



Typhoid associated Ileal Perforations following the Introduction of Typhoid Conjugate Vaccine in Pakistan:

Findings from a Multi-Center Surveillance Study

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Introduction

- World Health Organization (WHO) estimates that there are 14.3 million typhoid cases and 222,000 typhoid-associated deaths per year, globally.
 - Stanaway JD et al. Clin Infect Dis. 2010;50(2):241-6.
 - Crump JA et al. Clin Infect Dis. 2010;50(2):241-6.
- South and Southeast Asia are the most affected regions, accounting for ~90% of the disease mortality.
 - Mogasale V et al. Lancet Glob Health. 2014;2(10): e570-80.
- Typhoid-related ileal perforations are more prevalent in low-middle income countries and occur in 0.8%–39% of cases. (700-1200 \$USD)
 - Qazi et al. Clin Infect Dis. 2020 Nov 1;71: S232-8.

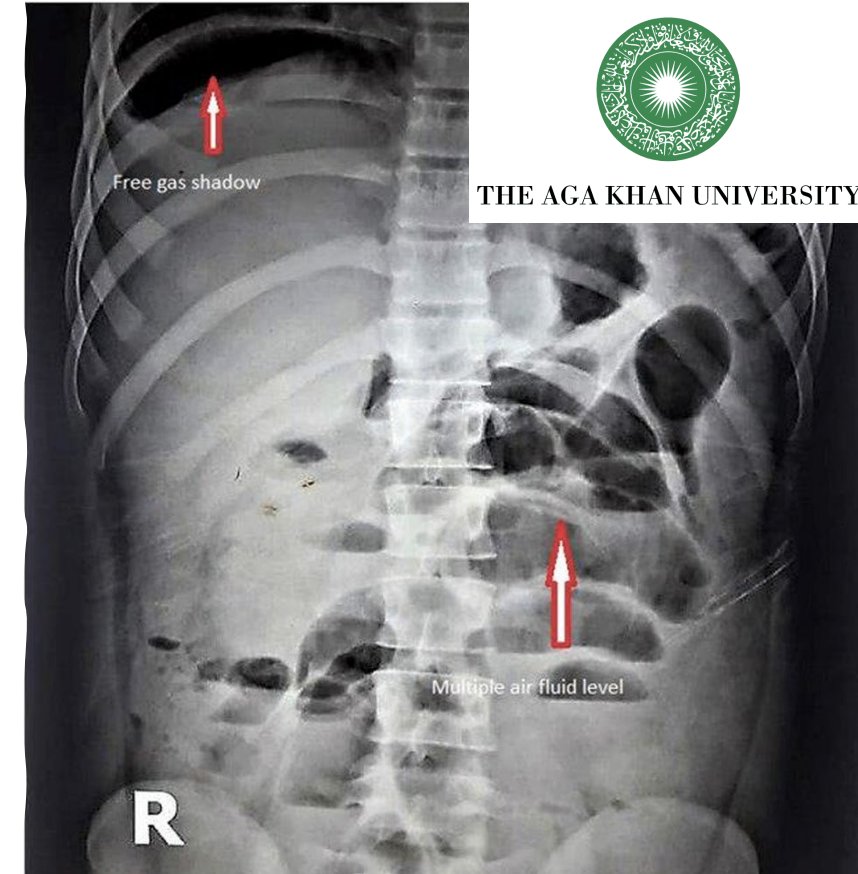


Background

- XDR outbreak in 2016 → limited treatment options in Pakistan
- TCV introduction in Pakistan in
 - 2019/20 in Sindh province,
 - 2021 in Punjab province and
 - 2022 in other provinces
- Routine immunization at 9 months
- Catch up campaign 9 mo to 15 years (Nov-Dec 2019 in Sindh)

Typhoid Ileal Perforation

- Presents late
- Exploratory Laparotomy
- Longitudinal perforation on anti-mesenteric border of ileum
- Ileostomy
- Reversal of ileostomy – 6-8 weeks
- Hospital stay – 10 – 14 days



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Aim



- This study aims to measure the burden of ileal perforations post TCV introduction in Sindh, Pakistan



Study Setting

- **NICH**
- **AKUH**
- **JPMC**
- **CHL Lahore**



National Institute of Child Health, Karachi

600 Beds

Jinnah Postgraduate Medical Center

- 2,208 bedded



Aga Khan University, Karachi

721 beds



Institute of Child Health & CH Lahore

- 1100 Beds





Study Duration

- **March 2022 – Surveillance started in Sindh Province**
- **June 2023 – Surveillance Punjab Province**
- **Active surveillance from Monday to Saturday**



Eligibility Criteria

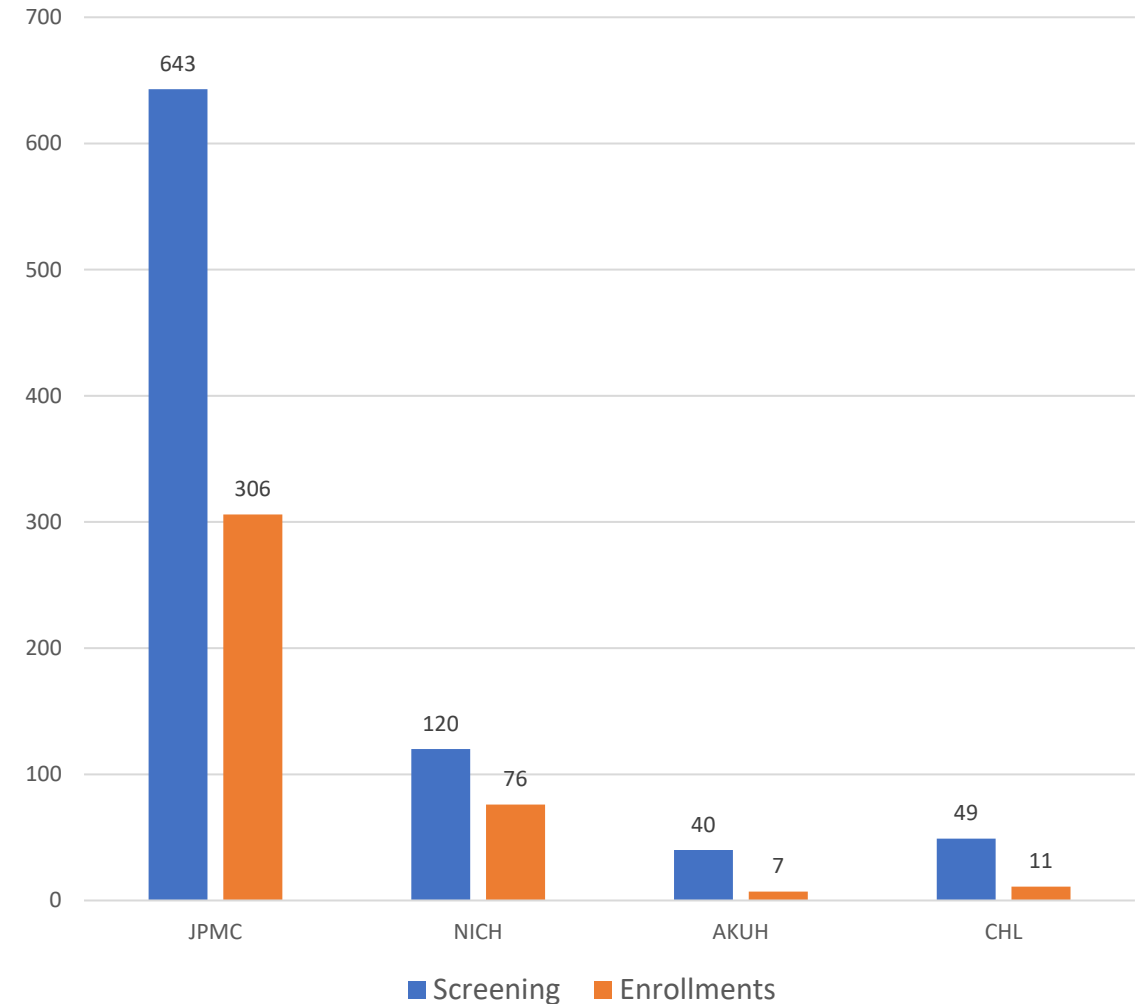
- Screening of all suspected and confirmed cases of non-traumatic ileal perforation admitted in the surgical wards
- Non-ileal perforations and perforations due to trauma, malignancy or tuberculosis are excluded
- Blood culture is obtained from enrolled participants
- Tissue samples are collected for histopathology and archived at AKU

Screening and Enrollments of ileal perforations (Mar 2022 – 30th Sep 2023)



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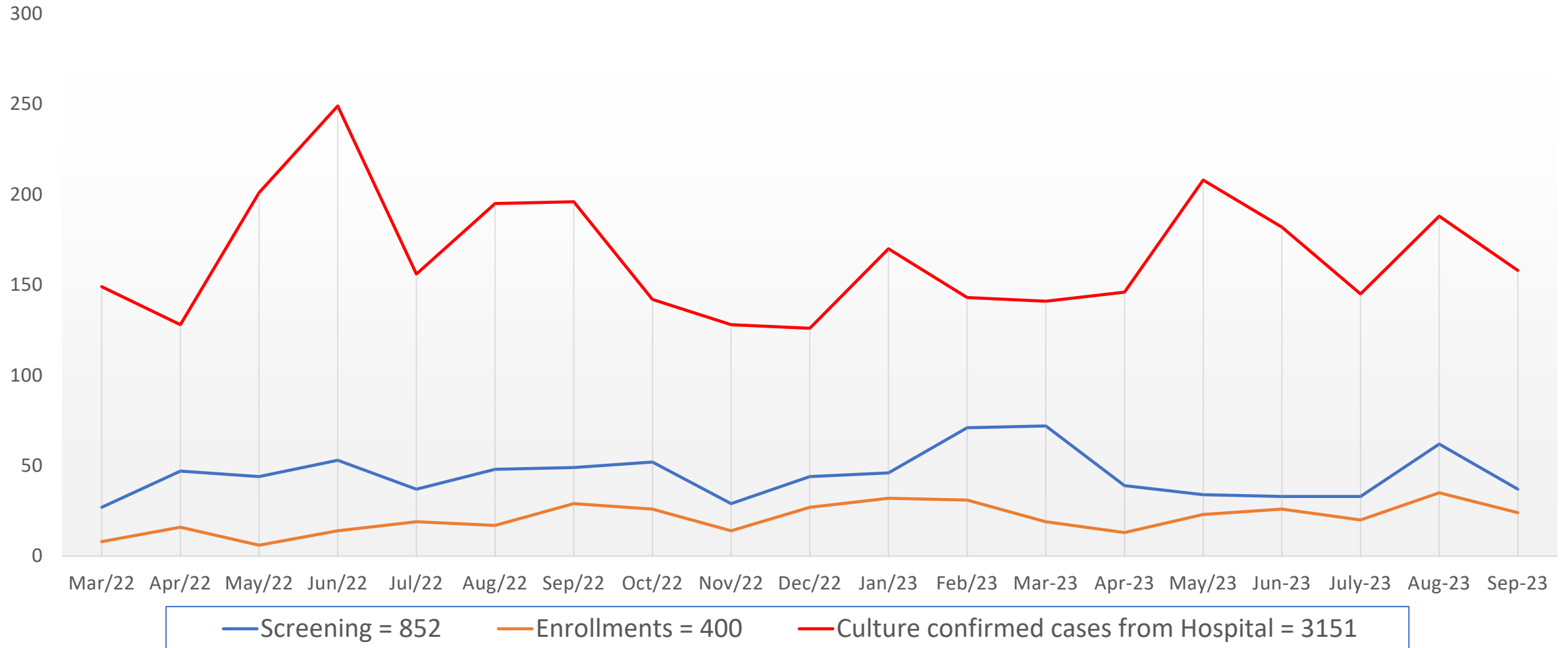
S#.	Site	Screening	Enrollments
1	JPMC	643	306
2	NICH	120	76
3	AKUH	40	7
4	CHL	49	11
Total		852	400



Monthly trend of ileal perforations (Mar 2022 – 30th Sep 2023)



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Sociodemographic characteristics of ileal perforations (Mar 2022 – 30th Sep 2023)

Characteristics of Patients	AKU	NICH	JPMC	CHL	TOTAL
n =	7 (2)	76 (19)	306 (76)	11 (3)	400
Gender					
Male	6 (2)	55 (14)	256 (63)	10 (3)	327 (82)
Female	1 (0)	21 (5)	50 (13)	1 (0)	73 (18)
Year of Surveillance					
2022	6 (2)	35 (9)	135 (34)	0 (0)	176 (44)
2023	1 (0)	41 (10)	171 (43)	11 (3)	224 (56)
Age Groups					
< 2 years	0 (0)	1 (0)	0 (0)	4 (1)	5 (1)
≥ 2-4 years	0 (0)	6 (2)	0 (0)	0 (0)	6 (2)
≥ 5-15 years	0 (0)	67 (17)	14 (4)	7 (2)	88 (23)
≥ 16-25 years	4 (1)	2 (0)	132 (33)	0 (0)	136 (34)
>25	3 (1)	0 (0)	160 (40)	0 (0)	165 (41)

Lab results among patients with ileal perforations (Mar 2022 – 30th Sep 2023)

S#.	Site	Total Enrolled	BLCs	S. Typhi	S. Paratyphi	Other Pathogen	Tissues Collected	Deaths
1	JPMC	306	277	19	1	127	241	44
2	NICH*	76	70	8	0	36	53	9
3	AKUH	7	6	0	0	5	5	0
4	CHL	11	5	0	0	0	0	0
Total		400	358	27	1	168**	233	53 (14%)

• One 1 S.typhi's tissue not collected only BLCs done in NICH.

** *Staph.Spp,E.Coli,K.Pneumoni,Acubetibac,Bac.Sp(Fr),E.Cloacae,Entb.Spp,Burak, Cepac, Candida Spp,Aerom.Spec, Coryneb.Sp,Pseudomonas Stut Entb.Spp,Candida Lusitaniae,Entb.Spp,K.Pneumoni, Pseu.Aerug, E.Cloacae,Klebs.Spec, Acinetobac Enterococc*

Health care seeking before presenting at the hospital (Mar 2022 – 30th Sep 2023)

S#.	Site	Total Enrolled	Physician	Pharmacy	Other *
1	JPMC	306	206 (67)	110 (32)	4 (1)
2	NICH*	76	42 (55)	15 (20)	19 (25)
3	AKUH	7	3 (44)	2 (28)	2 (28)
4	CHL	11	5 (45)	5 (45)	1 (10)
<ul style="list-style-type: none"> • Traditional Healer/Lab/Self Medication 					

Clinical presentation at the time of hospitalization (Mar 2022 – 30th Sep 2023)

S#.	Site	Total Enrolled	Fever	Abdominal pain	Vomiting	Diarrhea	Constipation	Other *
1	JPMC	306	295 (73.75)	299 (74.75)	183 (45.75)	48 (12)	157 (39.25)	122 (30.5)
2	NICH*	76	76 (19)	74 (18.5)	55 (13.75)	22 (5.5)	29 (7.25)	29 (7.25)
3	AKUH	7	7 (1.75)	7 (1.75)	3 (0.75)	2 (0.5)	1 (0.25)	5 (1.25)
4	CHL	11	10 (2.5)	10 (2.5)	8 (2)	3 (0.75)	6 (1.5)	7 (1.75)
Total		400	* Abdominal distention, Loss of appetite, Nausea, Headache, Fatigue, Urine retention, Body pain, SOB					

Antibiotics use before presenting to the hospital (Mar 2022 – 30th Sep 2023)

S#.	Site	Total Enrolled	Yes	No
1	JPMC	306	254 (83)	52 (17)
2	NICH*	76	61 (80)	15 (20)
3	AKUH	7	3 (43)	4 (57)
4	CHL	11	6 (55)	5 (45)
Total		400		



Conclusion & Recommendations

- Burden of ileal perforation is high in Pakistan
- 75% of ileal perforations are among age group > 15 years (non-vaccine eligible group)
- There were 14% deaths associated with ileal perforations
- TCV eligible age needs to be expanded
- TCV should be made available in private market

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- EPI Sindh, Punjab and Federal
- Provincial disease surveillance & response units



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