.

RESULTS

A total of 76 (1.12 %) NTS isolates were recovered by screening 6732 rectal swabs from children with acute gastroenteritis. A total of 15 serovars were identified of which *S.* Typhimurium was predominant (*n* = 22; 28.94 %) followed by *S.* Kentucky (*n* = 11; 14.47 %). Resistance to ≥ 1 antimicrobials was found in 54% of NTS isolates, of which 28% were MDR. Among the serovars, MDR was predominantly observed in *S.* Kentucky (n=10/11; 91%) with a high rate of resistance towards Ampicillin, Nalidixic acid, Ciprofloxacin (100% each), Tetracycline (91%), Streptomycin (45%), Cefotaxime, Ceftazidime, Ceftriaxone and aztreonam (36% each). Less resistance was seen in Gentamicin, azithromycin and cotrimoxazole (< 30%). WGS analysis of MDR *S.* Kentucky revealed the presence of following AMR genes $bla_{CTX\text{-}M\text{-}15}$, $bla_{TEM\text{-}1}$, $bla_{OXA\text{-}9}$, *tetA*, *aadA1* and *aadA2*. Double mutation in *gyrA* (D87Y, S83F) and single mutation in *parC* (S80I) was responsible for ciprofloxacin resistance in this MDR isolates. A single plasmid of IncC type and sequence type 198 was found in all the isolates.

CONCLUSIONS

Increasing AMR was observed against cephalosporins and fluoroquinolones which are the current drug of choice for infection control. The results indicate continuous monitoring of the AMR profiles of the resistant organisms to prevent further spread of AMR gene in other organisms.

33. Urban Rats as Carriers of Invasive *Salmonella* Typhimurium Sequence Type 313, Kisangani, Democratic Republic of Congo

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BACKGROUND

Invasive non-typhoidal *Salmonella* (iNTS-mainly serotypes Enteritidis and Typhimurium) are major causes of bloodstream infections in children in sub-Saharan Africa, but their reservoir remains unknown. We assessed iNTS carriage in rats in an urban setting endemic for iNTS carriage and compared genetic profiles of iNTS from rats with those isolated from humans.

METHODOLOGY/PRINCIPAL FINDINGS

From April 2016 to December 2018, rats were trapped in five marketplaces and a slaughterhouse in Kisangani, Democratic Republic of the Congo. After euthanasia, blood, liver, spleen, and rectal content were cultured for *Salmonella*. Genetic relatedness between iNTS from rats and humans-obtained from blood cultures at Kisangani University Hospital-was assessed with multilocus variable-number tandem repeat (VNTR) analysis (MLVA), multilocus sequence typing (MLST) and core-genome MLST (cgMLST). 1650 live-capture traps yielded 566 (34.3%) rats (95.6% Rattus norvegicus, 4.4% Rattus rattus); 46 (8.1%) of them carried *Salmonella*, of which 13 had more than one serotype. The most common serotypes were II.42:r:- (n = 18 rats), Kapemba (n = 12), Weltevreden and Typhimurium (n = 10, each), and Dublin (n = 8). *Salmonella* Typhimurium belonged to MLST ST19 (n = 7 rats) and the invasive ST313 (n = 3, isolated from deep organs but not from rectal content). Sixteen human S. Typhimurium isolates (all ST313) were available for comparison: MLVA and cgMLST revealed two distinct rat-human clusters involving both

six human isolates, respectively, i.e. in total 12/16 human ST313 isolates. All ST313 Typhimurium isolates from rats and humans clustered with the ST313 Lineage 2 isolates and most were multidrug resistant; the remaining isolates from rats including S. Typhimurium ST19 were pan-susceptible.

CONCLUSION

The present study provides evidence of urban rats as potential reservoirs of S. Typhimurium ST313 in an iNTS endemic area in sub-Saharan Africa.

34. Ceftriaxone-Resistant Typhoid Fever in the United States, 2018–2023

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BACKGROUND

Typhoid fever is a severe systemic infection caused by *Salmonella* enterica serotype Typhi. Antimicrobial treatment is important in the management of typhoid fever to prevent complications and mortality. The recent emergence of ceftriaxone resistance in Typhi isolates has made these strains extensively drug-resistant (XDR), limiting treatment options. In 2018, we initiated a retrospective search and began prospective surveillance for ceftriaxone-resistant typhoid fever cases in the United States.

METHODS

The U.S. Centers for Disease Control and Prevention collects epidemiological and resistance information for all cases of typhoid fever diagnosed in the United States. We considered cases to be travel-associated if patients traveled internationally in the 30 days before illness began. We considered isolates to be resistant to an antimicrobial if the results of susceptibility testing by broth microdilution had a minimum inhibitory concentration in the resistant range or if the isolate's genome harbored a resistance mechanism known to confer resistance to that antimicrobial. Isolates with resistance to ampicillin, chloramphenicol, ciprofloxacin, and trimethoprim-sulfamethoxazole in addition to ceftriaxone were considered XDR.

RESULTS

As of March 31, 2023, we identified 145 ceftriaxone-resistant typhoid cases, with the earliest in 2018; 108 (74%) were XDR. Patients with ceftriaxone-resistant infections had a median age of 11 years (interquartile range, 5–24) and 52% were male. Among 142 patients with known travel history, 114 (80%) traveled to Pakistan, 6 (4%) to Iraq, 4 (3%) to India, 1 (1%) to Afghanistan, and 5 (4%) to multiple countries; 12 (8%) did not travel. Most (88%) patients with XDR infections traveled to Pakistan. Two XDR isolates collected in 2022 and 2023 were also resistant to azithromycin; no ceftriaxone-resistant isolates were also resistant to carbapenems.

CONCLUSIONS

Ceftriaxone-resistant typhoid fever has emerged in the United States; most infections are XDR and associated with travel to Pakistan, but cases have also been observed among travelers to other countries and non-travelers. Ceftriaxone-resistant Typhi isolates remain largely susceptible to azithromycin and carbapenems, agents recommended for the management of XDR strains, but the documentation of XDR isolates with additional resistance to azithromycin underscores the need for clinical vigilance and close public health monitoring.

35. The Anti-Vi IgG Antibody Profile of Typhoid Fever Patients and Their Household Contacts in the Northern Division, Fiji

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BACKGROUND

Vi, the capsular polysaccharide of *Salmonella* Typhi, induces antibodies in some infected individuals but high levels of anti-Vi antibodies are typically associated with vaccination or carrier status. This study was conducted in the Northern Division of Fiji to investigate the anti-Vi IgG antibody levels among residents before the implementation of the typhoid conjugate vaccine (TCV) and to assess the utility of anti-Vi IgG antibody for detection of chronic carriers.

METHODS

The anti-Vi IgG antibody (anti-Vi IgG) profiles of three cohorts were analysed: Group A — acute typhoid fever patients who were followed prospectively. The anti-Vi IgG titre was determined at a median time of one day after diagnosis (IQR 0-4 days) and three months post diagnosis (IQR 2.7-4 months). Group B — included individuals who recovered from culture-confirmed typhoid fever and their serum sample taken at 12-months post diagnosis (median 14 months, IQR 12-17). Group C — household contacts, where the sample was taken from asymptomatic and afebrile household contacts within three weeks after the diagnosis of the index case. All sera were tested at a single dilution (1:100) using an in-house ELISA method. A purified Vi capsular polysaccharide (5 mg/ml, GSK) was used as the capture antigen in the ELISA. Pooled Fijian sera with high anti-Vi IgG titre from a previous study were used as positive control (reference sera) while sera from non-endemic setting were used as the negative control. The anti-Vi IgG positivity cut-off threshold was set at 1.8 $\log_{10}$ reciprocal dilution, which is equivalent to 63 ELISA unit (EU). The reference standard was estimated at 2.4 $\log_{10}$ reciprocal dilution or 251 EU.

RESULTS

Overall, 382 serum samples were analysed to determine anti-Vi IgG titres from 295 study participants (65 in Group A, 110 in Group B and 120 in Group C). The median anti-Vi IgG titres were significantly higher among patients with acute typhoid fever in Group A (1.51 $\log_{10}$, IQR 0.93-1.88) and recovered cases in Group B (1.52 $\log_{10}$, IQR 1.86-1.79), compared with asymptomatic household contacts in Group C (1.28 $\log_{10}$, IQR 0.69-1.65), p=0.004. In Group A, 8% (n=5) of patients had anti-Vi IgG titres > 2.4 $\log_{10}$ which is greater than the cut off threshold of the standard positive reference sera. There was no significant difference in the median anti-Vi IgG titre at diagnosis (1.464 $\log_{10}$, IQR 0.927-1.855) and at three months follow up (1.436 $\log_{10}$, IQR 0.919-1.808), p=0.659 among Group A participants. In Group B participants, *S.* Typhi was isolated from the stool cultures of three asymptomatic individuals with high anti-Vi IgG titre, (>2.4 $\log_{10}$). These individuals were classified as asymptomatic chronic carriers and treated accordingly.

CONCLUSION

The study revealed mixed anti-Vi IgG antibodies levels among patients with acute culture-confirmed typhoid fever, or in recovered individuals. The study confirmed that serum anti-Vi IgG titres were maintained but with no marked increase during the short-term convalescence period after infection. The protective efficacy of anti-Vi IgG antibodies was incomplete as adults with high titres developed symptomatic and culture-confirmed disease although the anti-Vi ELISA deployed could not differentiate the fine specificity of these high titre antibodies. The study demonstrated that an anti-Vi ELISA in combination with stool culture could be used to identify asymptomatic carriers in the study area where the typhoid burden is high, although the value of the ELISA component will likely diminish with the implementation of the TCV.

36. Typhoid Fever and Concurrent Infections with Vector-Borne Diseases Among Patients Presenting with Febrile Illnesses in North India

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INTRODUCTION

Infectious diseases are the leading causes of morbidity and mortality in India. Acute undifferentiated fever is a temporary febrile illness characterised by vague, non-specific symptoms caused by varying etiological agents presenting with overlapping signs and symptoms like high fever, generalised body ache, nausea, vomiting, rash etc. Differentiating patients with typhoid fever from other co-infections such as malaria, dengue and chikungunya on clinical grounds alone is challenging. Typhoid, malaria, dengue and chikungunya share overlapping epidemiological patterns with most cases being reported from tropical/sub-tropical regions of the world, mainly in the monsoon season. Concurrent infection of typhoid with any of these infections may cause diagnostic dilemma for treating physicians.

METHODS

This observational study was conducted over 10 months in a tertiary care hospital in North India. A total of 3182 patients presenting with complaints of fever for 2-14 days were included and evaluated for typhoid fever, malaria, dengue and chikungunya. For typhoid fever, rapid card test (Typhidot) was done; for malaria — rapid antigen testing (RMAT) and thin smear examination was done; dengue and chikungunya testing was performed by IgM ELISA.

RESULTS

Of 3182, 791 patients tested positive on Typhidot (IgM/IgM and IgG) (25.28%). Amongst these 791 cases, typhoid-malaria co-infection amounted to 4.7% (37 patients); typhoid-dengue co-infection were seen in 10.5% (83 patients); typhoid-chikungunya co-infections were reported in 5.9% (47 patients); while typhoid-dengue-chikungunya co-infections were recorded in 7.5% (59 patients). Remaining 71.4% (565) patients tested positive for only typhoid infection.

CONCLUSION

Concurrent infections of typhoid with other infectious agents is a major concern since it can lead to increased incidence of complications. False positives due to cross-reactivity for typhoid with malaria, dengue and chikungunya is another possibility that creates diagnostic ambiguity. Co-infection and cross-reactivity — both pose a challenge to accurate diagnosis leading to mismanagement — in terms of over or under-treatment. So, diagnosticians and treating physicians need to be made aware of both — especially in endemic

regions — to prevent misdiagnosis and mistreatment of patients. Further research can help us comprehend the nature, consequences and pathogenesis of co-infections. It is imperative to conduct additional laboratory tests with gold standards to ensure accurate diagnosis to institute appropriate treatment in a timely manner.

37. Environmental Surveillance for *Salmonella* Typhi in Rivers and Wastewater From an Informal Sewage Network in Blantyre, Malawi

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BACKGROUND

Environmental surveillance (ES) for S. Typhi can provide essential and timely information on the community-level dynamics of typhoid fever, especially in resource poor regions experiencing a high burden of disease. However, many knowledge gaps concerning the feasibility and effectiveness of ES as a tool in public health monitoring remain, especially throughout areas lacking formal sewage systems.

METHODS

We established a standardised protocol for S. Typhi ES. From May 2021 to May 2022, we collected monthly grab and trap (Moore swab) samples from 43 river and informal sewage sites in Blantyre, Malawi. Additionally, water quality measurements, ES site and catchment characteristics and presence of HF183, a marker gene from a human-restricted Bacteroides, were recorded. Their association with S. Typhi detection was investigated in a logistic mixed effects regression analysis. Autoregressive moving average models, accounting for site specific random effects and covariates were fitted to identify whether increases in detection over time corresponded to increases in clinical cases.

RESULTS

Prevalence of S. Typhi in ES samples was 2.1% (1.1-4.0%) and 3.9% (1.9-7.9%) for grab and trap samples, respectively. The presence and abundance of HF183 was a significant predictor of S. Typhi positivity, with presence increasing the odds of finding S. Typhi by a factor of 5.3 (p=0.00241), and each unit increase in the log genome copy number, increasing the odds of finding S. Typhi by an estimated 40.2% (p=4.14e-7). The log catchment population estimate was weakly predictive of HF183 positivity at each site; a unit increase in the log population size corresponded to an estimated 15% increase in the odds of HF183 positivity for any sample at each site (p=0.00882). We could not find any significant relationship between water quality measurements and S. Typhi detection.

CONCLUSIONS

Our findings suggest that routine wastewater surveillance can be used to detect S. Typhi in the natural environment and provide valuable information on the burden of typhoid throughout a target population. This data can be used as an early warning system to detect outbreaks of typhoid fever as well as inform the deployment of and evaluate the impact of typhoid conjugate vaccines in low-income settings.

38. Economic Burden Associated with Typhoid Fever in Chhatarpur Area—Qualitative Assessment

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BACKGROUND

Typhoid fever is a significant contributor to infectious disease mortality and morbidity in low- and middle-income countries, specially in Southeast Asia. With increasing antimicrobial resistance, commonly used treatments are less effective, and risks increase for complications and morbidity. During an episode of typhoid fever, households experience multiple social and economic costs that are often undocumented. In the current study, qualitative interview data from Kathmandu and surrounding areas provide important insights into the challenges that affect those who contract typhoid fever and their caregivers, families, and communities, as well as insight into prevention and treatment options for health providers and outreach workers.

METHODS

Overview

In August 2022, qualitative interviews were conducted with 22 households (case studies) and 8 physicians. Three focus group discussions were conducted—1 with public health center (PHC) providers and 2 with female community health volunteers (FCHVs) at rural and urban PHCs. In addition, a brief instrument was used to assess household monetary and time costs associated with each disease episode. The study research team included 2 US-based social scientists and the director and staff from a Chhatarpur-based nongovernmental organization.

Research Sites

Research sites included 11 urban and peri urban in Chhatarpur town.

Sampling and Recruitment

Qualitative data sampling strategies require identification of salient dimensions for identification of a representative group of respondents. For the household case studies, these dimensions included blood culture diagnosis within the

past 6 months of a permanent household member, location (urban/rural), and demographics of the typhoid fever patient (sex/age). The physician sample included various specialists and private and public clinic– and hospital-based practitioners. Non-physician medical providers included nurses, medical assistants, and midwives from a single PHC. FCHVs were recruited from 2 additional PHCs.

Data Management and Analysis
Recordings were transcribed and Nepali interviews were translated into English. A coding dictionary was developed and all data were coded in a qualitative data management program. Data searches were conducted based on key research constructs including disease severity, barriers and facilitators to care, diagnosis and testing, use of medications and treatments, social support networks, and prevention practices. Searched data sets were analyzed for patterns within and across respondent groups. Texts were organized within these patterns and are presented in the Results section. Demographic data were entered into Excel software and household cost data were entered into SPSS 22 software. Descriptive statistics were conducted for demographic data and for reported indirect and direct house- hold monetary and time costs.

Ethical Considerations
The proposed study was reviewed and approved by the Nepal Health Research Council, government of Nepal. All participants consented and signed a written consent form prior to data collection. Data collectors were trained in research ethics and consenting procedures.

RESULTS

22 household case study respondents, 12 (55%) were female. Fifty-five percent (12/22) of patients were female and 50% were aged ≥18 years. Seventy-five percent (6/8) of participating physicians were male. All FCHVs were female and 67% (4/6) of PHC providers were female.

While services and medications at PHCs are free or only require a small fee, for some households, even a minimum charge is more than they can afford. In addition, nontreatment costs such as travel can be expensive. FCHVs also discussed low literacy combined with poor economic conditions as barriers to seeking healthcare.

39. A Glycoconjugate Vaccine Against Typhoidal and Non-Typhoidal *Salmonella*

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BACKGROUND

Available *S.* Typhi vaccines have limited long-term efficacy, while no commercial is currently available for *S.* Paratyphi and *S.* Typhimurium. Our laboratory previously reported robust immunogenicity and protective efficacy of a subunit vaccine, containing *S.* Typhi/*S.* Paratyphi outer membrane protein, T2544. To expand the coverage to non-typhoidal *Salmonella* serovars, we generated a glycoconjugate vaccine containing T2544 and *S.* Typhimurium O-specific polysaccharides (O-specific polysaccharide -T2544).

METHODS

O-specific polysaccharide, purified from lipopolysaccharide by acid hydrolysis was chemically linked to recombinant T2544 expressed in *E.coli.* The purity and structural conformation of O-specific polysaccharide-T2544 was studied by size exclusion chromatography, western blots, and nuclear magnetic resonance. Afterwards, the glycoconjugate vaccine was administered subcutaneously into mice and serum antibody titers against O-specific polysaccharide and T2544 were measured by enzyme-linked immunosorbent assay. Vaccine protective efficacy was evaluated by oral challenge with *S.* Typhi, *S.* Paratyphi, and S. Typhimurium in iron overload and streptomycin pre-treated mouse models.

RESULTS

A smear-like pattern in Coomassie stain and western blot with T2544 and O-specific polysaccharide, antibodies confirmed the identity of O-specific polysaccharide -T2544. Further, nuclear magnetic resonance showed the characteristic O-acetyl group of the polysaccharide antigen. O-specific polysaccharide -T2544 induced a four-fold higher serum IgG titer than O-specific polysaccharide g, with antibody avidity significantly greater on the 120th day after a booster dose than after the 3rd immunization dose, suggesting affinity maturation and memory response. Bacterial challenge study showed 75% to 80% protection of O-specific polysaccharide -T2544 immunized mice for different *Salmonella* serovars.

CONCLUSIONS

A glycoconjugate vaccine of intrinsic *Salmonella* protein may be strongly immunogenic and confer long-term protection against both typhoidal and non-typhoidal *Salmonella* serovars.

40. A Bivalent *Salmonella* Typhi and Paratyphi A Ghost Based Vaccine Induces Protective Immune Response in Mice Model

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BACKGROUND

Salmonella Typhi and *Salmonella* Paratyphi A are the leading causative agents of enteric fever worldwide. At present, prolonged use of multiple antibiotic leads to the development of multi drug resistant *Salmonella* strain. Currently, there is no combination vaccine which could protect infection from both the strains. Therefore, we have developed a novel bivalent bacterial ghost based vaccine that confers protection against typhoidal and paratyphoidal infection.

METHODS

Bacterial ghost were prepared from *Salmonella* Typhi and *Salmonella* Paratyphi A by minimal inhibitory concentration of chemical treatment. Scanning electron microscopy and western blot were performed to characterize the immunogen. Cytotoxicity assay was performed in murine macrophage cell line by lactate dehydrogenase assay. The bivalent vaccine was administered intraperitoneally into the mice and serum antibody titers against anti-outer membrane protein and anti-lipopolysaccharide were measured by enzyme-linked immunosorbent assay. Protective efficacy of the vaccine was evaluated by the challenge with heterologous wild type strain in intraperitonial mouse model.

RESULTS

Chemical treatment inducing trans-membrane tunnel on the cell surface of bacteria confirmed bacterial ghost formation determined by electron microscopy. The cytotoxicity assay was determined against bivalent bacterial ghost was less cytotoxic. Western blot analysis supported the detection of immunogenic bands against cell lysate, outer membrane protein, lipopolysaccharide by vaccinated sera. Induction of serum IgG, IgA titter also correlates these results. Cell mediated immune response specially Th1/Th17 specific cytokine expression was observed in immunized animals. Successful reduction of bacterial growth was observed by serum bactericidal assay with vaccinated serum. In efficacy study, 80-100% protection was observed in bivalent bacterial ghost immunized mice.

CONCLUSION

All these findings reflect that our newly formulated bivalent bacterial ghost immunogen could be used as a novel candidate vaccine against enteric fever in our near future.

41. Real-Word Effectiveness of Typhoid Conjugate Vaccine in Children: A Systematic Review and Meta Analysis

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INTRODUCTION

Typhoid fever, caused by *Salmonella* typhi, has remained a global health problem, especially in children. According to WHO estimates, about 11-21 million annual cases occur, and 128-161 thousand annual deaths occur globally, primarily in children. Without treatment, the case fatality rate of typhoid fever is 10–30%, dropping to 1–4% with appropriate therapy. Since 2018, the World Health Organization has recommended typhoid conjugate vaccine (TCV) because of its high efficacy and long-term immunogenicity. However, currently only 6 countries have already introduced TCV into their national immunization programs. Therefore, this study aims to estimate real-world effectiveness of TCVs to support the immunization introduction around the world and to serve as important parameter in vaccine modeling.

METHODS

The major databases MEDLINE, EMBASE, Web of Science, and Cochrane Library databases were searched. In this systematic review and meta-analysis, we included observational, cluster randomized trial, post-licensure studies of TCVs, published up to 19 August 2023, in English, with laboratory-confirmed typhoid as the endpoint. Two WHO-prequalified typhoid conjugate vaccines, Typbar TCV® (Bharat Biotech) and TYPHIBEV® (Biological E), were anticipated when the review process was conducted. Data was pooled in statistical meta-analysis using Review Manager software by Cochrane. The PRISMA checklist was used for the meta-analysis. Pooled estimates of Odds Ratio (OR), Vaccine Effectiveness (VE) and 95% CIs were calculated. Protocol and search strategy have been registered to PROSPER on 31 August 2023 with ID : CRD42023456130.

RESULTS

We identified 1181 articles (400 duplicates removed) and screened 780 studies, of which 5 studies from 4 countries (Pakistan, Malawi, Zimbabwe, and Bangladesh) were . All the vaccine effectiveness studies used Typbar TCV® and compared with unvaccinated (3 studies), Japanese Encephalitis vaccinated (1 study), or meningococcal capsular group A conjugate vaccinated (1 study) populations. The overall odds ratio (OR) for TCV against

laboratory-confirmed typhoid fever among children was 0.11 (95% Confidence Interval 0.05 – 0.24) or vaccine effectiveness of 89% (95% Confidence Interval 76-95%). Lower effectiveness was found for the outcome of suspected typhoid fever.

CONCLUSION

TCVs were effective in preventing laboratory-confirmed and suspected typhoid fever among children in endemic countries.

42. Serologic Response Using ELISA Anti-Vi IgG Antibodies at Several TCV Among HIV Infected Children in Karachi Pakistan Time Points Following Immunisation with TCV Among HIV Infected Children in Karachi Pakistan

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INTRODUCTION

Associated with outbreaks, complications and the evolution to novel strains that are extensively drug resistant, enteric fever remains a major public health concern in Pakistan. WHO recommends programmatic use of typhoid vaccines for the control of typhoid fever in typhoid endemic countries, however, individuals infected with HIV generally have a lower response *to immunization as compared to the general population, but unfortunately, there is no data to corroborate the post-vaccination serologic response of TCV in HIV infected children. Therefore, this study was designed to assess the serological response of typhoid conjugate* vaccine (TCV) in HIV infected children in Ratodero, Larkana in Sindh.

METHODOLOGY

A prospective cohort study was conducted in HIV-positive children who receive a single dose of the Typbar-TCV at Taluqa Hospital in Ratodero Larkana, Pakistan. A total of 336 HIV positive children aged 6 months to 15 years were vaccinated and followed-up for 1 year, from December 2019 till January 2021.

We measured the serological response using ELISA anti-Vi IgG antibodies at several time points following immunization with a single 0.5ml intramuscular injection of Typbar-TCV. Blood samples were collected at baseline, 6 weeks, 6 months and 12 months post-immunization with TCV and tested for anti-Vi IgG titers and change in antibodies level at different time points was compared to baseline antibodies, and the seroconversion rates were calculated. Seroconversion was defined as four times increase in the Vi IgG antibodies titers after vaccination as compared to the baseline antibodies level.

RESULTS

The mean age of the participants was 52.04 months (standard deviation (SD) ± 29.96) and 206 (62.6%) of them were male and the mean CD4 count was 841 (IQR: 404 , 1303) cells/mm^3. The GMT were 1.4 U/ml, 97.65 U/ml and 21.8 U/ml and 21.4 U/ml at baseline, 4 weeks , 6 months and 1 year post immunization with TCV. The observed GMT titers were significantly lower in children aged 6 months to 5 years of age as compared to the children aged >5 years to 15 years of age at 6 months and 1 year post vaccination. Seroconversion rates were 75% at day 28, 51% at 6 months, and 40% at 1 year post immunization. The seroconversion rates were significantly different among different age groups, 45% versus 75% 6 months post vaccination, and 33% versus 68% 1 year post vaccination among children of 6 months to 5 years of age and >5 to 15 years of age respectively. Besides age, high immunosuppression was significantly associated with lower seroconversion rates, 57% versus 41% 6 months post vaccination, 48% versus 27% 1 year post vaccination among children with high immunosuppression and low immunosuppression respectively. Seroconversion rates were similar in males and females.

CONCLUSION

HIV-infected children with high immunosuppression and younger age were associated with low seroconversion rates and failure to remain seroconverted at 6 months and 1-year post-immunization with TCV. Thus, it can be concluded that the overall seroconversion rates of TCV among HIV-positive children are lower as compared to HIV-negative children. Therefore, the need for a booster dose of TCV should be assessed and administered accordingly amongst immunocompromised patients.

43. Stakeholder Perspectives on Giving Additional Injectable Vaccines in a Single Visit Under Universal Immunization Programme (UIP) in India

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BACKGROUND

Typhoid is endemic in India and remains a predominant cause of morbidity and mortality. As typhoid is vaccine-preventable, investing in vaccines has been sought to control the disease in the country. WHO recommends the introduction of Typhoid Conjugate Vaccine (TCV) to be prioritized in countries with the highest burden of typhoid disease. In June 2022, the National Technical Advisory Group on Immunization (NTAGI), considering the high burden of typhoid disease, recommended the introduction of TCV under the Universal Immunization Programme (UIP).

However, introducing TCV, another injectable vaccine, will increase the number of injections administered in a single visit to a maximum of 5 (if given at 9 months) or 4 (if given in the second year of life). This might lead to hesitancy and reluctance in acceptance amongst caregivers. Besides this, it might result in a lack of confidence in administering multiple injections among vaccinators. The study aims to gather stakeholder (program managers, private practitioners, vaccinators, community mobilizers, and caregivers) perspectives on giving additional injectable vaccines in a single visit and understand the schedule followed in the private sector for better acceptability.

METHODOLOGY

The study includes a scoping review of the published literature on the acceptance of additional injectable vaccines under the immunization schedule and a mixed-method exploratory study in urban areas identified as typhoid surveillance sites across 8 states in the country. Over 100 key informant interviews are being conducted among service providers. Quantitative data is being collected through a telephonic survey of 875 caregivers to gather their perspectives. The qualitative data will be thematically analyzed using NVIVO 14 software, the quantitative data will be analyzed using SPSS software version 21.

RESULTS

The preliminary findings suggest including evidence-informed training of vaccinators to enhance vaccinator-caregiver communication and improve the management of infants' pain. However, the comprehensive findings are under review.

CONCLUSION

As the study is currently underway, it is anticipated that the findings obtained will inform policymakers in developing a suitable vaccination strategy for multiple injectable vaccines in a single visit, especially in the context of the proposed introduction of TCV in the UIP.

44. Antibiotic Susceptibility Patterns of Typhoidal Salmonellae Isolates From Uncomplicated Out-Patients of Three Tertiary Care Hospitals in Dhaka, Bangladesh

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BACKGROUND

South Asia is considered as the largest hub for typhoid fever in the world. Antimicrobial resistance has become a critical issue for typhoid and paratyphoid and the increasing observance of bacterial isolates that are resistant or intermediate susceptible to certain potent antibiotics is alarming. At present, fluoroquinolones and third generation cephalosporins are widely used to treat typhoid and paratyphoid fever in Bangladesh. However, this changing antibiotic susceptibility among typhoidal Salmonellae poses a particular challenge to the therapeutic management of enteric fever. The recent emergence of a particularly resistant typhoid strain in Pakistan, and subsequent international spread, adds urgency to this problem and *Salmonella* is now listed as a high (Priority 2) pathogen by WHO. The objective of this study was to assess the antibiotic susceptibility patterns of *Salmonella typhi* (*S. typhi*) and *Salmonella paratyphi* (*S. paratyphi*) isolates.

METHODS

This observational study was conducted on uncomplicated febrile patients with clinically suspected typhoid or paratyphoid fever, attending the out-patient department of three tertiary care hospitals of Dhaka city, i.e., icddr,b Dhaka Hospital (icddr,b), Dhaka Shishu Hospital (DSH) and Shaheed Suhrawardy Medical College and Hospital (ShSMCH) as a part of an ongoing randomized controlled clinical trial between the period of May, 2022 to September, 2023. Antimicrobial susceptibility pattern was tested on 70 blood culture cases positive for *S. typhi*, *S. paratyphi A* and *S. paratyphi B* and zone of diameter (ZoD) was assessed using disk diffusion method for Ciprofloxacin, Azithromycin, Cefixime, and Ceftriaxone. E-test was performed for minimum inhibitory concentration (MIC) values of Azithromycin, Cefixime and Ceftriaxone.

RESULTS

Out of 70 blood culture positive cases (mean age 16±10 years, range 3–55), 55 (79%) were positive for *S. typhi*, 13 (18%) were positive for *S. paratyphi A*, and 2 (3%) were positive for *S. paratyphi B*. 100% isolates were found susceptible to Azithromycin, Cefixime, Ceftriaxone, Co-Amoxiclav and Meropenem. The isolates were either resistant or intermediately susceptible by 96% for Ciprofloxacin, 94% for Nalidixic Acid, 15% for Ampicillin, and 7% for Cotrimoxazole. MICs for Azithromycin, Cefixime and Ceftriaxone ranged from 0.094 µg/ml to 8 µg/ml, 0.016 µg/

ml to 1 µg/ml, and 0.023 µg/ml to 0.47 µg/ml, while the corresponding zone diameters ranged from 14 mm to 28 mm, 19 mm to 36 mm, and 19 mm to 34 mm, respectively. Zone of diameter for Ciprofloxacin ranged from 6 mm to 32 mm. Overall, multi drug resistance (i.e., co-resistance to the fluoroquinolones, Ampicillin, and Cotrimoxazole) was present in 8/70 isolates (11.4%).

CONCLUSIONS

The current practice of using third generation cephalosporins for typhoid and paratyphoid in Bangladesh seems effective as both Cefixime and Ceftriaxone has shown to be 100% susceptible against *S. typhi* and *S. paratyphi* in the current study. However, a very high rate of fluoroquinolones, i.e., Ciprofloxacin and Nalidixic Acid resistance as well as reduced susceptibility to both the drugs was observed. This is most likely due to an increased use of Ciprofloxacin as a first line drug of choice over more traditional antimicrobial agents for the treatment of typhoid fever in recent times. Azithromycin, Co-Amoxiclav and Meropenem was also found to be fully susceptible against the typhoidal Salmonellae.

45. Survival of *Salmonella Enterica* Serovar Weltevreden in Household Water From Ibadan, Nigeria

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BACKGROUND

Salmonella enterica subsp. *enterica* serovar Weltevreden is an emerging cause of intestinal and invasive diseases. This non-typhoidal serovar is most commonly reported from Asia and associated with aquatic environments and seafood. The Severe Typhoid in Africa node in Ibadan, Nigeria recently identified *S.*Weltevreden ST365 as the second most common invasive non-typhoidal *Salmonella* serovar, after Enteritidis. Salmonellae were recovered after enrichment from seven of 250 household water samples analyzed in 2018-19 within the SETA Ibadan catchment area and in three of these instances, *S.*Weltevreden ST365 was cultured. This study tested the hypothesis that exceptional aquatic viability accounts for *S.*Weltevreden prevalence and transmission in Ibadan.

METHODS

Water samples from three households from which *S.*Weltevreden was previously recovered were aseptically collected, evaluated for microbiological quality and then sterilized. Aliquots of the sterilized water samples were inoculated with an *S.* Weltevreden bloodstream isolate, an *S.* Weltevreden isolate from household water, *Salmonella* Typhimurium ATCC 14O28 or *Escherichia coli* ATCC 35218. Survival of the inoculated bacteria in the sterilized household water samples, and in sterile distilled water, at ambient temperature, was monitored over time using plate counts.

RESULTS

None of the samples were potable at collection and their coliform counts were above 10^3 cfu/mL. Over the course of 36 days, all the bacteria inoculated into sterilized household water samples maintained viability. By contrast, survival in distilled water declined by 2-4-logs within a week of inoculation, with *E. coli* and *S.* Typhimurium showing better viability after 2-3 weeks than either *Salmonella* Weltevreden isolate. Both *Salmonella* Weltevreden isolates showed comparable survival in borehole, well and stored water samples from the Ibadan households to *E. coli* and *S.* Typhimurium.

CONCLUSIONS

Water from different households in Ibadan permits the survival of non-typhoidal *Salmonella* and *E. coli* for extended periods. Recovery of *Salmonella* Weltevreden from household water in Ibadan is more likely to be a feature conferred by the water, rather than an inherent characteristic of this serovar of *Salmonella*. Systematic efforts to improve both the microbiological and physico-chemical characteristics of household water in Ibadan are needed to impact the epidemiology of salmonellosis and other potentially waterborne infections.

46. Direct and Indirect Costs of Typhoid Fever in Indonesia

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INTRODUCTION

Typhoid fever is a life-threatening infection caused by the bacterium *Salmonella* typhi and *Salmonella* Paratyphi. The WHO estimates the global typhoid fever disease burden at 11-21 million cases annually, resulting in about 128

000–161 000 deaths per year, compared to an estimated 6 million cases of paratyphoid fever and 54 000 deaths annually. Despite the high efficacy, safety, and long-term immunogenicity, currently Typhoid Conjugate Vaccine (TCV) has only been introduced in 6 countries worldwide, not including Indonesia. Therefore, this study aims to estimate direct and indirect costs of typhoid fever in Indonesia to support vaccine introduction into National Immunization Program (NIP) in Indonesia.

METHODS

This study was a multisite, health facilities (sentinel) based surveillance (hospitals and primary health centers) to estimate direct and indirect cost of typhoid fever among children and adults. The study was done in two parallel phases, a retrospective clinical record review and a prospective surveillance study. The study included hospitalized patients during the period of January 2019 – Maret 2023.The data was collected from 24 health facilities (tertiary, secondary, private hospitals, and primary health centers) from 6 provinces (Central Java, West Java, South Sumatera, South Sulawesi, South Kalimantan, and East Nusa Tenggara) in Indonesia.

RESULTS

Of the 891 children aged 6 months-17 years old hospitalized with typhoid on Jan 2019-February 2023, 474 patients were girls (53.0%). The complicated typhoid was reported in 49 child patients (5.0%). Of the 647 adults aged >18 years old hospitalized with typhoid on Jan 2019-February 2023, 403 patients were female (62.3%). The complicated typhoid was reported in 56 adult patients (8.7%). The weighted average direct medical costs of typhoid fever are estimated at USD 177 in children and USD 174 ± in adults. Furthermore, the weighted indirect costs of typhoid fever are estimated at USD 20.4 for children and USD 15.3 for adults.

CONCLUSION

This direct and indirect cost data of typhoid fever in Indonesia can be used to estimate potential healthcare cost savings within future cost-effectiveness analysis of programs, including introducing typhoid conjugate vaccines.

FUNDING

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47. Genomic Characterization of *Salmonella* Paratyphi C Around the Globe

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BACKGROUND

Salmonella enterica serovar Paratyphi C (*S.* Paratyphi C), an enteric fever-causing pathogen, exhibits diverse clinical manifestations ranging from asymptomatic bloodstream infections to severe septicemia. Although relatively uncommon in Europe, and North America, *Salmonella* Paratyphi C is frequently encountered among travellers originating from South and East Asia or Africa, where the prevalence is much higher. Despite this, limited genomic data is available about *S.* Paratyphi C. Our study examines genetic diversity and geographic distribution, offering insights into the epidemiology and evolution of *S.* Paratyphi C isolates in different countries.

METHODS

We obtained 217 isolates from diverse regions, including Africa, Asia, South America, and Europe, downloaded from the NCBI Sequence read archive (SRA) database. To detect antimicrobial resistance (AMR) genes and plasmids, we used SRST2-v0.2.0 software, ARGannot, and PlasmidFinder-v2.0.1 databases. We constructed a maximum-likelihood (ML) phylogenetic tree using the rAxML SSE3-v8.2.8 software, rooted with an S. Typhi isolate and performed 100 bootstraps for tree reliability.

RESULTS

AMR analysis revealed 86.3% (188/217) isolates as pan-sensitive. Among the remaining isolates, 05 were resistant against ciprofloxacin with *parC* (T57S) mutation, 07 against ampicillin (*bla*TEM-1B, *bla*TEM-116 and *bla*TEM-117), six against ceftriaxone and seven were multidrug-resistant (MDR). Surprisingly, ceftriaxone–resistant isolates lack plasmids like IncY, IncQ, or IncH, which usually carry ceftriaxone-resistance genes, indicating chromosomal genes' presence (*bla*ACT-16, *bla*OXA-1, *bla*DHA-1, and blaMIR-3). Among the resistant isolates, streptomycin, sulfonamides, trimethoprim, and chloramphenicol resistance were observed in 44.8%, 41.4%, 41.0%, and 10.3% of isolates, respectively. Predominantly, *Inc*FIB plasmid was identified in 138 out of 217 isolates. Phylogenetic tree analysis unveiled distinct clades from sensitive strains, mainly from Africa and Europe.

CONCLUSION

This study comprehensively presents the genetic diversity and geographic distribution of *S.* Paratyphi C, detailing antimicrobial resistance profiles and plasmid prevalence. Further research is necessary to understand chromosomal resistance mechanisms and their implications for managing Paratyphi C infections globally.

48. Exploring Diversity and Environmental Dynamics of *Salmonella* Typhi and its Bacteriophages

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BACKGROUND

Bacteriophages (or phages) are viruses that infect bacteria and regulate their abundance, phenotypic characteristics, and long-term evolutionary trajectory. Recently, our group has shown that Typhi-specific phages are abundant in surface water collected from high typhoid burden settings in Bangladesh and phage abundance correlates with typhoid burden. However, no information is available regarding the infecting mechanisms of Typhi-phages and the role these phages play in the evolution and dynamics of *Salmonella* Typhi in the environment. In this study, we used a combination of whole genome sequencing and bacterial killing assays against a diverse panel of *Salmonella* Typhi isolates to characterize the Typhi-phages present in Bangladesh.

METHODOLOGY

From 2021 to 2022, 114 phages were isolated from 1100 environmental surface water from seven districts in Bangladesh. All phages were spotted against 19 genotypes of *Salmonella* Typhi circulating in Bangladesh to profile their infectivity spectrum. 14 phages with unique activity spectrums and sampling locations were propagated from their respective phage plaques. Upon propagation, the genomic DNA was extracted using QIAamp DNA minikit. 150 bp paired-end library was prepared using NEBNext UltraII FS Library Preparation Kit and sequenced in Illumina NextSeq2000. The raw sequences were assembled and annotated using Unicycler and Kraken2, respectively.

RESULTS

We found that certain genotypes of *Salmonella* Typhi such as 1.2.1. to be completely resistant to all Typhi phages tested, while 2.5. and 4.3.1. were susceptible to all the Typhi-phages. Certain genotypes such as 2.2., 3.3.2.BD1/BD2 and 4.3.1.3.BDq showed a high resistance pattern whereas, 3.0.2., 3.2.2. and 4.3.1.2. were infected by most of the phages. We conducted whole genome sequencing of 14 phages, and phylogenetic analysis indicated that 10 phages belonged to the Kayfunavirus genus, while 2 were Teseptimavirus and 2 were Macdonaldcampvirus.

CONCLUSION

Taken together, the present study highlights the diversity of Typhi-phages present in a typhoid-endemic setting. Based on genomic sequencing, Kayfunavirus is the most common genus of Typhi phages, an observation also made by a related study from Nepal. To further dissect the phage-Typhi interaction, we are currently expanding this study on phages isolated from all 64 districts of Bangladesh.

49. Real-World Data for Decision-Making: Data Collection and Synthesis to Illuminate the Need for Typhoid Conjugate Vaccine

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BACKGROUND

Typhoid is a serious public health issue in Kenya—evidence shows nationally endemic typhoid transmission alongside persistent outbreaks through the country. Evidence increasingly shows multi-drug resistant typhoid strains. In October 2020, the Kenya National Immunization Technical Advisory Group (KENITAG) recommended the introduction of typhoid conjugate vaccine (TCV) into routine immunization through a nationwide campaign. To reach this recommendation and successfully apply for support to Gavi, the Vaccine Alliance, the KENITAG considered and triangulated various typhoid data and risk factors to reach their decision.

METHODS

Due to lack of strong surveillance and difficulties with accurate typhoid diagnostics, myriad data sources were gathered and weighed together to reach the decision about TCV introduction. Modeled data and estimates were gathered alongside surveillance data from national systems and local surveillance projects. Data also include rates of ileal perforations and other risk factors, including access to safe water and improved sanitation.

RESULTS

Analysis of the available data and risk factors identified typhoid as an ongoing public health problem with the potential to get worse, considering rising rates of drug-resistant typhoid, increased climate change events, and migration into already crowded cities with over-stretched water and sanitation infrastructure. When compared to the potential opportunity from TCV—including cost effectiveness and vaccine efficacy—the KENITAG recommended TCV as a priority public health intervention in Kenya. The example of typhoid data collection and analysis from Kenya show how policymakers can make strategic public health decisions with data and information already available.

CONCLUSIONS

The data collection, analysis, and triangulation from Kenya is a strong example of how other countries in the Africa region can gather various data and identify the potential for TCV, even without having strong national surveillance or data collection systems. Typhoid data are imperfect, yet the success from Kenya shows that the opportunity to gather data and bring together various data points to illustrate a comprehensive typhoid context. The KENITAG decision and subsequent successful application to Gavi show that together, many small data sources can highlight the overwhelming need for vaccine introduction. Kenya is now slated to introduce TCV in 2024.

50. Hyper-Reactive MAIT Cells in People Living with HIV Could Contribute to Protective Immunity Against Typhoid Fever in Malawian Adults

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BACKGROUND

People living with HIV are at an increased risk of many bacterial infections including *Mycobacteriumtuberculosis, Streptococcus* pneumoniae and *Salmonella* typhimurium. Paradoxically, the risk of typhoid fever is lower in people living with HIV (PLHIV) than in HIV-uninfected individuals. However, the mechanisms behind this apparent protective effect of HIV on typhoid fever are unclear. Mucosal-associated-invariant T (MAIT) cells are an abundant part of the intraepithelial lymphocytes (IELs) that provide rapid responses against pathogens encountered at the mucosal sites thereby contributing to early-stage control of infections.

OBJECTIVE

To determine whether gut and systemic MAIT cell responses to *Salmonella* typhi (*S.* Typhi) are augmented in PLHIV compared to HIV-uninfected controls.

METHODS

We collected peripheral blood and duodenal tissue biopsies from healthy HIV-uninfected adults (n=18), ART-naïve PLHIV (n=19), and PLHIV on ART (n=18). We measured the frequency and function of MAIT cells using flow cytometry. In addition, mononuclear cells were co-cultured with *Salmonella* typhi H58 strain for 18 hours, and intracellular cytokine (IFN-γ and TNF-α) staining assay was used to assess MAIT cell responses.

RESULTS

The frequency of TNF-α and IFN-γ-producing blood MAIT cells responding to *S.* Typhi was higher in ART-naïve PLHIV than in HIV-uninfected adults (TNF-α, p=0.027; IFN-γ, p<0.001). However, PLHIV on ART had a comparable proportion of TNF-α and IFN-γ-producing blood MAIT cells to that of HIV-uninfected adults (all p>0.05). While, in the duodenal mucosa, the frequency of TNF-α-producing MAIT cells was higher in ART-naïve PLHIV and PLHIV on ART than in HIV-uninfected adults (p=0.001, p=0.044; respectively). In contrast, the frequency of IFN-γ-producing duodenal MAIT cells was similar in ART-naïve PLHIV and PLHIV on ART compared to HIV-uninfected adults (p=0.15, p=0.68, respectively).

CONCLUSION

Our findings show the presence of responding blood and duodenal MAIT cells in ART-naïve PLHIV that respond to *Salmonella* Typhi H58 infection than in HIV-uninfected controls. However, only in blood and not the duodenum, this increased effect is reversed in PLHIV on ART. These hyper-reactive MAIT cells could in part contribute to protective immunity against typhoid fever in PLHIV.

51. Evolutionary Analysis of *Salmonella* Paratyphi A in India, 1991 – 2008 Reveals the Endemic Sub-Clones Associated with Paratyphoid Infections

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ABSTRACT

Paratyphoid fever caused by *S.* Paratyphi A is endemic, particularly in parts of Asia and Sub-Saharan Africa. In spite of the substantial rise in enteric fever cases caused by *S.* Paratyphi A, limited information is available regarding the genetic diversity and population structure of these strains. Also, data regarding the genomic epidemiology of paratyphoid fever in India are scarce. We have investigated the genomic epidemiology of *S.* Paratyphi A in Vellore, India during the 1990s when Paratyphoid fever caused seasonal disease. The study was conducted using the archived *S.* Paratyphi A isolates reported at Christian Medical College Vellore between 1991 and 2010. We used whole genome sequencing (WGS) and phylogenetic analysis to compare the genotypes of *S.* Paratyphi cultured from cases of paratyphoid fever during the 1990s (n = 34) versus 2000 - 2010 (n = 20). Phylogenetic analysis has clustered the study isolates into two major clades (2.3 & 2.4). Genotype distribution between historical isolates (1990s) and modern isolates (2000-2010) was similar, although the older historical isolates could not be classified into subclades. Additionally, phylogenomically 'ancient' genotypes 1, 2, 2.2 and 2.4 were uncommon in our historical collections, while modern isolates showed the re-emergence of genotype 1. Also, a significant number of isolates were fluoroquinolone non-susceptible with single mutations (S83F/Y) in the quinolone-resistance-determining region (QRDR). Since *S.* Paratyphi A is human-restricted, high levels of evolutionary changes are not expected. However, public-health investigations and interventions by means of genomic surveillance still need to be continued.

52. Transmission Dynamics for Invasive Non-Typhoidal *Salmonella* serovars in Africa (TiNTS)

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BACKGROUND

Nontyphoidal salmonellae are the leading cause of community onset bloodstream infection in Africa and Asia. *Salmonella* Typhimurium Multilocus Sequence Type 313 ("ST313") comprises the vast majority of sequenced invasive isolates, and exhibits genetic adaptation toward host adaptation/invasion. Food production pathways, animals, and household environments do not appear to present a viable nidus for ST313. The genomes of *Salmonella* Typhimurium shed in stool are near-identical to bloodstream isolates from the same individual; two case-control studies have recovered genomically conserved isolates of ST313 from household contacts of children with bloodstream infection. We hypothesise that ST313 exploits humans for transmission. Here we present TiNTS, a prospective household cohort study that will investigate this. We will simultaneously examine other circulating nontyphoidal *Salmonella* serovars, and determine the duration of *Salmonella* stool shedding.

METHODS

We will recruit individuals of all ages residing in at least 60 households in an informal settlement in Malawi between October 2023 and April 2025.

We will follow households for 28 days, obtaining stool on alternate days. At baseline we will collect nasopharyngeal swabs, perform bootsock sampling of household environments, conduct household / individual questionnaires, and obtain samples of water used for cooking, washing and drinking. We will test for *Salmonella* Typhimurium and Enteritidis O-Ag IgG at day 28 (and 28 days after any *Salmonella* positive stool culture). We will follow individuals who have *Salmonella* in stool at weekly intervals until two consecutive negative stool samples are demonstrated.

We will serotype recovered salmonellae. We will perform whole genome sequencing on bacterial isolates, and combine this with epidemiologic data to construct transmission networks.

(ANTICIPATED) RESULTS

We anticipate identifying prospective household *Salmonella* transmission events, inferring routes using genomic and epidemiologic data. We will obtain information on the duration of stool shedding, serologic responses to de novo colonization, proportions of participants with diarrhoeal and asymptomatic *Salmonella* carriage, and risk factors for individual/household *Salmonella* colonization.

(ANTICIPATED) CONCLUSIONS

Transmission data generated through TiNTS will inform public health interventions including modelling the impact of future vaccines.

53. Development and Qualification of Methods to Assess Immunogenicity of *S.* Paratyphi A Component of a Bivalent Paratyphoid A-Typhoid Vaccine

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BACKGROUND

Vaccines targeting paratyphoid fever are in clinical development; including a bivalent Paratyphoid A-Typhoid vaccine (Sii-PTCV). Such vaccines aim to reduce the burden of enteric fever caused by both *S.* Typhi and S.Paratyphi A. Assessing immunogenicity induced by these vaccines is an important outcome in clinical trials.

METHODS

We developed, optimised and qualified two assays to assess immunogenicity against *S.* Paratyphi A in human serum samples using; 1) an indirect ELISA to measure IgG responses against *S.* Paratyphi A lipopolysaccharide and, 2) a Serum Bactericidal Assay (SBA) to measure anti-*S.* Paratyphi A antibody mediated bacterial killing.

RESULTS

Our standardised ELISA allows for rapid evaluation of anti-lipopolysaccharide IgG levels using a single serum dilution. This medium throughput approach will be ideal for assessing larger sample sets e.g. from Phase II and III studies. Using our optimised SBA, we show effective killing of two different *S.*ParatyphiA strains (one strain used in vaccine manufacturing and one used as challenge strain in controlled human infection studies) in sera from Sii-PTCV vaccine recipients. We demonstrate inter-day and inter-operator precision with both assays. Finally, we compare the anti-LPS IgG responses post vaccination and post *S.* Paratyphi A infection.

CONCLUSIONS

We present robust assays to assess both level and function of anti-*S.*Paratyphi A antibody in human sera and demonstrate use of these assays to assess immunogenicity of a candidate bivalent Paratyphoid A-Typhoid vaccine. These assays will be further utilized in the ongoing clinical development of Sii-PTCV.

54. Global Evaluation of Tubex Kit Performance: A Comprehensive Meta-Analysis Across Diverse Study Settings

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BACKGROUND

Typhoid fever is a global health concern, particularly in regions with limited access to clean water and sanitation facilities. The Tubex Typhoid Kit, an IMBI Inhibition Magnetic Binding Immunoassay detects antibodies specific to *Salmonella* Typhi antigens in patient serum or plasma. The Tubex Typhoid Kit has shown promise in the rapid diagnosis of this debilitating disease and offers advantages in terms of simplicity, speed, and potential utility in resource-constrained settings. However, the diagnostic accuracy of the Tubex Typhoid Kit varies across different epidemiological and clinical settings. To address this issue, we conducted a comprehensive meta-analysis to evaluate the performance of the Tubex Typhoid Kit in diagnosing typhoid fever across diverse study settings. The main objective was to systematically review relevant studies to identify and critically assess the diagnostic performance of the Tubex Typhoid Kit in the context of typhoid fever diagnosis.

METHODS

The study employed a systematic meta-analysis approach to assess the diagnostic performance of the Tubex Typhoid Kit in the diagnosis of typhoid fever. Relevant studies were identified through systematic searches of electronic databases, including Peer reviewed journals and regional databases. Search terms encompass variations of "Tubex Typhoid Kit," "typhoid fever," and "diagnostic accuracy." Studies were screened based on predefined inclusion and exclusion criteria, and duplicate publications were meticulously removed. Extracted information encompassed sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), sample sizes, study populations, geographical locations, and demographic characteristics. The study exclusively involved the synthesis of data from existing studies, with no primary data collection involving human participants. As such, ethical approval was not required for this meta-analysis. No individual patient data was collected or disclosed in the study, ensuring the confidentiality of patient information. The analysis solely involved aggregate data from published studies.

RESULTS

The study findings suggest significant diagnostic accuracy of the Tubex Typhoid Kit across different study settings. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) estimates ranged widely. the sensitivity and specificity of Tubex Typhoid kit varies across different studies and regions. The kit appears to perform differently in Asia and Africa, with varying levels of sensitivity 92%-100% and specificity 95-98%.

CONCLUSION

The global evaluation of the Tubex Typhoid Kit's performance in diagnosing typhoid fever is essential for optimizing its utility in diverse healthcare settings. This meta-analysis provides critical insights into the diagnostic accuracy of the Tubex Typhoid Kit, allowing healthcare practitioners, policymakers, and researchers to make informed decisions regarding its use in typhoid fever diagnosis and control programs.

55. Environmental Surveillance for Typhoid Using Wastewater in Vellore, Tamil Nādu, India, 2021-2022

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BACKGROUND

Environmental surveillance has the potential to be a cost-effective alternative to blood culture surveillance for *Salmonella* Typhi (*S.* Typhi), especially in lower-and-middle income countries like India, which has low blood culture surveillance resources. We established environmental surveillance for typhoid using wastewater in Vellore, a city in southern India. We examined the association of the water quality parameters and site characteristics with the *S.* Typhi detection by different sample collection methods.

METHODS

Sewage water samples were collected from 40 selected sampling sites in Vellore across 18 urban wards and one rural area, covering a population of 164,886 at monthly intervals between May 2021 and April 2022. Overall, 1037 samples (520 grab samples by the bag-mediated filtration system and 517 trap samples using Moore swabs) were tested for three *S.* Typhi targets using quantitative polymerase chain reaction. Positivity rates were estimated, and the association of water quality, climate, and site characteristics with *S.* Typhi detection accounting for repeat observations was tested using mixed effects logistic regression and expressed using adjusted odds ratio (aOR). Agreement between grab and trap methods was calculated using the Kappa statistic.

RESULTS

Of 1037 samples, 118 (11.4%) tested positive for *S.* Typhi. The sample positivity was >10% from July to December and peaked during October (24.7%). The detection was higher in trap samples (15.3%, 79/517) than in grab samples (7.5%, 39/520). The agreement between the two methods was 85.3% (kappa-0.283, p-value<0.001). The sampling sites' catchment population size was significantly associated with higher *S.* Typhi detection in both grab samples (aOR=1.32; P value =0.01) and trap samples (aOR=1.97; P value <0.01). While fecal contamination in wastewater, indicated by the

log HF183 copy number, was associated with higher *S.* Typhi detection from trap samples (aOR=1.67; P value <0.01), high flow speed in the drains was associated with S. Typhi detection from grab samples (aOR= 7.11; P value = 0.04).

CONCLUSION

Wastewater surveillance showed ongoing transmission of S. Typhi in Vellore. Such surveillance can identify hotspots in the community and guide public health control measures. Preference can be given to sites with high catchment populations while selecting sites for surveillance.

56. Multidrug-Resistant *Salmonella* Typhi in Endemic Settings in Nairobi County, Kenya: 2013-2022

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KEMRI

BACKGROUND

A significant global problem that affects countries where typhoid fever is widespread is the emergence and persistence of multidrug-resistant typhoid infections. With an incidence rate of 263 per 100,000 people per year (95% CI: 199-347), multidrug-resistant *Salmonella* Typhi is a significant public health challenge in Kenya. Seemingly, in low- and middle-income countries with limited resources, the burden of multidrug-resistant typhoid infections has continued to persist. Concurrently, *S.* Typhi carriage, which affects 3 to 5% of individuals with Typhoid disease, has also increased in frequency in these environments.

However, little is known about the part that carriers play in *S.* Typhi transmission in low-income areas, including Kenya. This study utilized *S.* Typhi isolates from urban informal settlements collected from 2013-2022.The study sought to identify the most prevalent resistance phenotypes, and prevalence of multidrug-resistant (MDR) *S.* Typhi in acute illness and chronic carriage in an endemic setting in Nairobi County, Kenya.

METHODS

Archived and prospectively isolated *S.* Typhi isolates from blood and stool collected in 2013–2018 and 2020–2022, respectively, were analyzed. Positively confirmed *S.* Typhi isolates were tested for susceptibility to 14 antibiotics using the Kirby Bauer disc diffusion technique.

RESULTS

A total of 421(100%) *S.* Typhi strains isolated from cases; 285 (68%) and controls (apparently healthy individuals residing in the same household as the cases) 136 (32%) were analyzed. *S.* Typhi isolates from both cases and controls showed resistance to ampicillin (58%), sulfamethoxazole-trimethoprim (56%) and chloramphenicol (48%). Reduced susceptibility to ciprofloxacin was observed due to increased nalidixic acid resistance at 26%. Multidrug-resistant *S.* Typhi was observed in 180 (43%) isolates of which cases were 125 (69%) and controls were 55 (31%) respectively.

CONCLUSION

This study reported a high number of multi drug resistant *S.* Typhi isolates. Due to increased resistance to nalidixic acid, this study also reported reduced susceptibility to ciprofloxacin. Although not as high a number as cases, the study also reported that controls (carriers) equally play an important role in typhoid disease transmission in the community.

57. Leaving No Child Behind: Tailored Support for Reaching Missed and Zero Dose Children during Typhoid Conjugate Vaccine Introduction in Pakistan

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PHC Global Pvt Ltd

BACKGROUND

Typhoid fever remains a significant public health concern in Pakistan, and the introduction of the Typhoid Conjugate Vaccine (TCV) offered an opportunity to alleviate the disease burden. This abstract highlights the critical role of PHC Global in ensuring equitable access to the TCV by providing tailored support in identifying and vaccinating missed and zero-dose children during TCV introduction campaigns in Pakistan.

OBJECTIVE

The objective of this effort was to provide targeted support to ensure equitable access to the life-saving vaccines in Pakistan.

METHODS

PHC Global employed a comprehensive approach to reach missed and zero-dose children during the TCV campaigns. This involved microplanning, community engagement, advocacy, and supportive supervision. Microplanning calculated targets, scheduled vaccination days, allocated resources, and coordinated campaign functions. Field validations ensured accuracy and updated micro-plans. Surveys identified missed population segments, while mobile teams reached children not added to micro-plans. Vaccine hesitancy and hard-to-reach areas were tackled through community engagement, awareness sessions, and mosque/school involvement. Influencers promoted vaccination, and grand jirgas addressed refusals. Supportive supervision and on-the-job training maintained quality and addressed issues for vaccination teams.

RESULTS

A total of 235,782 missed children were added to the micro-plans, while 369,739 children, including initial refusals, were vaccinated through field visits. Tailored support interventions, including microplanning, community engagement, and advocacy, significantly improved vaccine coverage and reached marginalized populations. Through rigorous desk reviews and field validation, the accuracy of more than 700 micro plans was enhanced, while community engagement and awareness sessions enabled vaccinating more than 50,000 children from vaccine-hesitant and refusal families. The use of supportive supervision ensured the quality of vaccination services.

CONCLUSION

The implementation of a multifaceted strategy, including tailored support, has been instrumental in ensuring equitable access to life-saving vaccines. By prioritizing the vaccination of missed and zero-dose children, significant progress has been made in ensuring equitable access and reducing the burden of typhoid and other preventable diseases. These experiences provide valuable insights for future immunization campaigns, highlighting the importance of targeted strategies to reach every child and enhance public health outcomes.

58. Typhoid Fever Surveillance in Urban Dhaka, Bangladesh: Risk Factors and Antimicrobial Resistance Pattern

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BACKGROUND

Typhoid fever is a serious and sometimes fatal systemic disease caused by *Salmonella enterica* serotype Typhi (*S.* Typhi). Millions of people in low- and middle-income countries are at risk where access to clean water, and proper sanitation are not adequate. Poor personal hygiene also facilitates transmission of *S.* Typhi. Emergence of antimicrobial resistance (AMR) *S.* Typhi also demands vaccination and WASH (water, sanitation and hygiene) interventions in such settings. Using data collected during the surveillance of typhoid conjugate vaccine (TCV) trial, we aim to describe an epidemiological summary including the effect of different predisposing factors of typhoid and AMR patterns.

METHODS

The trial, conducted in a slum area of Dhaka, Bangladesh, vaccinated children 9 months to >16 years. A total of 150 geographic clusters were randomised to TCV or Japanese encephalitis (JE) vaccine. A baseline census was conducted to collect demographic, socioeconomic and WASH-related information from study population. Febrile patients were enrolled in passive surveillance (PS). Data obtained from the population of JE clusters were utilized for this analysis. We estimated the odds of being blood culture-positive cases for different potential risk factors and used a random forest classification model to understand predictive value of typhoid risk factors.

RESULTS

A total of 8,213 patients were enrolled in the PS and we found 568 typhoid cases. The monthly average positivity rate was 5.25% and isolation was higher between September and November. Age group, duration of fever, prior antibiotic use, patients with gastrointestinal symptoms, and using shared toilets were significantly associated with typhoid fever. In a multivariate analysis, the odds for developing typhoid among young age groups (2-4 and 5-17 years) was more than 2 times higher compared to adults. The influential attributes in the random forest classification model were age and temperature to predict confirmed cases. We found an area under the curve of 94% for these influential factors. Analysis of AMR pattern indicates that multi-drug resistance *S.* Typhi could be a major threat in future.

CONCLUSION

This surveillance helped to determine the risk factors of typhoid fever that lead policymakers to take preventive measures in endemic areas like Bangladesh.

59. Interactions Between *Salmonella* and Protists in Wastewater Facilities in Zimbabwe

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BACKGROUND

Salmonella Typhi is endemic in Zimbabwe with outbreaks often associated with multidrug resistant strains. *S.*Typhi is transmitted primarily via contaminated water in areas with poor or inadequate water, sanitation and hygiene (WASH) infrastructure. An understanding of the mechanisms employed by *Salmonella* to transmit via the aquatic environment is needed to enable targeted interventions to improve WASH infrastructure. Previous laboratory studies have shown that *Salmonella* survival in the environment is enhanced by protists that serve as a protective niche in which *Salmonella* can escape environmental stress. Acanthamoeba spp., Tetrahymena spp. and Dictyostelium discoideum protists, commonly found in water environments, have been shown to aid *Salmonella* transmission and survival. Interaction is mediated by *Salmonella* virulence factors which play a key role in avoiding phagosome lysis when ingested by the protists, allowing them to survive and replicate.

METHODS

A total of 250 wastewater samples were collected from both the inflow and outflow from five treatment facilities across Harare, Zimbabwe over three months in catchment areas with the highest rates of Typhoid fever. Standard culture and enrichment for *Salmonella* and whole-genome sequencing of suspected *Salmonella* was carried out. For a subset of samples, metagenome DNA was extracted and 18S amplicon (n=107) and shotgun metagenome sequencing (n=97) was carried out to identify the protist and bacterial aquatic community structure and association with *Salmonella*.

RESULTS

A total of 34 suspected *Salmonella* strains were isolated across the five treatment facilities, with 20 confirmed as non-typhoidal *Salmonella* by whole genome sequencing. We defined the aquatic protist community which included over 300 taxa within phyla such as Apicomplexa, Cercozoa, Ciliophora, Euglenozoa and Heterolobosea. Samples from which *Salmonella* were isolated, formed distinct clusters with the protist community using principal component analysis. The richness of the protist community but not the overall bacterial community was greater in samples from which *Salmonella* were isolated.

CONCLUSIONS

A complex community of protists are present in wastewater, many of which have the potential to interact with *Salmonella*. Preliminary analysis is consistent with the potential of protists to play a role in survival of *Salmonella*. The data has been used to design observational and experimental studies to test the hypothesis that a viable protist community is needed to enhance the survival of *Salmonella* and transmission within the aquatic environment. This information may be useful to inform strategies for reducing *S.*Typhi in the environment.

60. Awry Achives — Using Historiographical Methods to Uncover Biases in Microbial Culture Collections, Typhoid Vaccine Trials, and Microbiological Research

Claas Kirchhelle

University College Dublin

BACKGROUND

This presentation shows how historical power imbalances in international microbiological sampling networks led to significant biases in the composition of major microbial culture collections and how these biases continue to impact current typhoid control and microbiological research.

METHODS

The author employed critical qualitative and quantitative historiographic methods to evaluate over sixty years of archival correspondence and phenotypic surveillance data generated by Institut Pasteur in Paris, the UK Health and Security Agency in Colindale, and the US Centers for Disease Control and Prevention in Atlanta.

RESULTS

Evaluation of deposited data reveals how the hierarchical nature of Cold War sampling and high-income biosecurity priorities led to nonrepresentative surveillance of global microbiota and deposits in microbial heritage collections. Biased taxonomies and microbial collections impacted biomedical research including the selection of strains for human challenge trials of new typhoid vaccines.

DISCUSSION

Drawing on these findings, the presentation highlights the importance of integrating critical historiographic methods into microbiological research when it comes to working with historically biased culture collections and exploring the microbial past.

61. "Serocalculator": A Novel R Software Package for Estimating Typhoid Seroincidence From Cross-Sectional Serosurveys

Kristina Lai[1], Farah Qamar[2], Denise Garrett[3], Jessica C. Seidman[3], Dipesh Tamrakar[4], Samir Saha[5], Peter Teunis[6], Jason R. Andrews[7], Douglas Ezra Morrison[8], Kristen Aiemjoy[9]

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BACKGROUND

Public health scientists and health professionals worldwide lack reliable data on the burden of enteric fever, which is a barrier to effective control measures and vaccine introduction. Seroepidemiology provides an efficient means to generate unbiased estimates of disease burden such as seroincidence, the rate at which new infections occur in a population. Unlike blood-culture surveillance, seroepidemiology is not biased by care-seeking behaviors, access to laboratory infrastructure, or antibiotic use and is far less expensive and time intensive to conduct. A fully-developed, publicly-available software to efficiently generate accurate typhoid incidence estimates can help generate data to inform vaccine policy and implementation.

METHODS

The R package "serocalculator" implements a novel seroincidence estimation approach that leverages pre-existing models of antibody decay dynamics from longitudinal studies of confirmed cases to estimate seroincidence from cross-sectional serosurveys. This estimation approach overcomes limitations of previous methods which analyze dichotomized antibody responses. The package also hosts de-identified longitudinal parameter sets, allowing users to easily generate incidence estimates for their communities. Users will input results from cross-sectional serosurvey data, including variables such as quantitative antibody results. The "serocalculator" package will use pre-written functions to apply disease-specific antibody decay models and generate the specified estimates.

RESULTS

The novel R software package "serocalculator" provides an open-source, no-cost resource for estimating seroincidence and disease burden from cross-sectional serosurveys. Our software meets a critical need in disease surveillance and control and includes (a) functions for estimating seroincidence from cross-sectional survey data, (b) a database of the disease-specific antibody decay models that are required for applying these methods, and (c) accompanying package documentation and training materials to allow users to apply this package to their own data. The package includes functions for loading and preprocessing data, performing exploratory data analysis, generating incidence estimates, visualizing results, and performing simulations.

CONCLUSIONS

The "serocalculator" package will equip a new community of users with effective tools to generate seroincidence estimates from cross-sectional surveys. This software will have an immediate impact on the typhoid surveillance research community, where there is an urgent need for tools to accurately and efficiently measure the incidence to inform vaccine program prioritization.

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62. Optimising Vaccination for iNTS Disease in Africa: OptiVaNTS

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BACKGROUND

Invasive non-Typhoid *salmonella* (iNTS) is pre-dominantly a disease of infants in sub-Saharan Africa, and responsible for >500,000 illnesses, 77,500 deaths. The key feature of severe infection is systemic spread from the gut to systemic sites. Children develop highly effective natural immunity by the age of 2-3 years, following natural asymptomatic gut exposure in the community, but remain at risk of invasive disease while they are under that age. Therefore, an optimal preventive strategy is vaccines, which are now in early clinical development.

BROAD OBJECTIVE

To comprehensively elucidate the effector functional humoral profiles and antigen-specificities of naturally developed protective antibody against iNTS disease among Malawian children.

METHODS

This is a cross-sectional study conducting systems serology assays utilising carefully clinically characterised serological samples from demographically mapped randomly-selected cohorts of susceptible and non-susceptible children aged 0-5y, from Malawi. Children were characterised for *Salmonella* enteric exposure, and for susceptibility characteristics including malaria exposure and positivity, and for nutritional indices. Assays include antigen-specific analysis of isotypes and subclasses using Luminex bead array, and functional cellular assays including antibody-dependent neutrophil/monocyte phagocytosis and complement deposition (ADCD).

RESULTS

Analysis of discovery cohort samples (n=700) analysed to date suggest that repeated natural enteric exposure to NTS results in gradual acquisition of antigen-specific humoral immunity from 6 months onwards, across IgG1, 2 and 3 subclasses. IgM responses to NTS peaked earlier in life. Results will next be stratified across different susceptibility-exposures and epidemiologies in a characterised validation cohort, and among mother-infant pairs, and correlated with functional cellular responses.

CONCLUSION

This approach enables us to understand functional natural immunity in relation to age, *Salmonella* exposure, and disease susceptibility, and will help develop correlates of protection for vaccine development and evaluation.

63. Modelling Using Stem-Cell Derived Gut Organoids and Macrophages Demonstrates a Unique Transcriptomic Response to Infection with Members of *S.* Typhi H58 Clade

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BACKGROUND

There are significant concerns about the spread of the multi-drug resistant H58 S. Typhi clade and its ability to cause severe disease. Modelling infections with this human restricted pathogen to learn more about its pathogenicity can be done using the intestinal 'organoid' system (iHO) wherein 3-D structures representative of the gut epithelium can be produced from human induced pluripotent stem cells (hiPSC). Macrophages can also be produced from hiPSC from the same host, thus allowing study of response to infection in both the epithelial and immune compartments.

METHODS

hiPSCs were differentiated to iHO via sequential culture with a specific series of cytokines and placed into a Matrigel-based pro-intestinal culture system. hiPSC from the same cell line were differentiated into embryoid bodies and later macrophages via culture with specific cytokines. Organoids were microinjected and macrophages stimulated with *S.* Typhi (Quailes strain), SGB90 (non-H58 clinical strain), Ty101 and Ty106 (H58 strains) and modified gentamicin protection assays were performed. Intracellular CFU counts were compared between pathogens. RNA was extracted from infected samples and control samples injected with PBS and sequenced on the HiSeq 4000 in dual indexed pools at Wellcome Trust Sanger Institute, Cambridge UK. Differential gene expression analysis was performed between stimulation conditions and PBS controls using the limma/voom pipeline, with significant genes identified at false discovery rate (FDR) <0.05. Principal components analysis (PCA) was carried out to characterise overall variation in gene expression profiles amongst stimulated and control samples using R software.

RESULTS

All strains appeared to interact with and invade the intestinal epithelium, with Ty116 being significantly more invasive than the non-H58 strains at the 1.5 hour timepoint ($p<0.05$). All pathogens were able to survive and replicate within macrophages, with maximum CFUs being recovered in cells stimulated with *Ty101* ($p<0.001$). Ty116 was also recovered at higher CFU than the non-H58 strains, but not significantly so. PCA plots for macrophage RNA-Seq data revealed separation of transcriptomic response to the strains by H58 status. There was a unique transcriptomic response to infection by H58 strains, with downregulation of genes involved in antibacterial response, vesicle trafficking, phagosomal maturation and pro-inflammatory response (S100A8, SLAMF1, IL-12B and IL-23A).

CONCLUSIONS

We report increased invasiveness in the gut iHO and macrophage models for serovars from the *S.* Typhi H58 clade. We also demonstrate the presence of a unique transcriptomic signature in response to macrophage infection with these strains, with downregulation of a number of genes involved in response to infection, suggesting that the ability of this clade to cause severe disease could lie in its ability to survive and replicate within macrophages.

65. Silica Vesicles Increase Stability of Multi-Drug Resistant *Salmonella* Enteritidis-Specific Phages in Simulated Digestive Systems and Chicken Model

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INTRODUCTION

Non-typhoidal *Salmonella enterica* serovar Enteritidis is one of the major causes of foodborne infections in Sub-Saharan Africa. This serovar is mainly transmitted to humans through poultry products. Bacteriophages (phages) are a promising alternative to antibiotics to reduce *Salmonella* incidences in poultry farms. Surviving the harsh environment encountered in the chicken gastrointestinal tract, such as low pH, high temperature, and enzymatic digestion can be valuable in selecting phages with high therapeutic potential.

METHODS

In this study, we characterized 13 newly isolated Kenyan *S.* Enteritidis-specific phages for their ability to survive in pH-adjusted media, different temperatures, and simulated gastric and intestinal fluids. Additionally tested was the capacity of silica vesicles to adsorb/encapsulate, release, and safeguard phages in artificial stomach juice. Finally, 3-day-old broiler chicks were used to assess their capacity for survival *in vivo* (24).

RESULTS

All phages showed a broader host range and were relatively stable for 12 hours at pH values between 5 and 9 and temperatures between 25 °C and 42 °C. Phages remained stable in simulated gastric fluid for 20 minutes before losing their ability to infect. For up to two hours, phages remained largely stable in simulated intestinal fluid. Phages significantly inhibited *Salmonella* growth in pH 2 and pH 3-adjusted media as well as in simulated gastric fluid at pH 2.5, but this effect was less pronounced in simulated

intestinal fluid at pH 8. The adsorption/encapsulation efficiencies of the three silica vesicles (SV 100, SV 140, and SV 140-C_{18}) were 57.4%, 60%, and 90%, respectively. They were able to shield phages in stomach fluid for an hour and had modest, steady phage release rates up until day 4. SV 140-C18 had the lowest log reduction of 4 logs PFU/ml. Up until day 8 following inoculation, silica vesicle-encapsulated phages in the chickens displayed larger phage titers than non-encapsulated phages. On day 28, SV-encapsulated phages K28 and K11 had the highest titres.

CONCLUSION

These findings imply that these phages may have a chance of surviving in living organisms' gastrointestinal tract and eliminating salmonellosis.

66. Stakeholder Survey to Define Evidence Priorities for TCV Implementation Plan in India

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BACKGROUND

Typhoid fever in India, constituting one-third of the estimated global burden, is one of the diseases of public health importance against which a vaccine is not yet deployed nationally. The National Technical Advisory Group on Immunization (NTAGI) of India has recommended the introduction of TCV in routine immunization programmes and suggested developing an evidence-informed implementation plan. Developing an evidence-informed plan needs the generation of critical and missing evidence from the stakeholder perspective. The stakeholder survey described below aims to assess the importance of different types of evidence from an Indian stakeholder's perspective and make a rank list of priorities.

METHODOLOGY

In parallel to a literature review, the importance of evidence was assessed quantitatively from a stakeholder perspective through an online survey, and a priority list was generated using multi-criteria decision analysis (MCDA) based on the perceived importance of evidence as reported by the stakeholders. First, using World Health Organization's (WHO) Evidence to Recommendation (EtR) framework, a list of 45 evidence factors was prepared considering the Indian context under seven WHO EtR criteria, namely, disease burden, safety and efficacy, acceptability, values and preferences of the target population, feasibility, health equity and resource use. Then, an anonymised online survey tool and consent forms were developed in Microsoft Forms, and ethical approval was obtained. Thereafter, a diverse range of survey stakeholders involved in decision-making were selected to rank the order of evidence factors listed under each criteria based on their importance for TCV introduction, irrespective of the availability of evidence. A snowball sampling method was used with a final target sample size of 40, where preidentified study participants will choose future participants among their professional acquaintances. Finally, the participants were contacted by telephone, followed up by emailing the participant information sheet, instructions, and a link to the online survey. Once the survey is filled, data is automatically stored in Microsoft Excel. Data were analysed using multi-criteria decision analysis (MCDA). Finally, evidence factors were organised in quintiles of importance, the first quintile being the most important and the fifth least.

RESULTS

The stakeholder survey tool was developed, pilot-tested, finalised, and the survey started in late June 2023. At the time of this abstract preparation, 7 (18%) of target responses were received. Based on the preliminary results rank order of WHO EtR criteria are as follows: disease burden, safety and efficacy, feasibility, resources use, acceptability to stakeholders, values and preferences and target population and finally, health equity. The topmost important evidence factors under each EtR criteria were typhoid fever incidence, vaccine efficacy, sustained vaccine availability, cost-effectiveness, NTAGI recommendations, disease perceptions in the target population, and increased health benefits to poor, vulnerable and people living in slums. The final results will be available and presented at the conference.

CONCLUSION

The stakeholder's perspective in this survey indicates evidence-generation priorities for TCV introduction in India with due consideration for online survey limitations. The stakeholder priorities represented in the EtR framework have applicability to other vaccine introductions in India and elsewhere.

67. Typbar TCV®: A Comprehensive, Most Clinically Evaluated Typhoid Conjugate Vaccine

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Bharat Biotech International

ABSTRACT

Typbar TCV® is the world's first WHO pre-qualified typhoid conjugate vaccine containing polysaccharide of *Salmonella* Typhi Ty2 conjugated to Tetanus Toxoid. WHO-SAGE recommended the Typbar TCV® vaccine's introduction for infants and children over 6 months of age as a single dose in endemic countries[1]. Typbar TCV® vaccine was evaluated in a pivotal Phase 3 study for its safety and immunogenicity in healthy Indian participants aged 6 months to 45 years. From this study, which is the largest clinical trial for TCVs conducted thus far, results established that the vaccine is safe and immunogenic[2]. Typbar TCV® vaccine is the

only typhoid conjugate vaccine which was followed for persistence and proven to be safe and immunogenic even after 7 years post-vaccination[3]. Later on, a Phase 4 study was conducted and found that the vaccine is safe and induces a similar immune response in elderly adults aged between 45- 65 years. In another Phase 4 study, Typbar TCV® was proven for its non-interference with the MMR vaccine when co-administered in children ages 10 months[4]. Typbar TCV® also found to be safely co-administered with meningococcal conjugate vaccine (MCV-A), measles-rubella (MR), and yellow fever (YF) vaccines without interference in African children[5,6].

With regards to the vaccine efficacy, BBIL collaborated with Oxford University and evaluated the protective efficacy in a human challenge study and reported 87.1% efficacy against typhoid infection[7]. Typbar TCV® vaccine safety was evaluated in ~9000 participants and found to be safe and no vaccine-related SAEs were reported[8] (Table 1). Based on this data, Global Advisory Committee on Vaccine Safety (WHO-GACVS) also recommended the Typbar TCV® vaccine to children ages over 6 months in typhoid endemic regions[9].

Based on all these results, it can be concluded that Typbar TCV® vaccine is reported to be safe and immunogenic in children and adults across the world. Typbar TCV® vaccine's efficacy was established (~80%) in non-endemic and endemic regions.

References & Tables to be added later.

68. Genomic Characterization and Transmission Dynamics of *Salmonella* Melaegridis and Kentucky From a Sewage-Based Environmental Surveillance Study in Karachi

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BACKGROUND

Non-typhoidal Salmonellosis (NTS) is a zoonotic infection resulting in millions of cases of acute gastroenteritis and significant global mortality. *Salmonella enterica* serovar Kentucky, primarily infecting animals like poultry and cattle, poses a growing threat to public health. Underestimated NTS serotypes, such as *S.* Meleagridis, can asymptomatically infect humans, with potential transmission through animal-derived foods. Presently, Pakistan lacks WGS data on *Salmonella*. This study presents a WGS analysis of *S.* Melaegridis and S. Kentucky, aiming to uncover their genetic composition, diversity, antimicrobial resistance (AMR) profiles, and transmission routes within sewage systems, offering insights into their persistence and spread.

METHODS

In this pilot study, 02 *S.* Melaegridis and 01 *S.* Kentucky strains isolated from sewage were whole-genome sequencing (WGS) using Illumina MiSeq. Raw reads underwent quality filtering to remove low-quality bases and adapter sequences. Genome assembly was performed to reconstruct complete genomes, followed by variant calling and SNP analysis for identifying genetic variations. Phylogenetic analysis elucidated evolutionary relationships. Virulence gene identification and antimicrobial resistance gene detection assessed pathogenic potential and resistance profiles. Comparative genomics identified unique genomic features and variations.

RESULTS

Antimicrobial resistance analysis revealed that two Melaegridis isolates were pan-susceptible, while *S.* Kentucky showed resistance to multiple antibiotics, indicating a multidrug-resistant (MDR) strain. MLST classified *S.* Kentucky as ST198 and *S.* Melaegridis as ST365. These sequence types were phylogenetically similar to clinical isolates and comparable to other globally available *Salmonella* clinical strains. The *S.* Kentucky strain carried the IncFII(S) replicon, whereas no replicons were found in *S.* Melaegridis. All three isolates exhibited virulence genes associated with fimbriae adherence, stress adaptation, and plasmid-borne spv genes, highlighting their potential role in the pathogenicity of NTS strains.

CONCLUSION

This study highlights the importance of investigating *S. enterica* foodborne outbreaks, providing insights into host-restricted serovars' genetic diversity and antimicrobial resistance.

69. Genomic Analysis and Antimicrobial Resistance of Environmental Non-Typhoid *Salmonella* Serovars in Pakistan

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BACKGROUND

Non-typhoidal *Salmonella* (NTS) are zoonotic pathogens that cause millions of acute gastroenteritis cases and are responsible for a significant global mortality rate. *Salmonella enterica* serovar Kentucky, which primarily infects animals such as poultry and cattle, is an emerging human pathogen. Meanwhile, under-studied NTS serotypes, such as *S.* Meleagridis, can asymptomatically infect humans and potentially be transmitted through animal food. In this study, we performed whole genome sequencing (WGS) analysis of environmental (sewage-isolated) *S.* Meleagridis and *S.* Kentucky isolates.

METHODS

We have sequenced two *S.* Meleagridis and one *S.* Kentucky strain that was previously isolated from sewage samples collected in Karachi using Illumina MiSeq. Raw reads were filtered to remove low-quality bases and adapter sequences. Subsequently, we performed assembly to reconstruct complete genomes, variant calling, and SNP analysis to identify genetic variations. Further analysis was conducted to identify antimicrobial resistance (AMR) and virulence genes and determine the evolutionary relationship of these strains with other sequenced strains.

RESULTS

Antimicrobial resistance analysis showed that both *S.* Meleagridis isolates were pan-susceptible, while *S.* Kentucky demonstrated resistance to multiple antibiotics. Multi-locus sequence typing (MLST) identified *S.* Kentucky as ST198 and *S.* Meleagridis as ST365. Both sequence types exhibited phylogenetic similarities with clinical isolates and global *Salmonella* clinical strains. The *S.* Kentucky strain carried the IncFII(S) replicon, while the *S.* Meleagridis strain did not. All three isolates exhibited virulence genes related to cellular invasion, fimbriae adherence, and stress adaptation genes, highlighting their potential to cause human or animal infection.

CONCLUSION

Our study revealed significant antimicrobial resistance in *S.* Kentucky and potential virulence genes in both *S.* Meleagridis and *S.* Kentucky strains from Pakistan. The phylogenetic similarities with global clinical strains underscore the potential zoonotic threats and transmission paths. These findings emphasize the need for a more extensive genomic study of these serovars.

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70. Prospective Evaluation of a Novel DPP Typhoid Assay for Rapid, Low-Cost Diagnosis of Enteric Fever

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**Both authors contribute equally*

BACKGROUND

Enteric fever, caused by *Salmonella* Typhi and Paratyphi A, is a major cause of preventable mortality and morbidity in many resource-limited countries. Currently, there is a lack of rapid, accurate, and low-cost assays for diagnosing enteric fever. To address this need, the Dual-path Platform for Typhoid (DPPT) assay was developed for rapid detection of anti-Hemolysin E and anti-lipopolysaccharide IgA antibodies in blood. We performed a prospective study to evaluate accuracy of this assay in children with acute febrile illness.

METHODS

From August 2022 to July 2023, we conducted this study at a tertiary pediatric hospital in Dhaka. We enrolled children <18 years who visited outpatient clinic with ≥3 days of fever. We collected venous blood, finger stick capillary blood, and nasopharyngeal swab at enrollment. We performed blood culture and serologic assays (DPPT, Widal, and Test-It) for typhoid, as well as molecular assays for RSV, Influenza, Dengue, and Rickettsia. To evaluate the accuracy of DPPT system, we calculated the area under curve (AUC), specificity, and balanced accuracy at Youden's-optimal threshold.

RESULTS

Among 501 participants, we identified 77 enteric fever cases (62-typhoid, 15-paratyphoid) and 70 alternative etiologies (34-Influenza A/B, 24-dengue, 7-RSV, 5-Rickettsia). Accuracy of the DPPT was high in all patients (AUC 0.90; Youden's-optimal sensitivity 95%, specificity 80%) and those with confirmed etiologies (AUC 0.96; Youden's-optimal sensitivity 95%, specificity 90%). Balanced accuracy was higher for DPPT (88%) than Widal test (71%) and Test-It (64%) among all patients and confirmed etiologies (DPPT: 93%; Widal: 73%; Test-It: 66%). Assay performance remained high for individuals with or without prior antibiotic use (AUC: 0.98, 0.95), fever <5 or 5 days (AUC: 0.96, 0.98), ages <5 or 5 years age (AUC: 0.97, 0.96), and for typhoid or paratyphoid cases (AUC: 0.98, 0.97). DPPT gave consistent results when tested with plasma, venous and capillary blood (Pearson's r >0.92 compared with plasma ELISA for all).

CONCLUSIONS

The point-of-care DPPT system demonstrated higher accuracy in detecting enteric fever in a high-endemic community than other available diagnostics. This promising result calls for further evaluation through field trials to assess its effectiveness in improving antibiotic usage among suspected enteric fever cases.

KEYWORDS

Enteric fever; Typhoid; Paratyphoid; *Salmonella* Typhi; *Salmonella* Paratyphi A; Diagnostic; Point-of-care; Hemolysin E IgA; Lipopolysaccharide IgA

71. Detection of Typhoid Burden Using Environmental Surveillance in Yogyakarta, Indonesia

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BACKGROUND

Typhoid can progress from an active outbreak to a latent epidemic, but clinical surveillance alone may not be sufficient to monitor the disease in populations, particularly in low and middle income countries (LMICs) where the available data are underreporting and the definition of cases is unclear. Hence, wastewater-based epidemiology (WBE) may be an alternative. This study aimed to assess the feasibility of conducting WBE to measure the burden of typhoid diseases in an LMIC setting.

METHODS

A routine WBE surveillance in 17 sampling locations in 3 districts in Yogyakarta province, Indonesia, for 12 months was conducted. Samples were collected on a fortnightly basis with grab and passive sampling methods. A positive case of *Salmonella* typhi was defined as having positive results for all three gene targets ttr, tviB, and staG. Water samples were collected from central and community wastewater treatment plants (WWTPs), including manholes flowing to the central WWTP, river, and the near-source tracking (NST) locations (i.e., public spaces where people congregate).

RESULTS

We collected 399 samples from 11 October 2022 – 31 August 2023 (24 batches of sampling). The positivity rate of S. typhi was relatively higher between October to December 2022, ranging from 58% to 31%. Throughout the study period, S. typhi was frequently detected in rivers (42%), manholes (up to 25%), market (25%), and communal WWTP (17%). Challenges included providing real-time results and the availability of imported reagents have delayed laboratory analysis.

CONCLUSION

A WBE surveillance system for typhoid in Indonesia is feasible to conduct for monitoring community burden of infections. In order to successfully implement a real time WBE surveillance for typhoid, the challenges will need to be addressed.

72. Age-Specific Concentrations of Anti-*Salmonella* Enteritidis and *Salmonella* Typhimurium Antibodies at Three Sites in Kenya with Different iNTS Disease Incidence

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BACKGROUND

Seroprevalence studies can indicate the age-distribution of first infection with non-typhoidal *Salmonella* (NTS) and estimate the rate of acquisition of these infections by age, parameters that are critical in the targeting of interventions, particularly vaccination.

METHOD

We collected 1254 paired samples of serum and stool from healthy children and adults (aged 0-82 years) in Kilifi, Nairobi and Siaya counties in Kenya, areas of low, medium and high incidence of invasive NTS disease (iNTS), respectively. We quantified the concentrations of IgG and IgA antibodies against *S.* Enteritidis O-antigen (O:9) and *S.* Typhimurium O-antigen (O:4,5) using an in-house standardised ELISA. A previously calibrated reference serum was used as an internal control. The threshold for seropositivity was determined using mixture modelling. The stool samples were cultured for NTS and resulting NTS isolates serotyped using Kauffman-White scheme.

RESULTS

Among infants, maternally-derived O:9 IgG and O:4,5 IgG antibodies were present and both decreased by 40% per month in the first 6 months of life while concentrations of IgA among the infants remained low. Thereafter, the geometric mean concentrations (GMC) of IgG against O:9 and O:4,5 antigens increased sharply with age across all sites, reaching a plateau in early adulthood. The increase in O:9 IgG antibody concentration by age was highest in Nairobi, while for O:4,5 IgG antibody concentrations, it was highest in Kilifi. Seroprevalence also increased by age. By 5 years of age, 80% of children in Kilifi, 55% in Nairobi and 80% Siaya were seropositive to O:4,5 IgG, while 50%, 65%

and 40%, respectively, were seropositive to O:9 IgG. Out of 1253 matched stool samples, 34 (3%) were positive for NTS carriage, the majority (28/34) of which were from Kilifi. The GMCs of O:4,5 IgG were 2 times higher for carriers of Group B *Salmonella* than non-carriers (p=0.04).

DISCUSSION

Primary infection with NTS occurs early in life during the decay of protective maternal antibodies. This, coupled with known high incidence of iNTS disease in infants, suggests that interventions against iNTS, including vaccination, should be designed to provide immunity in early infancy. A bivalent vaccine against both *S.*Enteritidis and *S.* Typhimurium would be appropriate for Kenya as both serotypes occur widely.

73. O-Antigen Variation in *Salmonella* Paratyphi A

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BACKGROUND

A proportionate increase of *Salmonella* Paratyphi has been observed in many South and Southeast Asia countries. Currently, there are no licenced vaccines against Paratyphi A; however, several are in development, with a few using Paratyphi A O-antigen (O2, O12) as the target antigen. O-antigen is the outermost part of LPS consisting of repeating units of a pentasaccaride, and can be modified by length (number of repeating units) as well as lateral modifications such as acetylation. To ensure effective vaccine design, we need to understand how these modifications affect antibody binding.

METHODS

LPS from clinical isolates was extracted and subjected to separation by SDS-PAGE and LPS staining and/or western blotting with an O2 monoclonal antibody. A selection of genomes was sequenced and analysed bioinformatically (presence of SNPs, indel modifications or larger recombinations). Antibody binding was investigated by high-throughput confocal microscopy (Perkin Elmer Operetta) using monoclonal antibodies, rabbit polyclonal sera, as well as a selection of sera from naturally infected patients from an endemic area. Serum bactericidal assays (SBA) were performed using a luminescent assay.

RESULTS

LPS was extracted from 84 Paratyphi A clinical isolates. Around 10% had either a structural variation or variable O2 antibody binding, as determined by LPS migration shifts on a gel or by immunoblotting, respectively. We did not identify any apparent link between genomic differences in the O-antigen encoding regions and the observed phenotypes. Analysis by confocal high-throughput microscopy suggested that, within a theoretically homogeneous population, a substantial proportion of single organisms were not bound by O2-specific monoclonal antibodies, suggestive of variable presentation of the respective epitope. Similar variations were seen in antibody binding by patient sera and SBA activity, but did not necessarily correlate with O-antigen phenotypes. Finally, we observed changes in LPS laddering when organisms were grown in different salt concentrations, bile concentrations, and carbon sources, and show whether these changes impact antibody binding.

CONCLUSION

S. Paratyphi A exhibit variation in their O-antigen which can impact antibody binding, but this does not seem to be driven by variations in O2 conformation. However, these preliminary results should initiate further investigations on the importance of different O-antigen conformations in humans, particularly following vaccine immunisation.

74. Presence of Phage-Plasmids in Multiple Serovars of *Salmonella*

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BACKGROUND

Antimicrobial resistance (AMR) genes can be transferred between microbial cells via Horizontal Gene Transfer (HGT) which involves mobile and integrative elements such as plasmids, bacteriophages, transposons, integrons and pathogenicity islands. Bacteriophages are found in abundance in the microbial world but their role in virulence and antimicrobial resistance has not fully been elucidated in the Enterobacterales. Whole genome sequencing has revolutionised the way we identify and characterise antimicrobial resistance genes and regions/elements in pathogens. Illumina sequencing coupled with Nanopore sequencing and careful data curation allows the mining of pathogen genomes to detect, characterise and track novel mobile elements involved in AMR transmission.

We have recently identified and characterised a circular P1-bacteriophage-like plasmid (termed phage-plasmid) harbouring a $bla_{CTX\text{-}M\text{-}15}$ gene conferring ESBL resistance in *S.* Typhi (Grieg et al, 2022. mGEN). It is the first time that such a DNA element has been described in this organism.

There is increasing evidence from the literature to show that the horizontal spread of AMR genes mediated by bacteriophages and bacteriophage-like plasmid elements is much more common than previously envisioned.

METHODS

In a surveillance study, a *repL* (phage replication gene) pipeline was developed at UKHSA to detect the presence and characterise phage-plasmids in *Salmonella* isolates present in the GBRU database between 2016 – 2021.

RESULTS

Preliminary data indicates that these phage-plasmid elements are present more frequently than previously thought. In the 47784 isolates screen, 248 *Salmonella* isolates belonging to 26 serovars showed the presence of *repL*(phage plasmid). Majority of the isolates (178/248) isolates belonged to *S.* Typhimurium ST34 and ST19. Phage-plasmids were present in isolates that were resistant and non-resistant to antimicrobials and characterisation of these mobile elements will determine its role in AMR transmission.

CONCLUSION

Long read sequencing of interesting isolates or serovars will be conducted to identify and characterise AMR mechanisms as understanding the structure of such genomic elements is essential to fully elucidate the biological mechanisms and transmission of AMR, and their clinical relevance.

75. Safety and Immune Response of a Trivalent Vaccine Against iNTS and Typhoid Fever in European and African Adults: A Phase 1/2a Observer-Blind Multi-Country Study

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INTRODUCTION

Invasive nontyphoidal *Salmonella* (iNTS) disease and typhoid fever are significant public health concerns, particularly in sub-Saharan Africa (sSA), where the burden of these diseases is substantial. Currently, there is no vaccine available for iNTS disease. This study aims to evaluate the safety, reactogenicity, and immune response of the trivalent vaccine against iNTS disease and typhoid fever in healthy European and African adults.

METHODS

This is a Phase 1/2a, observer-blind, randomized, dose-escalation, controlled, multi-country, two-staged, staggered study involving nine groups. The study will recruit 155 healthy adults aged 18 to 50 years in Europe and Africa. The GVGH iNTS-typhoid conjugate vaccine (iNTS-TCV) candidate vaccine is currently undergoing its initial evaluation in European adults as part of Stage 1 of the clinical trial. Subsequently, Stage 2 of the trial will be assessing the same vaccine in African adults. Participants will receive one intramuscular (IM) study intervention per arm on Day 1, Day 57, and Day 169. Randomization will occur in a 2:2:1 and 3:3:1 ratio in Europe and Africa, respectively. Each participant will be in the study for approximately 13 months, including a 6-month follow-up period after the third intervention. Adverse events and serious adverse events will be recorded.

ANTICIPATED RESULTS

Ethical approval has been sought from the local ethics committee and the Stage 2 start date is anticipated to be August 2023 in Malawi. We plan to report the safety and reactogenicity profile of the GVGH iNTS-TCV vaccine in healthy Europeans and study progress from the African site at the conference. The study will provide valuable data on the safety and immunogenicity of the GVGH iNTS-TCV vaccine in both European and African populations.

CONCLUSION

This study represents a crucial step in evaluating the GVGH iNTS-TCV candidate vaccine in humans. The findings will contribute to the development of an effective vaccine against iNTS disease, addressing the urgent need for preventive measures in Africa. The results will provide insights into the safety, reactogenicity, and immunogenicity of the vaccine, paving the way for further clinical trials and potential implementation in high-risk populations.

FUNDING STATEMENT

The study is sponsored by GSK Biologicals SA and funded by Combating Antibiotic Resistant Bacteria-X (CARB-X)

Trial registration number: NCT05480800

76. Antimicrobial Resistance in Blood Culture Isolates of *Salmonella* Typhi and Paratyphi Received From Laboratories Across Pakistan From January to December 2021

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BACKGROUND

Antimicrobial resistance in Typhoid fever threatens the effectiveness of our existing arsenal of antibiotics thus limiting treatment options, prolonging illness, and increasing healthcare costs. Resistant strains can spread globally, further limiting treatment options and exacerbating the burden of typhoid. The study examined the prevalence of antimicrobial resistance of *S.*enterica serotypes Typhi and Paratyphi in blood culture isolates received from laboratories located at different sites across Pakistan.

METHODS

Blood culture reports of *S.* Typhi and *S.* Paratyphi, obtained through either the BACTEC™ automated system or manual subculture technique on macConkey and blood agar, were subsequently subjected to antimicrobial susceptibility testing using disc diffusion assay. These reports were compiled and analyzed on SPSS version 22.0, with data collected from laboratories situated at various sites across Pakistan from January 2021 to December 2021.

RESULTS

A total of 2,558 positive blood cultures were analyzed for serotyping, with 2,375 (92.8%) identified as *Salmonella* Typhi and 183 (7.2%) as *Salmonella* Paratyphi. Among the *S.* Typhi isolates the resistance rates exhibited to Ampicillin (AMP),Ciprofloxacin, Chloramphenicol, third-generation Cephalosporins and Azithromycin were 74%,68%, 66%, 59% and 1.6% respectively. In contrast, *S.* Paratyphi showed resistance rates of 36%,20%, 6%, 3.3% and 2.7% to Ciprofloxacin, Ampicillin, Azithromycin, Chloramphenicol and Cephalosporin respectively.

Age distribution analysis revealed that 63% of *S.* Typhi and 8% of *S.* Para Typhi samples were of children aged 0-12 years. Among all, 35% were classified as extensively drug-resistant (XDR), while 11% were identified as Multidrug-resistant (MDR) only. Remarkably, 67% of MDR and 60.5% of XDR samples among *S.* Typhi infections were detected in children below 12 years old.

CONCLUSIONS

A high prevalence of antimicrobial resistance to *Salmonella* Typhi and Paratyphi was found in the blood samples. Additionally, disproportionate distribution of MDR and XDR among children underscores the need for targeted preventive (vaccination and WASH) and treatment strategies. Concrete efforts should be made to raise awareness about prudent antimicrobial use and implement effective surveillance systems to monitor the changing patterns of enteric fever and antimicrobial resistance.

77. An Outbred Mouse Model of Invasive *Salmonella* for Study of Pathogenesis and Development of Vaccines

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Institut Pasteur de Dakar

ABSTRACT

Invasive nontyphoidal *Salmonella* (iNTS) infections constitute an important public health concern in sub-Saharan Africa. This significantly fatal disease is caused by serotypes of *Salmonella* that are typically associated with gastroenteritis and are widely present in food animals and the environment. Our goal is to develop an outbred mouse model of iNTS to study pathogenesis and construct vaccine strains. For this purpose, we use Swiss Webster (SW) mice that are fully immunologically competent rodents that better simulate natural *Salmonella* infection, contrary to mouse strains commonly used to study *Salmonella* pathogenesis like BALB/c and C57/BL6 rodents that harbor genetic mutations that make them highly sensitive to *Salmonella* infection. In order to identify lethal and non-lethal isolates among clones circulating in Senegal, we have screened 64 *Salmonella* enterica strains belonging to 31 serovars from our collection of strains originating from human patients, animals, food and environment. Ten isolates were able to cause death when administered by the intraperitoneal route with varying lethality. Four isolates of serovar Typhimurium and of sequence type (ST) 19 caused 80-100% death in repeated experiments. Similarly, five isolates of serovar Enteritidis ST11 caused 20-50% death, while one strain belonging to serovar Banana ST683 killed 50% on average. Interestingly, none of the lethal isolates caused death when administered by the oral route. To identify clones that can serve as potential vaccine strains, we evaluated the ability of non-lethal isolates to protect SW mice against challenges with virulent clones. For this purpose, groups of mice were administered with a non-lethal isolate and challenged four weeks later with a virulent strain. One isolate belonging to Kentucky ST198 fully protected SW mice against virulent Typhimurium strains in repeated experiment. Additionally, two isolates of serovars Brancaster and Schwarzengrund conferred a partial protection against virulent Typhimurium. Details investigations on the ability of these and other non-virulent strains are currently ongoing.

78. Characterization, and Comparative Genomic Analysis of Two Lytic Bacteriophages Infecting *Salmonella Typhi*

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BACKGROUND

Typhoid fever caused by *Salmonella Typhi*, remains a significant cause of morbidity and mortality in low and medium income countries. Multidrug-resistant *S.*typhi have been reported in Nigeria and across Africa. There is, therefore, need to explore alternatives to antibiotics in the control and management of typhoid fevers. In this study, we report the isolation of two lytic phages against *S.*typhi isolates and genome characteristics.

MATERIALS AND METHODS

The phages were isolated from sewage and stool samples obtained from hospital environments in Jos, Plateau state. The phages were sequenced on the illumina platform and the genomes were assembled using spades. Bacphlip was used to determine the life cycle of the phages and

viridic(web version) was used to determine the taxonomy of the phages. Prokka was used for annotation. The stability of the phages were tested in various pH, Temperature and salt concentration

RESULTS

The phages Jerseyvirus ijeoma is similar to Jerseyvirus SS3e. Jerseyvirus ijeoma is genome has 56CDS and a genome size of 41kbp. Apdecimavirus ayanbimpe is similar to Apdecimavirus AP10(KT852574.1) it has a molecular size of 39kbp, and it has 48 CDS. The phages lysed *Salmonella* typhi and *Salmonella* typhimurium isolates. The phages are lytic and stable at various conditions

CONCLUSION

The phages isolated have huge potential for further development against *salmonella typhi* infections.

79. Mama Put Joints Increases the Causes and Spread of Typhoid Fever to People of Aba Town in Abia State of Nigeria

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[1]Primary Health Care System, [2]ECEWS

BACKGROUND

Aba people are being fed with poisons in the name of food. People remain attached to local food vendors commonly known as Mama Put Joints in Aba despite the health risk involve. Aba town is commonly known for industrialization, markets, and transportation, for this reason; the people "love to eat on the go" to catch up with their daily duties. The Joints are mostly located close to unhygienic areas like toilets, gutters, and waste disposal areas. Most often, foods are dished and served with bare hands, and the water for drinking customers is unsafe. We set out to investigate the reason people patronizes roadside food vendors despite the health risk.

This study is carried out in Aba town of Abia state, Nigeria. We identified three popular common Joints in different areas that people patronize a lot. We randomly selected 150 people as the respondents to the questionnaire. The sample size was 50 questionnaires for each site. Data collected included age, no food at home, gender, employment, variety of food, education level, marital status, etc. We dichotomized responses for data analysis.

RESULTS

Results of the study revealed Median age of respondents was 35 years (range: 14-55 years) and a total number of 91(60.7%) were male. 97 people (64.7%) were employed and 54 (55.7%) of them were self-employed, 53 (35.3%) were students of both secondary and tertiary schools. 138 (92%) visit side food vendors regularly because the food is affordable and cheap. 113 (75.3%) due to the variety of food and 109 (72.7%) because of the availability of food. 77 (51.3%) due to no stale food and 96 (64%) no segregation. 75 (50%) due to no food at home and only 42 (18%) are aware of health challenges.

Government should embark on enlightenment campaigns on a regular basis and health hygiene training for these food handlers to create awareness about the importance of health hygiene and the risks associated with noncompliance with the rules and regulations that govern food handlers.

80. Genomic Characterization of *Salmonella* Strains Isolated From Household Water in Municipal Ibadan, Oyo State, Nigeria

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BACKGROUND

Household water quality contributes to human health, as fecally contaminated water can transmit enteric pathogens, including *Salmonella*. This study is aimed at determining whether *Salmonella* enterica can be recovered from household water in Ibadan and characterizing the isolates.

METHODS

Water from 250 randomly mapped households in municipal Ibadan was cultured for *Salmonella* by enriching in Selenite F for 24 hours and isolating on Xylose-Lysine-Deoxycholate agar. Total aerobic and coliform counts were done by spread plate method to assess water potability. *Salmonella* were confirmed by standard biochemical methods and polymerase chain reaction for invA, before whole genome sequencing, using the Illumina platform. Following quality assurance, the sequence reads were assembled using SPAdes. Reads were mapped, variants were determined, and single nucleotide polymorphisms (SNP) phylogeny was done using publicly available Nextflow pipelines. Multi-locus sequence types (MLST) and serovar prediction were performed using the *Salmonella* in silico typing resource (SISTR). Antimicrobial resistance genes and plasmid replicons were predicted using ARIBA analysis.

RESULTS

Twelve *Salmonella* isolates were recovered from 7 of the 250 water samples, only 33(13.2%) were deemed potable. Among the 12 *Salmonella* isolates, 6 (50%) were identified as *Salmonella* Weltevreden, while the remaining six strains belonged to five different serovars (Anatum, Saintpaul, Tenessee, Agona and Montevideo). *S.* Weltevreden ST365,

which has also been recovered from blood cultures in Ibadan, was isolated from groundwater in two of the five local governments (Ibadan Northeast and Ibadan Northwest). All 12 *Salmonella* isolates were devoid of horizontally-transmitted antimicrobial resistance genes but six (50%) of the strains (including four *S.* Weltevreden) harbored plasmids with IncFII-type replicons, while two (16.7%) harbored IncFIB replicons. All but two of the isolates carried quinolone resistance-conferring *parC*_T57S single-nucleotide polymorphisms.

CONCLUSIONS

Salmonella enterica, which are often not culturable when present in water, could be isolated from multiple household water specimens in Ibadan. *S.* Weltevreden, historically uncommon in Nigeria but has recently been reported from blood cultures in Ibadan, was recovered from groundwater in northern Ibadan. This study points to household groundwater as a possible reservoir for *Salmonella* and the need to improve water and sanitation facilities in Ibadan and other Nigerian cities.

81. Factors Associated with Nontyphoidal *Salmonella* Infection in Children Below 5 Years in an Urban Informal Settlement in Nairobi, Kenya

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BACKGROUND

Non-typhoidal *Salmonella* (NTS) is a significant global health challenge, particularly in low- and middle-income countries in Asia and sub-Saharan Africa. In Kenya, *Salmonella enterica* serovars Enteritidis and Typhimurium accounts for a substantial burden of bacteremia cases in children ≤ 5 years. Populations in urban informal settlements are particularly vulnerable to NTS due to limited access to clean water, poor sanitation and hygiene. We aimed to investigate the factors associated with NTS infection in children under 5 years of age living in Mukuru informal settlements in Nairobi, Kenya.

METHODS

This was a cross-sectional study conducted in Mukuru informal settlement in Nairobi, Kenya. Children presenting with fever (≥ 38° C) for more than 24 hours, with or without diarrhea, at four outpatient health facilities were recruited. A thorough history and physical examination of the participants was documented on a structured data form. Questionnaires were administered to the guardians which captured data on their background information, environmental risks, infrastructural risks, general wash, and social-economic risk factors. Rectal swabs and blood samples collected from the children, were subjected to culture for isolation of NTS, while identification was done through serotyping. Data was then subjected to descriptive statistics, chi-square tests, odds ratio calculations, and multivariable binary logistic regression to identify associations and risk factors for NTS infection.

RESULTS

A total of 3071 participants were recruited. The isolation rate of *Salmonella* Enteritidis and *Salmonella* Typhimurium was 1.4% (43/3071); *Salmonella* Enteritidis 0.8 %(25/3071) and *Salmonella* Typhimurium 0.6 %(18/3071). There was no significant association between the occurrence of *Salmonella* Enteritidis and Typhimurium with gender, age, and contact with animals. The use of open containers for water storage was significantly associated with NTS (2.0%; OR=1.93 (CI: 1.02-3.65); p=0.040). There was a significant association between households that did not regularly practice hand washing before eating and the occurrence of NTS in children (7.7%; OR=10.43 (CI: 1.13 – 96.23); p=0.039). Bloody diarrhea had a significant association with the occurrence of infection with NTS (4.6%; OR=3.64 (CI: 1.27-10.49); p=0.010).

CONCLUSION

This study highlights the importance of improving WASH infrastructure to reduce risk factors associated with transmission of NTS in the community. In the short-to medium-term, there is need for introduction of vaccine in the prevention and control of NTS.

KEYWORDS

Nontyphoidal *Salmonella*; Children; Informal settlement; Risk factors; Bacteremia; Hygiene practices

82. Burukutu as a Major Cause Factor and Spread of *Salmonella* Typhi in Wukari Town of Taraba State, Nigeria

Pascal Ofiri

ECEWS

BACKGROUND

Burukutu is an indigenous alcoholic drink locally brewed from the grains of Guinea corn/millet, ginger, and sugar. The age-long Burukutu serves as a source of alcohol for those who lack the financial means to consume refined beer in the region. The price of 5liter of the product is about four times cheaper than that of refined beer which makes it accessible and generally affordable to members of the community. Producers do not adhere to basic rules of hygiene in the preparation/storage of Burukutu and the joints are mostly located close to unhygienic areas like toilets, gutters, and waste disposal areas, giving access to flies/insects to fetch on it. The drinks are served in a small half-calabash bowl. However, the social system and the influential nature of social order have put a mixed category of classes of people into the target market and further

worsen the health protection of any typical household. We set out to investigate the reason people patronize Burukutu despite the health risk.

This study is carried out in Wukari town of Taraba state, Nigeria. We identified three popular common Burukutu joints in different areas that people patronize a lot. We randomly selected 150 people as the respondents to the questionnaire. The sample size was 50 questionnaires for each of the joint's sites. Data collected included age, the fun of drinking Burukutu, gender, employment, health risk, marital status, etc. We dichotomized responses for data analysis.

RESULTS

Results of the study revealed Median age of respondents was 31 years (range: 16-45 years) and a total number of 101(67.3%) were male. 97 people (64.7%) were not employed and 54 (55.7%) of them were self-employed. 53 (35.3%) students of both secondary and tertiary schools. 138 (92%) visit Burukutu joints regularly because the drink is affordable and cheap. n=113 (75.3%) Burukutu serves as breakfast (thickness), and 109 (72.7%) because of availability. 77 (51.3%) due to no stale drinks and 96 (64%) no segregation. 75 (50%) for the fun of drinking Burukutu. Out of the 100 people who volunteer for Stool Culture, 67(67%) tested positive, and only 22 (22%) are aware of health challenges.

Burukutu production provides a source of income to the producers who account for a very small percentage of the population but leaves behind long-term negative health impacts and increased public health burden. Having a multi-sectoral collaboration involving awareness creation, and demand creation on health promotion using local, administrative, and religious leaders, health policy stakeholders, and implementers of health regulations are key to providing a sustainable innovative solution.

83. Homemade Water Filter and Boiling to Reduce the Level of Typhoid Fever and Other Water-Borne Diseases in the Wukari Area of Taraba State in Nigeria

Pascal Ofiri

ECEWS

BACKGROUND

Safe potable water is a major deficiency in the Wukari area of Taraba State in Nigeria. The semi-arid nature of the location is largely responsible. Access to potable water for domestic use is out of reach of the inhabitants who must depend on poorly dug open wells that are only produced during the rainy seasons. In the dry season, the wells are all dried up. The inhabitants are then left at the mercy of ponds and small lakes with turbid waters. The lakes unfortunately also service free-grazing cattle and other animals. Such a situation has left the populace exposed to many illnesses among which are the rampant cases of enteric fevers.

In this study, the turbid water was made clean using homemade water filtration apparatus before boiling. Water mostly used by the communities usually comes from lakes, rivers, ponds, and groundwater. Before we can use this water domestically, it must be cleaned. This process generally has four main steps, coagulation, sedimentation, filtration, and disinfection.

The effectiveness of this method was confirmed by assessing bacterial typhoid such as treated water. Bacterial load was found to be less than 0.5 X 10^{1}cfu/ml as compared to well and pond water samples which showed 2.5 x 10^{12} and 1.0 x10^{18}cfu/ml respectively. Biochemical tests show that the treated water does not contain *Salmonella typhii* compared to the raw water from the ponds as well as water from the wells. Physicochemical parameters for both treated and untreated water (well water) show that the treated water is free of objectionable taste and odor. The pH is 7.84 which is within acceptable standards and can be improved using locally sourced agents like morning seeds.

RESULTS

The results of the study highlight that the use of homemade water filters and boiling water will greatly address the problem of lack of potable water as well as reduce the incidence of enteric fever in the study area.

84. Widal Test as a Typhoid Fever Diagnostic Test in Most Health facilities at Onitsha Town of Anambra State, Nigeria has Led to Ciprofloxacin Misuse and Resistance

Pascal Ofiri

ECEWS

BACKGROUND

Most Health facilities especially Private Laboratories conduct the Widal test which is not reliable in the diagnosis of Typhoid fever because it is easy, time safe, and profitable. The town is commonly known for businesses, and the inhabitants "are always on the go" to catch up with their daily activities. People always request Widal and Malaria tests once they have a fever. The widal can be carried out within 10 minutes, and the Patient proceeds to buy Ciprofloxacin for treatment. This has led to easy accessibility to substandard ciprofloxacin. Therefore, the wrong diagnosis has led to Ciprofloxacin misuse and resistance. We set out to investigate the reason people/ Facilities prefer the Widal over the standard culture test.

This study is carried out in Onitsha town of Anambra state, Nigeria. We identified three popular Communities with a lot of Health Facilities that people patronize a lot. We randomly selected 150 people as the respondents to the

questionnaire. The sample size was 50 questionnaires for each of the sites. Data collected included age, employment, time, affordable, treatment delay, etc. We dichotomized responses for data analysis.

RESULTS

Results of the study revealed Median age of respondents was 37 years (range: 18-55 years) and a total number of 94(62.7%) were male. 93 (62%) of them were self-employed, and 53 (35.3%) were students of both secondary and tertiary schools. 138 (92%) visit health Facilities regularly because the Widal Test is affordable and time-saving to avoid treatment delay as compared to the Culture test. 109 (72.7%) of healthcare workers said is profitable, in high demand, and has no delay in producing results. 129 (86%) said the Culture test is a time constraint and people do not want to visit the hospital a second time. 117 (78%) of individuals request for Widal test and self-medication. 97 (65%) of them do not complete Ciprofloxacin dosages.150 (100%) of them are not aware Widal test is not reliable, and they always take Ciprofloxacin once their Widal test is positive.

The is an urgent need for renewed scrutiny and adherence to diagnosis guidelines by Health facilities, Drug quality assurance, strict laws, regulations for the manufacturing, and sale of ciprofloxacin required to prevent misuse and resistance.

85. Slow-Growing *Salmonella Enterica* Typhi Mistaken for *Salmonella* Gallinarum in Ibadan, Nigeria

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BACKGROUND

Salmonella enterica serovar Typhi is endemic and *S.* Gallinarum rarely reported in Ibadan Nigeria. Routine invasive *Salmonella* surveillance in Ibadan detected three "*S.* Gallinarum" isolates within ten days, precipitating an outbreak investigation.

METHODOLOGY

Three isolates recovered from different patients within 10 days were identified as presumptive S. Gallinarum based on routine testing. Address and other metadata were retrieved for each patient. Isolates were reidentified using VITEK-2 and compared to extended biochemical profiles of other *S.* Typhi isolates. Motility testing, initially negative by hanging-drop method, was repeated using SIM (Sulphide-Indole-Motility) semi-solid medium. The isolates were whole genome sequenced on Illumina and Nanopore platforms. Short reads were used to determine sequence type, serotype identity by *Salmonella* In-Silico Typing Resource (SISTR), and phylogenetic relationships to previously characterized *S.* Typhi from Nigeria. Colony morphology was observed on nutrient agar.

RESULTS

The three isolates initially identified as *S.* Gallinarum were re-identified as *S.* Typhi genotype 3.1.1 by VITEK-2 and whole genome sequencing. Epidemiological evaluation determined that two infections with the isolates occurred at the same address and the third at a distant location. All three isolates differed from the majority of local Typhi isolates by gamma glutamyl transferase positivity. Isolates from two individuals in the same household had no SNP differences, suggesting a point-source infection. The third isolate differed by 14 SNPs, pointing to an independent infection event. Motility testing using SIM media was negative at 24h but positive after 48h incubation. The three isolates formed significantly smaller colonies than typical *Salmonella* strains and were shown to represent slow-growing *S.* Typhi.

CONCLUSION

A cluster of slow-growing, blood culture-derived *S.* Typhi was mistaken for *S.* Gallinarum in a diagnostic laboratory. Two patients were victims of household transmission and the third was infected by an independent slow-growing isolate. *S.* Typhi and *S.* Gallinarum are biochemically similar group D serovars. As many resource-limited laboratories may not have anti-Gallinarum sera on site, suspected *S.* Gallinarum isolates in typhoid endemic areas should be evaluated for motility in semi-solid media after extended incubation and verified by serological or molecular methods.

86. *Salmonella* Surveillance Cases at Nyahera Sub County Hospital, Kisumu County, Kenya

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BACKGROUND

Typhoid is a serious and sometimes fatal enteric fever spread through contaminated food and water. The disease causes fever, fatigue, headache, abdominal pain, and diarrhea or constipation. While it used to devastate major cities in the United States and Europe, it was largely stamped out in industrialized countries in the 1940s with the advent of antibiotics and improved sanitation. However,

for millions of people living in low- and middle-income countries are at risk. According to the Global Burden of Disease Study, typhoid resulted in more than 9 million cases and more than 110,000 deaths globally in 2019, mostly among children and adolescents in Asia and sub-Saharan Africa. Low-resource communities are often the most susceptible. The study sought to assess the number of positive typhoid fever cases from the stool samples tested by salmonella antigen rapid test.

METHODOLOGY

This was a retrospective study conducted from January 2022 to July 2023 by abstracting data of the number of typhoid cases done from MOH 240 and 706 reporting tools. The data obtained was analyzed in Microsoft excel and represented in percentages

RESULTS

A total of 230 salmonella antigen tests were done out of which 10 (4.35%) tested positive of these 10 positives 40 %(n= 4) were males while 60 %(n=6) were females. The median age was 45 years. The positive samples were referred to a microbiology laboratory for culture and sensitivity, antimicrobiofilm and virulent factors for possible isolation salmonella sub species.

CONCLUSION

There was a significantly low typhoid positivity rate at 4.35% reported in the facility for the period, which was largely attributed to best practices that has were put in place like: infection prevention and control, hand hygiene, improved sanitation and hygiene, typhoid conjugate vaccine, proper cooking and boiling of drinking water and lastly health education of the community on the above mentioned best practices.

87. Development of a Live Attenuated Vaccine Against *Salmonella* Paratyphoid A Using a Human Challenge Model

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BACKGROUND

Paratyphoid fever causes over 3 million cases of enteric fever annually, yet there are currently no licensed vaccines against this pathogen.

An oral live attenuated vaccine against *Salmonella* Paratyphi A, CVD1902, has been shown to be safe and immunogenic in a phase 1 trial. The efficacy of this vaccine is being evaluated in a controlled human infection model trial at Oxford Vaccine Group.

METHODS

In this participant observer-blinded randomised controlled trial, 74-76 adult participants will be randomised 1:1 to receive either two doses of CVD1902 or placebo (sodium bicarbonate). Twenty-eight days after second vaccination, all participants undergo challenge with *Salmonella* Paratyphi A and are monitored with daily blood tests and symptoms for 14 days. Paratyphoid is diagnosed if participants have a positive blood culture or develop persistent fever. All participants are treated with ciprofloxacin at the time of diagnosis or at 14 days and are followed up for 1 year post-challenge.

Comparison of paratyphoid attack rate between the vaccinated and placebo group will allow an estimation of vaccine efficacy. Vaccine safety will be assessed by analysing adverse events following vaccination. To assess vaccine immunogenicity, IgG and IgA anti-O and anti-H specific responses will be measured. Functional antibody assays will also be performed.

RESULTS

Thirty-four volunteers have been enrolled and 28 participants challenged by June 2023. The median age is 28 and 16 (47%) are male.

Following vaccination, in the vaccine and placebo groups (data aggregated to maintain blinding), 27 participants reported symptoms, with only 2 reporting severe symptoms. Malaise is the most reported symptom, followed by headache and anorexia. Median time from vaccine to symptom onset is 2 days. Only one participant has developed fever following vaccination; this participant had Covid shortly after being vaccinated.

To date, 13 participants have been diagnosed with *S.* Paratyphi A. No participants have developed severe disease. Immunological assays are ongoing.

CONCLUSIONS

CVD1902 appears to be well-tolerated. This human challenge model of *S.* Paratyphi A infection will provide vital information on efficacy and immunological data, which may prove invaluable for the development of an oral *S.* Paratyphi A vaccine.

88. *Salmonella Enterica* Serovars From Environmental Samples Collected From Commercial and Smallholder Farms in Two Communities in the Ashanti Region of Ghana

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ABSTRACT

Salmonella enterica causes more than 1.2 million annual deaths worldwide with the majority occurring in resource-poor countries. In this study, we examined the frequency and antibiotic resistance of *Salmonella enterica* isolated from environmental samples (dust and soil) and farm animal feces collected from commercial and smallholder farm environments in two communities in the Ashanti Region of Ghana. All suspected *Salmonella* were confirmed using the automated VITEK 2 Systen and serotyped following the White-Kaufmann Le Minor scheme at the Robert Kochs Institute (RKI), Germany. A total of 1490 environmental samples, comprising 800 (53.7%) soil, 409 (27.4%) faecal and 281 (18.9%) dust samples, were collected from 30 commercial and 50 smallholder farms. The overall *Salmonella* prevalence was 6.0% (n/N = 90/1490); the prevalence varied according to the type of samples collected: 8.9% for dust (n/N = 25/281), 6.5% for soil (n/N = 52/800) and 3.2% for faecal (n/N = 13/409). The prevalence of *Salmonella* in clay soil was 4.3 (95% CI: 1.1 – 17.1) and 3.7 (95% CI: 2.1 – 6.7) times higher than in sandy and loamy soil respectively Also, more *Salmonella* were recovered from commercial farm environments (8.6%, n/N = 68/793) than smallholder farms (3.2%, n/N = 22/697) (PR = 2.7, CI: 1.7 – 4.4). Thirty-four different *Salmonella* serovars were identified with the two most common ones being Rubislaw (27.8%, n/N = 25/90) and Tamale (12.2%, n/N = 11/90). *Salmonella* prevalence was much higher in the rainy season (8.4%, n/N = 85/1007) than dry season (1.0%, n/N = 5/483) (PR = 8.4, 95% CI: 3.3 – 20.0). About 14.4% (n/N = 13/90) of the isolates were resistant to at least one of the tested antimicrobials, with 84.6% (n/N = 11/13) of them being multidrug-resistant (MDR). The findings of this study warrant the encouragement of good husbandry practices such as the removal of dust in poultry farms since there is a higher chance of isolating *Salmonella* from dust.

89. Serious Adverse Events Reported in a Phase III RCT of a Typhoid Conjugate Vaccine in Malawian Children

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BACKGROUND

An individually-randomised clinical efficacy trial of Typbar typhoid conjugate vaccine (TCV)® (Bharat Biotech) was conducted in Malawi, recruiting 28,130 children. The efficacy results are presented elsewhere. We here present details of 48-month severe adverse event safety data from the trial.

METHODS

Healthy children aged 9 months through 12 years were randomly assigned 1:1 to receive TCV or meningococcal A conjugate vaccine (MenA) and were under surveillance for 48-54 months. Passive surveillance was conducted throughout the trial to identify febrile presentations and serious adverse events (SAEs). SAE are events resulting in death, life-threatening situations, hospitalization, persistent disability, or requiring medical intervention. An international Data and Safety Monitoring Board (DSMB) monitored safety outcomes.

RESULTS

Between 21 February and 28 September 2018, 28,051 participants were vaccinated. In 120,720 person-years of follow-up until 30 Sep 2022, there were 548 SAE events, including 33 deaths. Of these, 512 were hospitalizations from 451 participants, none being related to vaccination. Among these 451 participants, 239 received MenA and 212 received TCV. Of these, 62 hospitalisations occurred in children <2 years old, 221 in children aged 2-5 years, and 168 in children aged >5 years. Infections and infestations were the leading cause of hospitalisation (337, including respiratory tract infections (n=124), gastroenteritis (n=57), malaria (n=77) and other infections (n=79)). Other SAE categories included: injury, poisoning and procedural complications (n=63); nervous system disorders (n=44); surgical and medical procedures (n=15); other (n=53). The SAE events in all categories were evenly spread between the 2 vaccine groups. The incidence of hospitalisation was 16.8 per 1000 for TCV and 19.6 per 1000 for MenA.

Up to 30 Sep 2022, 136 of the 10,136 (1.3%) blood cultures were positive for *Salmonella* Typhi, and 21/136 (15%) were

hospitalized (6 in the TCV group, 15 in the MenA group). One typhoid case, in the MenA group, resulted in death. No typhoid perforations were recorded.

CONCLUSION

SAEs represented a range of common childhood illnesses, and were equally distributed between vaccine groups. There were no TCV-related SAEs. These safety data support TCV introduction in typhoid-endemic settings.

90. Measuring the Effectiveness and Impact of Typhoid Conjugate Vaccine in Malawi

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BACKGROUND

Typhoid Conjugate Vaccine (TCV) has demonstrated robust efficacy in randomized controlled trials in low- and middle-income countries (LMICs), including Malawi. Liberia and Zimbabwe became the first sub-Saharan African countries to introduce (Typbar-TCV) in April and May of 2021, respectively. In May 2023, Malawi became the third African country to introduce TCV and the first to use TyphiBev in Africa. We aim to measure the effectiveness and impact of TCV after introduction in a typhoid-endemic sub-Saharan African setting to demonstrate the safety and effectiveness of TCV are consistent with the clinical trial results, and to inform policy decisions across Africa.

METHODS

We are conducting passive surveillance in Ndirande and Zingwangwa townships. Children and adults aged 9 months to 45 years presenting with febrile illness (subjective fever for ≥72 hours, axillary temperature ≥38°C, or hospitalization with a history of fever), have blood collected for culture. Vaccine effectiveness will be measured using a test-negative study design, and impact assessed using an analysis of incidence before and after the vaccine campaign.

RESULTS

Between 18 April 2022 and 31 May 2023, 121,864 participants were screened during passive surveillance, 3646 were enrolled, and 3603 blood cultures taken. The results showed 148 cases of *Salmonella* Typhi and 11 cases of *Salmonella* Typhimurium. Among the cases, 99% were multidrug-resistant, 2.03% were fluoroquinolone-resistant, and only 1% were fully susceptible to first-line antibiotics. A total of 61% of these cases occurred in children eligible for the national vaccine campaign (09 months to 15 years), which occurred in May 2023; the rest occurred in non-vaccine-eligible older individuals. This study data includes one year of surveillance before the campaign, alongside multi-year baseline surveillance data from the Malawi Liverpool Wellcome Programme, the Strategic Alliance Across Africa and Asia (STRATAA) and the Typhoid Vaccine trial in Malawi.

CONCLUSION

This study will demonstrate real-life effectiveness and impact of TCV in an endemic setting. Pre-campaign baseline data consistently suggests ongoing high incidence and transmission. Surveillance continues after the TCV campaign, and current data will be reported. Vaccine effectiveness and impact in Malawi will provide important information across Africa.

91. Invasive Non-Typhoidal Salmonellosis: Data From a South Asian country

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BACKGROUND

Salmonella spp. are widely distributed in nature. It is found in the gastro-intestinal tract of wild and domesticated animals. Non-typhoidal *Salmonella* typically cause mild gastroenteritis. Febrile invasive salmonellosis can present in the absence of diarrhoea in the form of bacteremia, meningitis or focal infections. However significant proportion of invasive disease can lead to life threatening complications.

According to recent meta-analyses on invasive non-typhoidal salmonellosis, the most common complication is septicemia. Case fatality rate remains 14.7%.

Salmonella laboratory surveillance was established in 2016 in Sri Lanka in order to comprehensively understand the current situation and trend of the salmonellosis including the predominant serotypes, incidence of invasive salmonellosis and antimicrobial sensitivity.

METHODS

Under the *Salmonella* laboratory surveillance, all non-typhoidal *Salmonella* isolates from clinical and food testing laboratories in the country are sent to the Enteric Reference Laboratory, Medical Research Institute for further identification. In addition, the laboratory receives stool samples from hospitals which do not have facilities to carry out stool cultures.

All isolates received were sub-cultured on to Xylose Lysine Deoxycholate agar, Macconkey 3 and *Salmonella Shigella* media and incubated at 37oC for 18-24 hrs. Based on the typical morphology the suspected *Salmonella* isolates were phenotypically identified using biochemicals; mainly KIA, urease, lysine and indole tests. Presumptively identified isolates were subjected to serotyping using commercially available antisera. Antibiotic Sensitivity Test was performed and interpreted as per Clinical Laboratory Standards Institute manual for the relevant year. All data were entered and analysed using the WHONET software.

RESULTS

During the four-year study period 960 non-typhoidal *Salmonella* isolates were received by the reference laboratory. Of these 517 (53.8%) isolates were from human clinical samples. These isolates were from blood cultures, joint and other sterile fluid aspirates and pus samples in addition to isolates from stool samples. Out of 517 *Salmonella* isolates, 249(48.16%) isolates were from invasive diseases and only 247 (47.77%) isolates were from stool cultures. However, there was only one isolate from cerebrospinal fluid. From year 2018 to 2021, among the *Salmonella* isolates received from invasive disease, 225 (43.5%) isolates were from blood cultures. Further it was noted that in year 2021, invasive non-typhoidal salmonellosis rate has risen to 66.66%.

Predominant *Salmonella* serotype reported during this four-year period was *Salmonella* Enteritidis, while second most common serotype is *Salmonella* Typhimurium for the isolates from human clinical samples. Other predominant serotypes isolated from human clinical samples were *Salmonella* Kentucky, *Salmonella* Weltevreden, *Salmonella* Chester, *Salmonella* Corvallis and Salmonella Para Typhi B *Var* java.

When considering antibiotics sensitivity of non-typhoidal *Salmonella* species, ciprofloxacin resistance remains around 37.52% over these four years. However, in 2021 it was noted that 47% of isolates were ciprofloxacin resistant. During this study period, only three isolates from human clinical samples were resistant to third generation cephalosporins and all three isolates were reported in 2019.

The distribution of serotypes isolated are comparable in *Salmonella* isolated from clinical and food.

CONCLUSIONS

Out of 517 *Salmonella* isolates, 249(48.16%) isolates were from invasive diseases and 225 (43.5%) isolates were from blood cultures.

According to these data predominant *Salmonella* serotype from human clinical disease is *Salmonella* Enteritidis. Ciprofloxacin resistant of non-typhoidal *Salmonella* is 37.2% and Resistance to third generation cephalosporin remains very low.

Preventive measures need to be strengthened to slow down current invasive non-typhoidal salmonellosis. Vaccine against non-typhoidal *Salmonella*, specially for high- risk groups would be of significant benefit.

92. Distribution Patterns of Seafood-Borne Non-Typhoidal *Salmonella* Serovars in Fish Markets and Fish Landing Centres in Mumbai, India

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ABSTRACT

Non-typhoidal salmonella (NTS) is an important cause of food-borne infections worldwide and is often found as a secondary contaminant in seafood. The diverse NTS serotypes associated with seafood might vary in terms of their virulence potential. In this study, 82 seafood samples collected from three fish landing centres and seven retail fish markets in Mumbai were studied with respect to the distribution pattern of *Salmonella* serovars. A total of 94 *Salmonella* isolates were recovered from seafood samples using multiple enrichment broths and selective isolation media with an overall incidence of 20.73%. Altogether, contamination levels of fish markets and fish landing centres were 84.1% and 15.95%, respectively. All 94 isolates of *Salmonella* were serotyped. Of these, 89 isolates represented 10 different serovars and 5 isolates were not typeable. The dominant serovar was *S.* Bareilly (33 isolates, 35.10%), followed by *S.* Typhimurium (15 isolates 15.95%), *S.* Newport (10 isolates, 10.63%), *S.* Kentucky (9 isolates, 9.57%), *S.* Paratyphi B (8 isolates, 8.51%); *S.* Tennessee (7 isolates, 7.44%), *S.* Alachua, *S.* Weltevreden and *S.* Volta 2(2.12%) isolates each, and one *S.* Lindenburg (1.06%). *S.* Bareilly was the most common serotype encountered in fish markets in Mumbai. The high incidence and the serovar distribution of *Salmonella* in seafood suggests multiple and diverse sources of contamination.

93. Environmental Surveillance to Unravel the Spatio-Temporal Dynamics of *Salmonella* Typhi Bacteriophages in Dhaka

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BACKGROUND

Dhaka, the capital city of Bangladesh, with a population of 23 million, is one of the most densely populated cities in the world and is afflicted by an enormous burden of typhoid fever. A recent study has also revealed the presence

of *Salmonella* Typhi-specific bacteriophages (viruses that infect bacteria) in the environmental samples of Dhaka, and an overall positive correlation between phage prevalence in the environment and typhoid fever burden. To investigate the spatio-temporal dynamics of Typhi-phages in Dhaka, we initiated a study to collect wastewater from a large urban catchment area.

METHODS

A catchment area, consisting of 11 administrative thanas, around the two largest pediatric hospitals of Dhaka has been defined representing about 14% of the population of Dhaka. 120 sample locations have been chosen to cover the different wastewater facilities present in the catchment area. Starting from March 2023, from each selected location, 10 ml water samples are collected monthly. Water samples are filtered through a 0.22 µm filter and tested by a double-layer agar method for the presence of Typhi-specific bacteriophages.

RESULTS

Between March and May 2023, 360 water samples were collected, of which 21.3% (77 samples) were positive for Typhi-specific bacteriophages. Positivity ranged from 13% to 33% between thanas.

Preliminary results show that the highest proportion of Typhi phages was recorded in Mirpur and Kafrul thana (33% from each). A notable number of *Salmonella* Typhi-specific bacteriophages were also isolated from Mohammadpur (22%), Sher E Bangla (22%), Shah Ali (21%), and Darussalam (21%). Lower rates of Typhi positivity were obtained from Pallabi (19%), Hazaribagh (16%), Tejgaon (18%), Cantonment (17%), and Adabor (13%). The correlation between Typhoid burden and Bacteriophage number will be analyzed by obtaining hospital data from two pediatric hospitals in the region.

CONCLUSION

Environmental surveillance can complement traditional hospital-based surveillance and can reveal the spatio-temporal dynamics of *Salmonella* Typhi and phages in endemic regions. The proposed study will also help us to uncover the role of phages in the spread of *Salmonella* Typhi in high-burden endemic settings.

94. Application of a Novel Multiple Endpoints Approach to Assess the Efficacy of Typhoid Conjugate Vaccines Against Antimicrobial Usage

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BACKGROUND

Typhoid conjugate vaccines (TCV) have emerged as a powerful tool to combat antimicrobial resistance (AMR), which poses a significant burden in parts of Asia and sub-Saharan Africa. Emergence of AMR is driven in part by antimicrobial usage (AMU), and vaccines targeting *Salmonella* Typhi can reduce both the clinical syndrome and the need for antimicrobials. However, selecting relevant outcomes to evaluate the impact of TCVs on AMU in clinical trials can be challenging when multiple clinically significant endpoints exist. This study explores various approaches for analyzing multiple endpoints using real-world data from a TCV clinical trial.

METHODS

Data was collected from an individually randomized controlled trial conducted in Malawi by the TyVAC consortium. Selected endpoints included the total number of antimicrobial prescriptions in the TCV and control groups at different time points, the time from vaccination to the first prescription of an antimicrobial, and the total person-days for which antimicrobials were prescribed. Different approaches for multiple endpoint analysis were compared, such as permutation-based methods and Bonferroni tests, the latter treating each endpoint independently. Permutation tests included the well-established minP test, which uses the minimum P-value across all test statistics, and a novel approach, wavP test, that represents a weighted average of individual outcome test statistics.

RESULTS

Permutation tests, particularly wavP, were found to be preferable when the different endpoints analyzed exhibited similar characteristics in terms of incidence, effect size, and severity. However, when the outcomes differed in incidence and displayed high variability, more established methods such as minP or Bonferroni tests performed slightly better. The wavP approach had the greatest power to detect a significant effect of TCV on one or more of the AMU endpoints.

CONCLUSIONS

This study provides valuable guidance on incorporating multiple endpoints in the analysis of clinical trials, with a specific focus on the impact of TCV on AMU. Real-world examples from TCV are presented to illustrate the practical application of the findings.

95. Genomic Epidemiology of *Salmonella* Paratyphi B isolates from Bangladesh

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BACKGROUND

Salmonella species are among the most common causes of foodborne diseases, and the *Salmonella enterica subsp. enterica* serovar Paratyphi B (*Salmonella* Paratyphi B) is one of the causative agents for paratyphoid fever in humans. Depending on its ability to ferment D-tartrate (dT), this serovar has two biotypes – dT non-fermenting (dT-) *Salmonella* Paratyphi B sensu stricto and dT fermenting (dT+) biotype Java. Differentiating between these two biotypes is challenging by classical microbiology tests but they have different pathogenic profiles. Paratyphi B biotype Java is often considered to be non-invasive while the other cause paratyphoid fever. Hence, it is crucial to understand their genomic background.

METHODS

Our surveillance of typhoid and paratyphoid fever was conducted in Dhaka, Bangladesh, encompassing two major pediatric hospitals and one private clinic from 1999 to 2022. Blood cultures were performed at physicians' discretion, and confirmed cases were determined through microbiological, serological, and biochemical tests. Whole genome sequencing (WGS) was done for all detected *Salmonella* Paratyphi B isolates. Genomic characterization was done using multi-locus sequence types (MLST), core-genome MLST (cgMLST) phylogenetic groups (PG), and antimicrobial resistance (AMR) profiles.

RESULTS

15 *Salmonella* Paratyphi B isolates were detected in our surveillance. WGS analysis showed two different cgMLST profiles; one for *Salmonella* Paratyphi B (n=13), and another for Paratyphi B biotype Java (n=2). MLST results showed dominance of ST43 (n=14). None of the isolates showed presence of any AMR genes which matched the antimicrobial susceptibility testing results. Phylogenetic analysis showed that the *Salmonella* Paratyphi B sensu stricto isolates formed two clusters within phylogenetic group 4 (PG4). One cluster contained isolates from 1999 (n=4) and other contained isolates from 2004-onwards (n=9). Remaining two Paratyphi B biotype Java isolates were outside of these clusters- one in PG4 and the other in PG6.

CONCLUSION

Our results suggest that *Salmonella* Paratyphi B from the ST43/PG4 group is dominant in Bangladesh. Prevalence of AMR is also low in *Salmonella* Paratyphi B isolates. With introduction of Typhoid Conjugate Vaccine (TCV) in Bangladesh to control typhoid fever, the dominant enteric fever, it will be crucial to observe the genomic and AMR changes within *Salmonella* Paratyphi B population in the country.

96. Antibiotic Resistance Pattern of *Salmonella* Typhi and *Salmonella* Paratyphi Clinical Isolates From Dhaka, Bangladesh: A Retrospective Study

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BACKGROUND

Enteric fever caused by *Salmonella* enterica serovar Typhi and Paratyphi is still an important public health problem in developing countries including Bangladesh. The changing trend of antibiotic susceptibility of *Salmonella* Typhi and Paratyphi and emergence of multi-drug resistance has increased which is turning into a public health emergency due to improper use of antibiotics. The aim of this analysis was to determine the prevalence and susceptibility profile of *Salmonella enteric* (serotype Typhi and Paratyphi A).

METHODS

In this study, laboratory-based blood culture technique depicts an overview of total 11 antibiotics. The study was carried out in Mirpur, Dhaka, Bangladesh from February 2018 to December 2021.

RESULTS

A total of 18,664 blood samples were obtained from patients with suspected enteric fever. Among them 1000 (5.4%) were *S.*Typhi and 204 (1.1%) were *S.*Paratyphi A. Patients were divided in three age groups. The highest antimicrobial susceptibility to *S.*Typhi and *S.*Paratyphi A was observed for cefixime (100%) and ceftriaxone (100%). The new generation antibiotics gentamicin and meropenem were showed 99.6% and 99.8% sensitivity for *S.*Typhi respectively.100% sensitivity was also found in *S.* Paratyphi A for both gentamicin and meropenem. The maximum resistance was observed in nalidixic acid (91.5% in *S.*Typhi and 98.5% in *S.*Paratyphi A) for all age groups. The macrolide (azithromycin) was also found 98.5% sensitive for

*S.*Typhi and 87.7% for *S.* Paratyphi A. Moreover, 16.0% cases of MDR typhoid were found in this study. The highest MDR (19.8%) was seen in children less than 5 years of age.

CONCLUSIONS

Carbapenem type beta lactum (meropenem), aminoglycoside (gentamicin) and third generation cephalosporins (cefixime and ceftriaxone) were the most effective drugs for typhoid fever. The multidrug resistance typhoid is also a subject of concern. These findings are essential for a full description of the pathogens, their susceptibility to antibiotics and the selection of the best drugs for treating typhoid fever. Hence antibiotic susceptibility tests should be considered for appropriate therapy to prevent further emergence of drug resistance in Bangladesh.

97. Paratype Genotyping Framework Provides Better Understanding of the Population Structure of *Salmonella* Paratyphi A in Bangladesh

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BACKGROUND

Salmonella enterica serovar Paratyphi A (*S.* Paratyphi A) is an understudied cause of enteric fever which has started replacing *S.* Typhi in some endemic regions. Currently, there have been limited studies on genomic epidemiology of paratyphoid fever, especially from South-east Asian countries. Here, we have utilized a SNP based genotyping scheme "Paratype" (reported in Tanmoy et al. 2022) to investigate genotypic distribution among Bangladeshi population which were previously classified under a lineage scheme (designated as lineage A-G in Zhou et al. 2014).

METHODS

Maximum likelihood phylogeny was constructed with 309 *S.* Paratyphi A genome sequences from the global collection including 67 Bangladeshi isolates. Genotypes were assigned according to the genotyping scheme using the "paratype" python script. AMR mutations in *S.* Paratyphi A genomes were identified using "genoparatyphi" python script.

RESULTS

WGS analysis of *S.* Paratyphi A isolated between 2008-2018 from Bangladesh revealed the six distinct genotypes which were previously classified into only three lineages; A, C and F. Under the genotyping nomenclature, each lineage is now split into two distinct genotypes (i.e lineage A into 2.4.1, 2.4.4; lineage C into 2.3.2, 2.3.3 and lineage F into 1.2.1, 1.2.2). The majority of the Bangladeshi genomes (62.7%) formed a monophyletic sub-lineage A3 which is now assigned to genotype 2.4.4. This dominant genotype was mostly present in Bangladesh and closely related to genotype 2.4.3 isolates (previously sub-lineage A2) from Nepal (median distance ~70 SNPs). All Bangladeshi *S.* Paratyphi A isolates possessed a single point mutation in *gyr*A gene either at codon 83 or 87 associated with decreased fluoroquinolone susceptibility. Additionally, one *S.* Paratyphi A genome belonging to genotype 2.3.3 acquired azithromycin resistance gene acrB-R717L.

CONCLUSIONS

This data highlights the importance of "Paratype" tool for *S.* Paratyphi for future genomic surveillance efforts to track the spread of epidemiologically important genotypes to support public health measures.

98. Typhoid Conjugate Vaccine (TCV) Introduction in Madagascar (TyMA)

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International Vaccine Institute

ABSTRACT

Typhoid fever poses a significant public health challenge globally, especially in resource-limited settings. Based on previous prospective blood culture-confirming, facility-based surveillance, the burden of typhoid fever in Madagascar is estimated to be high, particularly among children and adolescents. To address this, Typhoid Introduction in Madagascar (TyMA) builds on surveillance studies of typhoid and other salmonelloses including Typhoid Surveillance in Africa Project (TSAP) and Severe Typhoid Fever Surveillance in Africa (SETA). Through TyMA, the real-world effectiveness of Vi-CRM_{197} typhoid conjugate vaccine (TCV) will be evaluated through the vaccination of 60,000 children between the ages of 9 months and 16 years. This will be the first real-world evaluation of Vi-CRM_{197} TCV (TyphiBEV) in the African continent. This Vi-CRM_{197} TCV is of particular significance as it can be offered to children under the age of two, thus highlighting the critical nature of these safety and immunogenicity data to be generated.

The baseline census spanning six communes was performed from May to December 2022 and encompasses a population and over 160,000 individuals and 55,000 households. Here, household-level demographic information and geolocation data was collected. TyphiBEV vaccination was launched in August 2023 and age-stratified participants recruited to safety, immunogenicity and antimicrobial resistance (AMR) cohorts. For participants in the immunogenicity cohort (n = 350), blood and DBS samples will be procured and levels of anti-Vi antibodies

determined. Stool and oral swab samples will be taken from participants in the AMR cohort (n = 180) and resistance markers assessed through whole genome sequencing.

This study enables the investigation of AMR, antimicrobial use (AMU) and healthcare-seeking behaviour in these rural and urban communities through household visits and questionnaires. Here, we present the key objectives, study design and preliminary results of TyMA, with an overall aim of generating sufficient data to facilitate the adoption of TCV into the Madagascar Essential Programme on Immunization (EPI).

99. Enhanced PCR Based Screening Prior to Culture of *Salmonella* Typhi From Natural Waters

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INTRODUCTION

Environmental surveillance (ES) of *Salmonella* Typhi (*S.* Typhi) was undertaken in Blantyre, Malawi from 2019-2020, using a culture-based method, isolating six *S.* Typhi. From 2020-2022, a second method using direct detection by PCR was introduced and performed in parallel. During this period, two *S.* Typhi were cultured, but 33 were detected by PCR; as such, we have revisited our laboratory methods to enhance PCR based screening prior to culture.

METHODS

Three variants of Magna Extract (ME0, ME1 and ME2), a low cost, bead-based DNA purification method, were evaluated alongside the Qiagen PowerFaecal Pro (QPFP) Kit. We challenged these protocols with 12 different isolates *S.* Typhi diluted 10-fold eight times from ~1.5 x 10^8 CFU/mL (MacFarland standard density 0.5); two different bile$^-$ broths were used as diluents: 1) pure bile$^-$; 2) a 1:10 inoculation of river water in bile$^-$ (RWB). Due to potential inhibitors, RWB was diluted 1:10 with nuclease free water for a third comparison. All four extraction methods, with all 3 challenges, were assessed by real-time PCR using *S.* Typhi target: *ttr*, *tviB* and *staG*.

RESULTS

ME0 performed most consistently, with the highest percentage positivity at all dilutions. At the lowest dilution 42% (pure bile-) and 25% (RWB) of the 12 samples had positive amplification for all three targets (ME0), compared to QPFP's 17% and 17%, ME1's 8% and 0% and ME2's 33% and 8% ($\chi2$ = 143.3, df = 21, $p < 0.0001$; and $\chi2$ = 273.9, df = 21, $p < 0.0001$). When RWB samples were diluted, ME0 dropped to 0% detection, compared to QPFP, ME1 and ME2 all having a 25% detection ($\chi2$ = 345.8, df = 21, $p < 0.0001$).

DISCUSSION

ME0 outperformed, or performed comparably to the QPFP, showing a viable alternative to the high cost and labour associated with QPFP, allowing easy implementation within ES programmes. By integrating this direct PCR step to screen samples, we can provide high quality molecular data and focus culture-based methods on samples that are PCR positive in order to obtain and whole genome sequence isolates, therefore increasing sensitivity whilst lowering overall costs of ES programmes.

100. Development of a Bivalent Glycoconjugate Vaccine Against *Salmonella* Typhi and Paratyphi A

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BACKGROUND

S. Typhi and Paratyphi A together are responsible for over 13 million cases and 133 thousand deaths per year, most of which occur in children in South and South-East Asia. After the successful development of a Typhoid Conjugate Vaccine (TCV), which was WHO prequalified in 2020 and is manufactured by Biological E, we are attempting to broaden its coverage by incorporating the *S.* Paratyphi A component. The increasing antibiotic resistance of *S.* Paratyphi A and the potential risk of *S.* Typhi serovar replacement with *S.* Paratyphi A, for which no vaccine is available, strongly advocate for the rapid development of this bivalent vaccine combination.

METHODS

In collaboration with Biological E, we have developed a new glycoconjugate vaccine for *S.* Paratyphi A, based on the serovar-specific O-antigen (O:2) conjugated to CRM_{197} (O:2-CRM_{197}), which we have formulated with TCV (Vi antigen conjugated to CRM_{197}). We have completed a robust preclinical assessment, by testing both monovalent and bivalent formulations in different animal models and investigating possible critical quality attributes. We performed a GLP toxicology study and manufactured GMP lots for clinical studies, which were fully characterized through a comprehensive analytical panel.

RESULTS

The preclinical data allowed to define which parameters (i.e., O:2 molecular weight, sugar/protein ratio, cross-linking, O-acetylation, alum adjuvantation) are most appropriate for an immunogenic O:2-CRM_{197} conjugate. In addition, we demonstrated the ability of the bivalent formulation to elicit functional antibodies, with lack of interference between the two components. The toxicology

study showed that the bivalent vaccine was well tolerated in rabbits with no evidence of local or systemic toxicity. A Phase 1 study in European healthy adults has commenced in November 2022.

CONCLUSION

We obtained satisfactory preclinical results with the bivalent vaccine, constituted by the WHO prequalified TCV and the newly developed *S.* Paratyphi A glycoconjugate, to progress this candidate to clinical development. The Phase 1 study will determine the vaccine's safety and immunogenicity and will provide indications on dose and formulation to be tested in a subsequent Phase 2 trial.

101. Progress in Expanding TCV Use Globally: Leveraging Gavi's Support for Vaccine Introductions and Improving Diagnostics for Vaccine Decision-Making

Allyson Russell, Lee Hampton, Francisco J. Luquero

Gavi

ABSTRACT

Gavi supports countries to introduce typhoid conjugate vaccine (TCV) into routine immunization schedules, accompanied by catch-up campaigns to build immunity in older age cohorts. Since funding became available for TCV introduction in 2018, five countries have introduced the vaccine nationally with funding and other support from the Gavi Alliance. Recent successful introductions have incorporated strategies to identify and reach zero-dose and under-immunized children with other antigens into catch-up campaigns, and to integrate TCV with other planned campaigns (bOPV, MR, Vitamin A) for efficient use of human and financial resources. In the wake of the COVID-19 emergency and with growing threat of the spread of antimicrobial resistant strains, momentum is building to expand the use of TCV worldwide; however, countries lack visibility on the availability of pre-qualified TCVs, funding support available from Gavi for TCV introduction, and how to successfully apply for Gavi support, which this presentation will address. Countries also have experienced difficulty in gathering sufficient data on typhoid burden of disease to inform National Immunisation Technical Advisory Group (NITAG) recommendations, and in prioritizing new vaccine introductions among the growing number of vaccines available. Gavi's new funding to bring fit-for-purpose typhoid diagnostic tests to market and make them available to Gavi-eligible countries seeks to help address this need. The Gavi Alliance and global partners will continue to support countries with typhoid burden evidence generation and assessment, new vaccine introduction and switch prioritization, improved typhoid diagnostics to inform TCV decision-making, and the implementation of successful TCV introductions.

102. Prevalence of Multi Drug Resistant Non Typhoidal *Salmonella* Among Different Species of Fish Collected From Wet-Markets of Lahore, Pakistan

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BACKGROUND

Seafood when exposed to contaminated water and processing practices can become a source of *Salmonella* posing a public health threat. The sustainability of fish resources and the concept of "One Health" depend on the promotion, policing, and supervision of ethical fishing methods.

METHODS

For this purpose, a cross-sectional study was designed in Lahore, Pakistan to determine the prevalence and antimicrobial resistance of non-typhoidal *Salmonella* isolates recovered from different species of fish (Rohu n=80, Tilapia n=60, and Gulfam n=60). Fish samples were collected from retail shops of the largest fish market in Lahore (Urdu Bazar and Mori Gate) from June to August 2022. Prevalence of *Salmonella* was checked by PCR and antimicrobial susceptibility testing was performed through the Kirby Disc-Diffusion method. A total of 10 commercially available and commonly used antibiotics were selected.

RESULTS

According to the results of our study, 32 (16%) of fish samples were found positive for *Salmonella*, with 11 from Rohu (13.8%), 10 from Tilapia (16.6%), and 11 from Gulfam (18.36%) samples. Antimicrobial susceptibility results showed a total of 12.5% of *Salmonella* isolates were resistant to all tested antibiotics while 87.5% were resistant to at least one of them. There was 100% resistance against Streptomycin(S) and Azithromycin (AZM), while 96.87% of the samples were resistant to Lincomycin (L), Oxytetracycline (OT), and Kanamycin (K). Among the other antibiotics used the highest resistance (90.62%) was found in Doxycycline followed by (84.37%) Trimethoprim (TMP), (59.37%) Ciprofloxacin, (53.12%) Cefotaxime, with the lowest (37.5%) in Amoxicillin. All isolates were Multidrug Resistant (MDR) and seven different resistance patterns were found. The most common MDR pattern (S+AZM) was 100%, followed by (S+D+AZM+OT) was 84.3%, and only four isolates showed (TMP+CTX+CIP+AZM+Amc) and (L+S+TMP+D+K+CTX+CIP+AZM+Amc+OT)was 12.5%.

CONCLUSION

The results of this study provide baseline data for *Salmonella* prevalence in fish which is essential for planning and implementing one health policy to preserve the health of the public. Our findings also show an alarming public health concern regarding high resistance in *Salmonella* isolates against the antibiotics which are used as first-line treatment for most of the bacterial infections in Pakistan. This research will help in the formation of standards for the appropriate use of antibiotics in aquatic systems and the environment.

103. Navigating Typhoid Fever Challenges in Pakistan: A Holistic Approach to *Salmonella* Typhi Drug Resistance, Proteomic Insights, and Diagnostic Prospects

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BACKGROUND

Typhoid fever, primarily caused by *Salmonella* Typhi, is a significant public health concern in Pakistan, ranking as the 6th major cause of mortality in the country. With an incidence rate of 451.7 cases per 100,000 populations per year, a strongly typhoid endemic Country-Pakistan faces formidable challenges in combating this disease. Several factors contribute to the worsening situation, including poor hygiene practices, antibiotic misuse, the emergence of drug-resistant strains, and the inadequacy of rapid diagnostic tests (RDTs) for accurate diagnosis.

OBJECTIVES

This study aimed to comprehensively characterize the causative agents of typhoid fever, explore their antibiotic susceptibility profiles, analyze the differential proteomes of drug-resistant and drug-sensitive *S.* Typhi strains, and characterize the immunoreactive proteins of clinical *S.* Typhi isolates along with their gene expression patterns. The findings of this study would have the potential to shed light on resistance mechanisms, facilitate the development of accurate diagnostics, and aid in the creation of reliable vaccines for the effective management of typhoid fever.

METHODS & RESULTS

Standard laboratory procedures, including blood culture, polymerase chain reaction (PCR), and 16S rRNA gene sequencing, were employed to identify and characterize *S.* Typhi strains in blood samples. The results confirmed the presence of bacteria in 43 out of 100 blood samples, highlighting the limitations of RDTs in diagnosing typhoid fever accurately. Antibiotic susceptibility testing using the disc diffusion method revealed that Imipenum, Azithromycin, and Ceftriaxone were the most effective antibiotics, with resistance rates of 0%, 0%, and 11% among the tested *S.* Typhi isolates, respectively. Conversely, Nalidixic acid, Ampicillin, and Co-trimoxazole were the least effective antibiotics, with resistance rates of 95.3%, 80%, and 74%, respectively.

Differential proteomic analysis, facilitated by liquid chromatography-mass spectrometry (LC-MS/MS) and bioinformatics tool Skyline, identified 23 proteins that were significantly up-regulated (p-value <0.05 and log2-fold change values of ≥1.5) in drug-resistant *S.* Typhi isolates compared to drug-sensitive ones. These differentially expressed proteins played diverse roles in biological processes such as virulence, pathogenesis, translation, antibiotic resistance, cell metabolism, and stress response.

The characterization of immunoreactive proteins in *S.* Typhi was achieved through immunoaffinity chromatography-based mass spectrometry, utilizing total cell proteins and sera from typhoid patients. This approach identified 28 immunoreactive proteins, including 14 captured by IgG, 4 by IgM columns, and 10 by both columns. These proteins were found to be enriched in carbohydrate metabolism, biosynthetic pathways, and cellular component localization. *In silico* analysis via VaxiJen 4.0 confirmed the antigenicity of these immunoreactive proteins.

Gene expression analysis using real-time quantitative polymerase chain reaction (RT-qPCR) demonstrated that the genes coding for selected immunoreactive proteins were more highly expressed in clinical *S.* Typhi strains compared to the ATCC strain. While some genes, such as 16S rRNA and *rfbH*, were equally expressed in both strains, others, including *trxB*, *glyA*, *pepD*, *tufA*, *groEL*, *pflB*, and *dapD*, exhibited higher expression in clinical strains. *In silico* predictions through C-IMMSIM indicated a strong immune response to these proteins, further validating their immunogenicity.

CONCLUSION

In conclusion, this study has provided valuable insights into typhoid fever by identifying 23 overexpressed proteins in drug-resistant *S.* Typhi and characterizing 28 immunoreactive, immunogenic, and antigenic proteins. These findings hold promise for enhancing our understanding of resistance mechanisms, serving as biomarkers for accurate diagnosis, and contributing to the development of reliable typhoid vaccines.

few years, particularly the pharmaceutical industry. Thus, prompted by the above, in the present study we have shown the development of a novel 1,3,5-triazine-pyrazole analog (TP15) against *S. Typhi* and *S. Paratyphi A* clinical isolates.

METHODS

Initially, a library of compounds was generated using the architecture of deep generative models, followed by neural network validation, and the most promising compound (TP-15) against the ompF (outer membrane porin F) protein target of *S. typhi* was identified using molecular docking, molecular dynamics simulations, and binding free energy calculations. The TP15 effect on the viability of *S. Typhi* and *S. Paratyphi A* was analyzed by broth microdilution assay and CFU assay. The anti-QS activity was determined using the swarming ability and violacein inhibition assay.

RESULTS

The artificial intelligence-based drug discovery model against ompF has been developed which yielded TP15 as the most promising compound among the generated library. The MIC and IC_{50} values of TP15 showed that they are very good inhibitors of human pathogenic MDR *S. Typhi*, and *S. Paratyphi A* strains in a concentration-dependent manner, with no cytotoxicity. TP15 showed a reduction of swarming motility in a dose-dependent manner and reduced the QS-regulated violacein production up to 49.4 - 62.3% in both isolates.

CONCLUSION

Our study has demonstrated the successful utilization of artificial intelligence in the discovery and development of a novel 1,3,5-triazine-pyrazole analog (TP15) as an anti-quorum sensing and antibacterial agent against *salmonella enterica typhi/paratyphi A* clinical isolates.

108. Development of a Nontyphoidal *Salmonella* Controlled Human Infection Model

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INTRODUCTION

Invasive nontyphoidal *Salmonella* (iNTS) disease is a leading cause of bloodstream infection in sub-Saharan Africa. iNTS is potentially amenable to vaccination and several candidate vaccines are in early-stage clinical testing. Controlled human infection models (CHIMs) have a proven track record of accelerating vaccine development for enteric infections, including cholera and typhoid fever. We have developed an iNTS CHIM, with the aim of providing a platform to test candidate vaccines and better understand host-pathogen interactions. Herein we describe expert consultation, preliminary challenge strain characterisation, and clinical study protocols underpinning this study.

METHODS

The Challenge NTS (CHANTS) study will deliver a CHIM using well-characterised clinical-case isolates of *Salmonella* Typhimurium. Key stakeholders were invited to an expert consultation meeting in July 2022 to discuss endpoints, inclusion/exclusion criteria, strain selection and prioritisation of assays. We have also engaged public focus groups in the UK to inform key aspects of study design.

RESULTS

An expert consultation recommended recruiting healthy volunteers in a non-endemic setting in the first instance, prior to potentially transferring the model to high-burden settings. Primary endpoints should mimic iNTS disease where possible. Public engagement activities emphasised clear risk communication and facilities available in the study site. Volunteer reimbursement was calculated based on nationally agreed tariff costs and time-lost-from work using the London living-wage. Two strains of *Salmonella* Typhimurium — 4/74 and D23580 — have been manufactured to GMP standard and have undergone preliminary characterisation testing. Healthy volunteers aged 18-50 will undergo screening and — if consenting and eligible — will be challenged with 4/74 or D23580 following a dose-escalation algorithm. Participants will be admitted to a quarantine facility for a minimum of 7 days. The primary objective of the study is to determine the dose of *Salmonella* Typhimurium required to achieve an attack rate of 60-75% using a primary endpoint of bacteraemia and/or persistent temperature ≥38°C for ≥12hrs. Secondary endpoints include the rate of gastrointestinal colonisation, diarrhoea, and systemic symptoms at different dose-levels, and to compare clinical, microbiological, and immunological features between challenge-strains.

CONCLUSION

The CHANTS study will commence Autumn 2023 and will provide a platform to assess candidate iNTS vaccines. It is anticipated that strain characterisation, in addition to preliminary clinical and safety data from a sentinel challenge cohort will be presented.

109. Typhoid Intestinal Perforation in Francophone Africa, a Scoping Review

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BACKGROUND

Typhoid intestinal perforation (TIP) is a leading cause of peritonitis and indication for emergency surgery in Africa,

with mortality rates up to 30% in pediatric populations. Most TIP studies in academic Western databases are conducted in countries that primarily speak English, due to non-English publication and citation biases. Despite the high burden of infectious diseases in Francophone Africa, data from these countries remain limited. This study aims to highlight incidence and morbidity of TIP in Francophone African countries using an extended search algorithm.

METHODS

We conducted a scoping review to investigate peritonitis, non-traumatic ileal perforation, and typhoid in Francophone African countries using PubMed, EMBASE, and Scopus databases. To expand beyond traditional databases, we reached out to surgeons in Africa and concurrently used citation chasing. Studies published after 2000 were included.

RESULTS

We identified 39 studies from 12 countries, across 28 different hospitals. A total of 22 manuscripts were published in French. Patient's median age was 20 years. TIP caused a median of 35% of acute peritonitis. Mortality rates ranged from 6 – 37% (median: 16%). Rate of complications ranged from 15 – 92% (median: 46%). Ileostomy creation as a treatment for TIP remains variable between hospitals (0 – 79%), with the highest rates noted in Niger.

CONCLUSION

In Francophone Africa, TIP is a common surgical emergency, associated with high morbidity and mortality, primarily in children and young adults. Unfortunately, in many countries, the lack of blood culture availability leads to underreported typhoid cases. Limited country specific data remains a major barrier to the introduction of typhoid conjugate vaccines (TCV), which are highly efficacious and safe. Using TIP as an indicator of typhoid disease burden, countries can support TCV inclusion in additional national vaccine programs. Interventions including improved sanitation and the introduction of TCVs have the potential to significantly decrease this preventable disease.

110. Paratype v1.1: Recent Updates to the Genotyping Tool for Paratyphoid Fever Surveillance

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Child Health Research Foundation

BACKGROUND

Paratyphoid fever, caused by *Salmonella* Paratyphi A, is a neglected tropical disease that disproportionately affects low- and middle-income countries. However, limited genomic information of this pathogen hindered the development of effective treatment and prevention strategies. In 2022, using all genomes published till 2021, we released an open access tool, *Paratype* (v1.0), to facilitate genomic epidemiological studies on paratyphoid fever. Here, we present updates to *Paratype* v1.0.

METHOD

Using *Paratype* v1.0, we analyzed *Salmonella* Paratyphi A genomes published since 2021. Phylogenetic analysis, conducted using RAxML, enabled the identification of novel genotypes. For any new genotype detected, a conserved allele was assigned, and the *Paratype* scheme was updated accordingly. We also introduced additional features to *Paratype*, including the ability to process large numbers of genomes in batch mode. Updated python and bash scripts are available on GitHub.

RESULTS

Since development of *Paratype* v1.0, 479 *Salmonella* Paratyphi A genomes have been published from Bangladesh, Cambodia, India, Malawi, Nepal, and Pakistan. *Paratype* v1.0 successfully assigned genotypes to all genomes from the above countries except India. For a subset of the genome dataset published by Jacob et al, 2023 (61 out of 152 genomes) from India, no subclade/genotype could be assigned beyond the assignment of primary and secondary clades. Through phylogenetic analysis, we identified six novel genotypes from this dataset: 2.3.4 and 2.4.5 - 2.4.9. Alleles were assigned for each of these genotypes and were included in the updated version, *Paratype* v1.1. We released this version on 25 May 2023.

To enhance user convenience, we updated the *Batch_run_paratype.sh* script in *Paratype* v1.1, enabling easier batch processing. Additionally, we introduced the *--mapq_cutoff* option to control the mapping quality of allele positions and improve genotype calling.

CONCLUSION

Six new genotypes have been incorporated in *Paratype* v1.1. Future developments of *Paratype*, v1.2 will include easy installation through using the Conda environment. The

inclusion of genome sequences from paratyphoid endemic regions, particularly Sub-Saharan Africa, will further improve the *Paratype* scheme. Collaborative efforts within the enteric fever research community are crucial in achieving this goal and enabling *Paratype* to inform prevention and treatment strategies for this neglected pathogen.

111. Challenges and Lessons Learned While Completing/Initiating Vaccine Clinical Trials During the COVID-19 Pandemic in a Developing Country: Experience From Nepal

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BACKGROUND

The global burden of vaccine-preventable infectious diseases is comparatively higher among developing countries than developed world. The COVID-19 pandemic has created many challenges in conducting clinical trials worldwide, especially in resource-limited countries. In this article, we describe the challenges and lessons learned in conducting vaccine clinical trials during COVID-19 pandemic in Nepal, a developing country.

METHODS

It is a study where researchers have shared their experiences while completing ongoing clinical trial for typhoid vaccine along with initiation of new clinical trial for COVID-19 vaccine in Nepal. In this study, researcher has used real time events, records and also secondary data to share the experience and prospect for future clinical trials in Nepal.

RESULTS

In March, government of Nepal decided to impose lockdown for rising case of COVID-19 which affected ongoing clinical trial for study titled, "A Phase III Multicenter, Observer-Blinded, Randomized, Active Controlled, Immune Non-inferiority and Safety Study of Diphtheria Toxoid Conjugated Vi-Polysaccharide Typhoid Vaccine compared to Typbar TCV® in healthy 6 months-45 years aged Nepalese participants" sponsored by International Vaccine Institute (IVI). This clinical trial was first ever large scale phase-3 clinical trial conducted in 4 different sites of Nepal. Out of 6 visits, 4th visits was almost completed and completion of remaining visits and retention of participants in the study was very challenging. IVI immediately responded by providing guidelines to complete remaining visits and providing personal protective equipment to all 4 sites. Similarly, site staffs were receptive to guidelines and tactful in planning follow ups and exploring the alternatives platform to review diary cards and safety assessment. With these initiatives, we could combat the situation and complete the study fulfilling both government and protocol safety requirements.

Similarly, in 2021, IVI submitted proposal for phase-3 COVID-19 vaccine trial in Nepal, where we faced various hurdles and challenges to initiate the study. From site selection to procuring logistics, staff training, participant recruitment/follow ups and monitoring of participants safety and data monitoring was challenging. However, making necessary changes as per the local requirements, collaborating with local stake holders, conducting community engagement program, pre-screening activities, continuous participants counselling, affiliating with various hospital departments, involving hospital staffs, etc. we were able to initiate and conduct the study amid the COVID-19 pandemic with highest enrolling sites among other countries and advanced to continue to the study.

CONCLUSION

Conducting a clinical trial in a developing country like Nepal during pandemic might be challenging, but by making necessary changes in study as per the local requirements, it is possible. High subject enrollment rate, subject safety monitoring plan and strategies, regular follow-ups, quick adjustment to new technology and sample shipment process, active and passive surveillance of covid-19 like illness have shown the optimal standard of proficiency of sites and its staffs.

112. Changes in WASH Properties and Health Seeking Behaviour: Pre and Post-TCV Mass Campaign in Asante Akim North District, Ghana

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BACKGROUND

Typhoid is a major public health issue in low- and middle-income countries; and its transmission has been well documented. Improving and monitoring WASH properties alongside typhoid conjugate vaccines (TCVs) and immediate treatment are considered key to its control. Therefore, we sought to examine the changes in the WASH properties and health-seeking behaviour in the pre and post-typhoid conjugate vaccine (TCV) mass campaign in a highly endemic area for typhoid fever in Ghana.

METHODS

A follow-up design of the households in a TCV trial site in the Asante Akim North district was used for the study. Questionnaires on the WASH properties and health-seeking

behaviour information were developed on Commcare running on tablets. With GIS maps of the catchment area, enumerators located and administered the questionnaire to every household in each structure for the two-time points (i.e., pre and post-TCV). Confidence intervals were estimated for the proportions and t-test was used to detect the difference in these two-time points.

RESULTS

The total number of households for pre- and post-TCV mass campaign were 13,266 and 13,393 respectively. There was no significant decrease (p-value=0.32) in the proportion of households who practiced open defecation in the pre-TCV campaign (6.78%) and the post-TCV campaign (6.45%). We observed a significant increase in the usage of sachet water as the main source of drinking water from 32.59% (32.2, 33.8) in the pre-TCV as opposed to 35.3% (34.1, 35.9) in the post-TCV (p-value<0.001). 88.54% (87.9, 89.1) of the households neither boiled nor filtered their drinking in the pre-TCV but this decreased significantly to 53.74% (52.8, 54.7) in the post-TCV mass campaign (p-value<0.0001). There was a decrease in the proportion of households who used traditional medicine to treat typhoid fever from 70% (60.1, 79.8) to 45% (31.5, 64.6) in pre- and post-TCV respectively (p-value=0.02). We observed a statistically c from 0.71% (0.67, 0.75) to 0.36% (0.34, 0.37) in the pre and post-TCV respectively (p-value <0.001).

CONCLUSIONS

Good practice of hygiene, improved sources of drinking water and its treatment and health-seeking behaviour might have contributed to the decline in the *S.* Typhi detection rate.

113. Isolation and Characterization of *Salmonella* From Nigerian Fruit Bats (Eidolon helvum) Using InvA Gene PCR, Sequencing and Serotyping

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BACKGROUND

Bat globally are identified as potential carriers and transmitters of both zoonotic and emerging pathogens amongst which include *Salmonella. Salmonella* species are amongst the most important zoonotic pathogenic organisms affecting both man and animals respectively generating a public and veterinary health risk.

OBJECTIVE

To determine the incidence and serovars of *Salmonella* in Fruit Bats (Eidolon helvum) from Nigeria using InvA gene PCR, Sequencing and serotyping.

MATERIALS AND METHODS

A total of 86 bats were captured from 6 small settlements of Plateau and Bauchi States, Nigeria. Ethical clearance was obtained. Bats were euthanized using chloroform and submitted for post mortem and the entire intestinal tract was removed and placed in sterile universal bottle. To detect *Salmonella* spp., inoculated selenite faeces were sub-cultured onto Xylose Lysine Desoxycholate agar and Brilliant *Salmonella* agar. Plates with growth of suspected pink or pink colonies with black centres on XLD agar and purple colonies on BSA were considered as *Salmonella* spp. Typical *Salmonella* colonies were confirmed by biochemical assays using Triple sugar iron, indole, Methyl Red Voges Proskauer, Citrate, Urease, glucose, mannitol, sorbitol. The confirmed isolates were analysed by PCR of detection of invA gene with expected band size of 284 bp. Sequencing of the invA gene of *Salmonellae*spp was determined, blasted and compared with the published sequences in the GenBank. *Salmonella* isolates were freeze-dried and shipped following WOAH guidelines to the WOAH *Salmonella* reference laboratory in Padova *Salmonella*.

RESULT

We screened 86 intestinal contents by conventional culture and phenotypic methods, only 10 (8.6%) samples were positive for *Salmonella* and only 4 samples were positive for invA gene confirming the presence of *Salmonella* by PCR. The homology percentage of the nucleotide sequence showed high similarity with other published sequences. *Salmonella* Kisarawe was the only serovars established by the serotyping analysis.

CONCLUSION

The confirmation and characterization of *Salmonella* spp. in this study, with further sequencing and serotyping analysis validates the presence of *Salmonella* in Nigerian fruit bats (Eidolon helvum). Bats can therefore play an important role in the geographical distribution of salmonellosis. The presence of *Salmonella* in the Nigeria fruit bat also implies a significant public health threat to humans and animals.

114. Evaluation of Impact of Health Education Intervention on Knowledge and Management of Typhoid Fever Among Patent Medicine Vendors in Ebonyi State, Nigeria

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BACKGROUND

Typhoid fever is a major public health concern in Nigeria. According to the World Health Organization, Nigeria is one

RESULTS

From 94 candidate sampling sites, we down-selected to 35 final sites spanning different types of waterways. Monthly sampling of 35 final sites has started in September 2022, and will continue for a year after the vaccination campaign (planned for Q3 2023). Since 2023, sampling in outbreak locations has been added to the regular sampling schedule. The container lab is operational, and DNA has been extracted from all samples collected to date. Initial PCR analysis are underway, and PCR results will be shown if available by the conference.

CONCLUSION

Here, we describe the design and practical implementation of a routine environmental surveillance system that will complement clinical surveillance to assess the impact of an island-wide mass vaccination campaign. We will focus on success and challenges to guide and inform similar endeavors in other locations, and show preliminary results if available.

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