

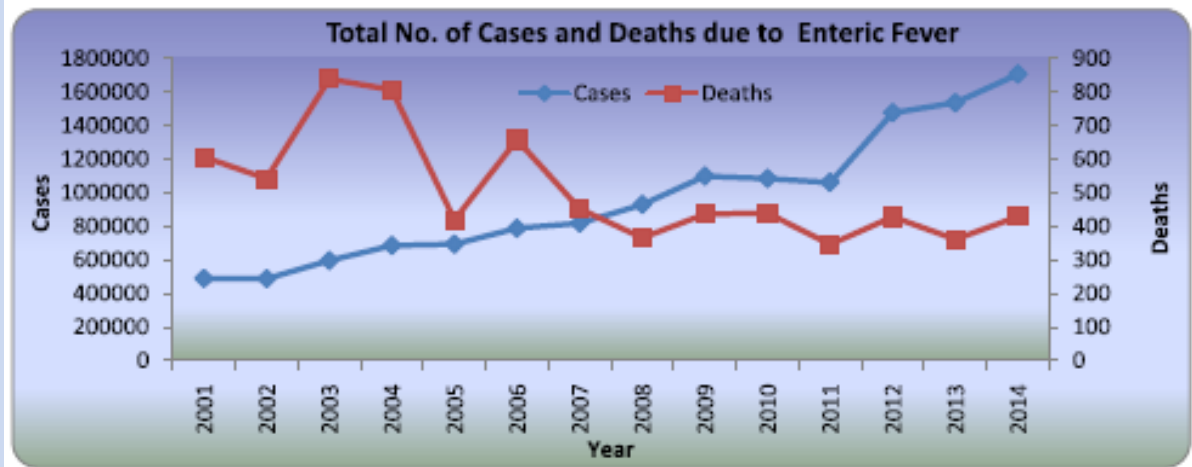
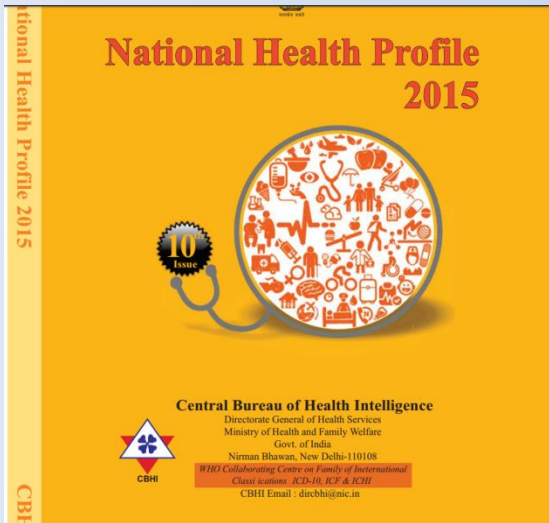


Seasonality, Antibioogram and Mechanism of Fluoroquinolone resistance Of Salmonella serotypes in a Tertiary care Hospital- Delhi



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India : Burden, Vaccination



Source : Monthly Health Condition Reports from Directorate of Health Services of State/UT.

2014
Total cases : 1707312
Deaths : 429

- EPI -Typhoid-paratyphoid Vaccine
1981: vaccine was dropped reportedly
- higher reactogenecity
 - low efficacy
 - perceived reduced burden of typhoid disease in the country

Salmonella Typhi and Paratyphi A isolated over a 10 year period (2004-2013):

A total of salmonella isolates-1266

- Trends seasonal distribution and clinical presentation
- antibiogram pattern
- mechanism of fluoroquinolone resistance

1266 (1012 ST and 254 STA) 2004-2013
Antibiotic sensitivity and MIC

characterized for FQ resistance

Based on of NAL and CIP MIC, year of isolation , MDR phenotype
N= 206 (162 ST , 44 STA)

Mutation

- Topoismerase gene (*gyrA*, *gyB*, *parC* , *parE*)
- DHPLC technique

PMQR genes

- *qnrA*, B and S
- *aac(6')Ib-cr*
- *qepA*

Efflux Pump

- Screening--
cyclohexane
tolerance., EPI
- Confirmation- PCR

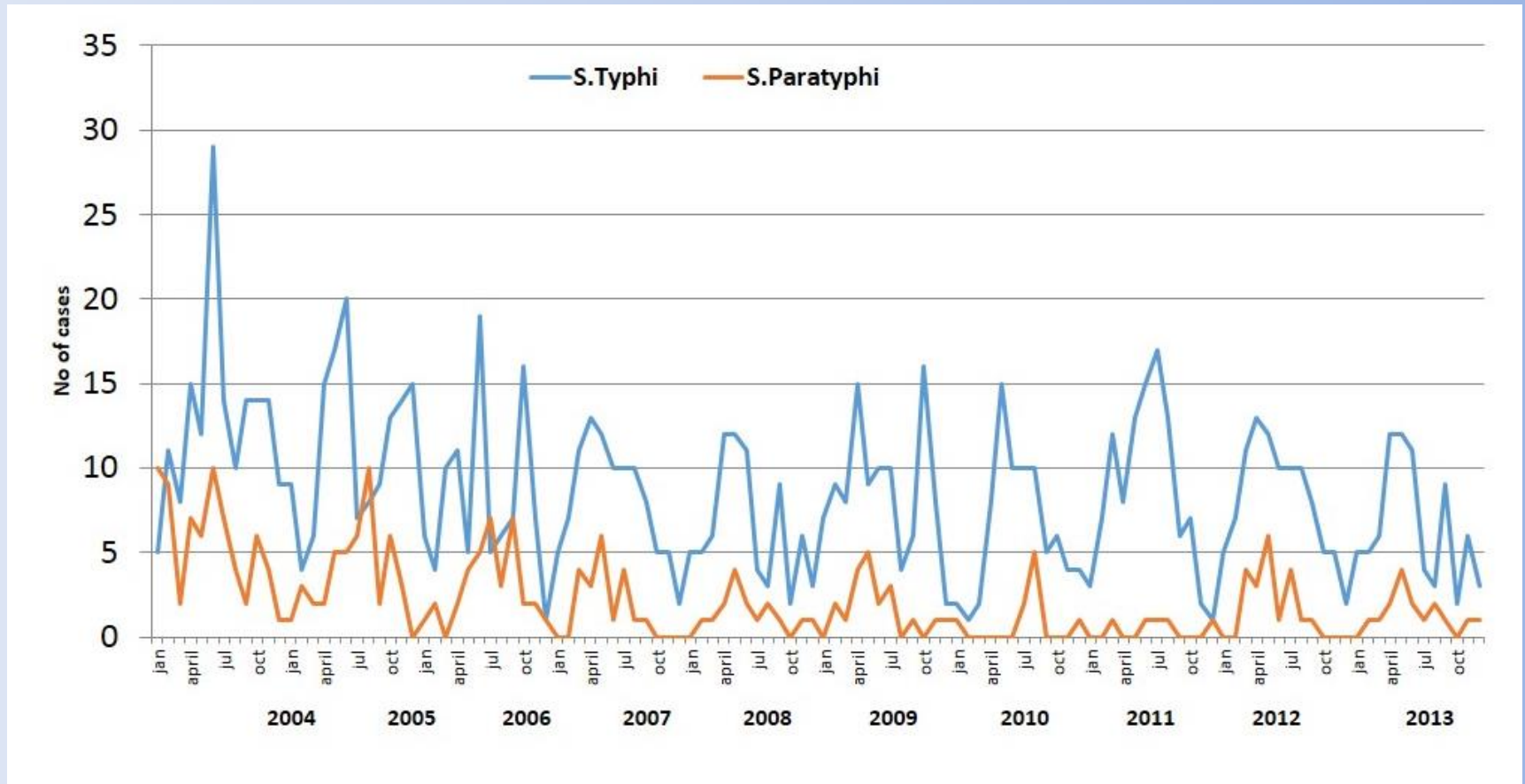
OMP : outer memb porins Screening

- Cefoxitin MIC
- Confirmation-SDS-PAGE.

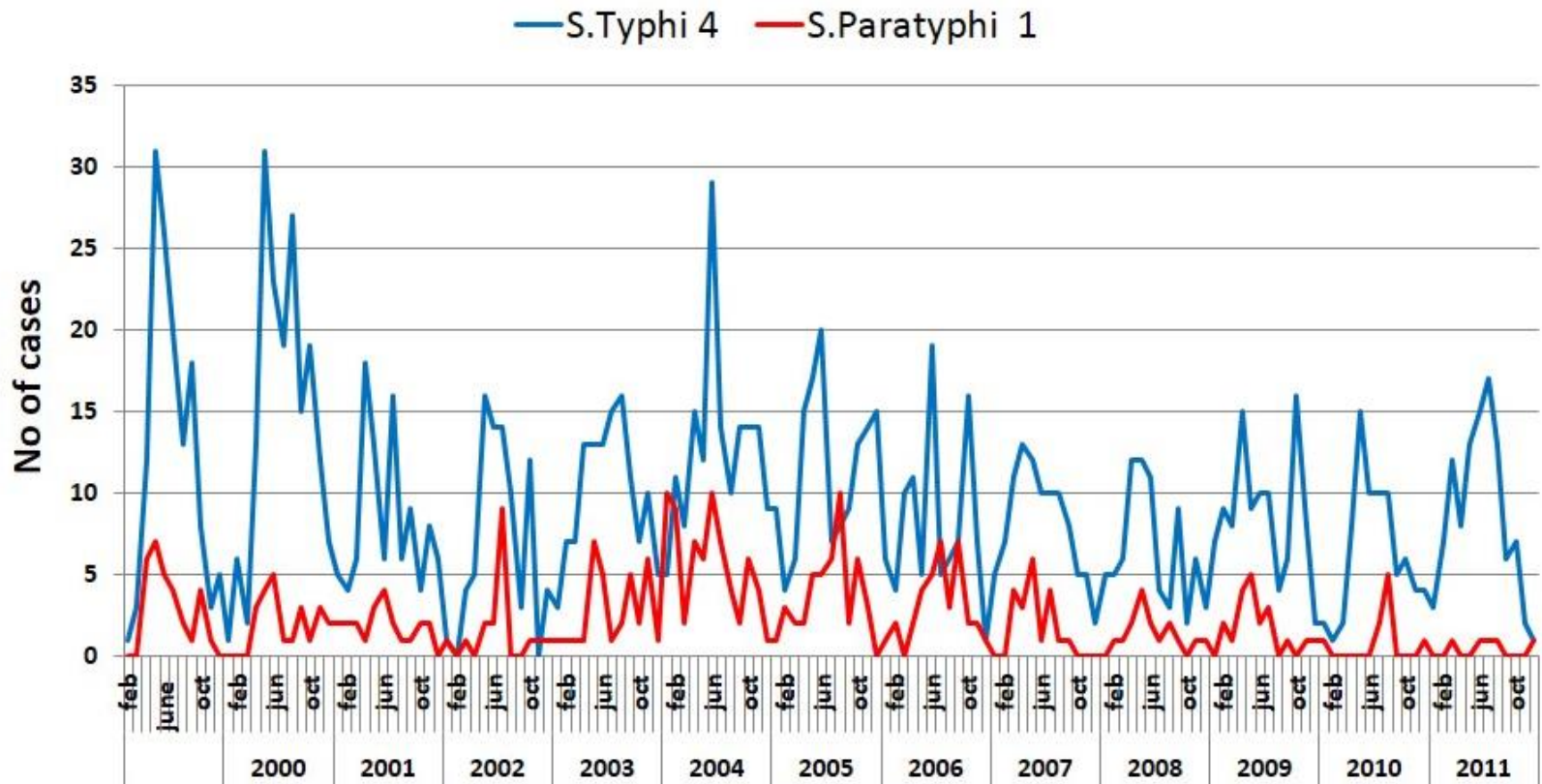
Molecular Epidemiology : MLVA-VNTR

Based different mutation, MIC , year of isolation 104/206 (80 ST and 24 STA) isolates

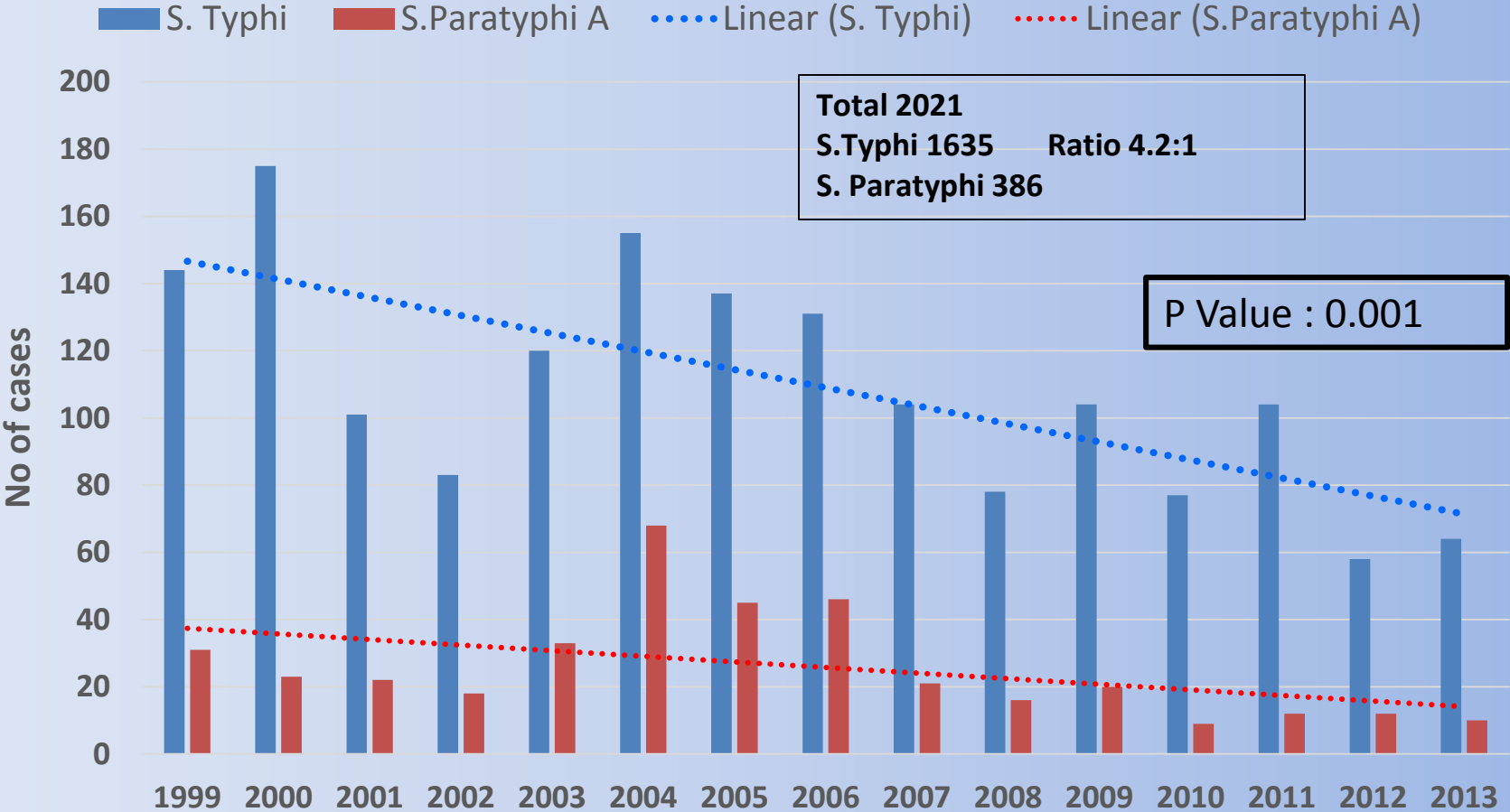
Seasonal variation



Seasonal variation

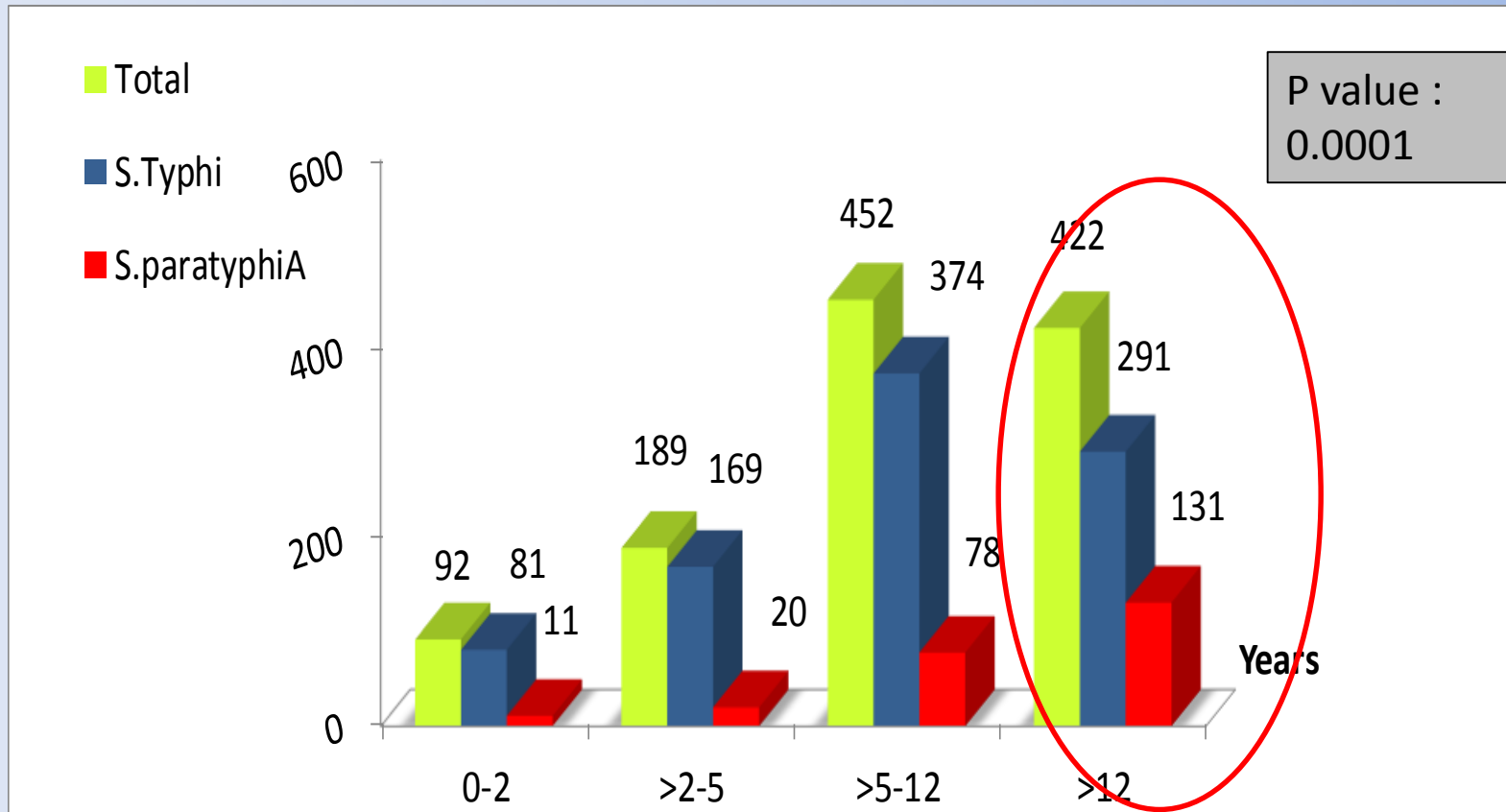


Trend : Serotype isolation 1999-2013



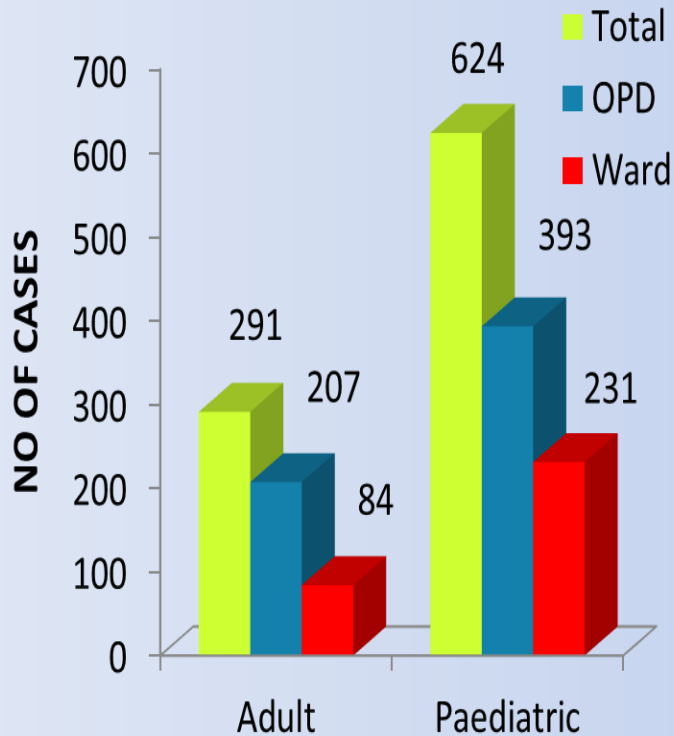
Year	Total Isolates	S.Typhi (%)	S. Paratyphi A(%)	Ratio
1999	175	144(82)	31 (18)	4.6:1
2000	198	175(88)	23(12)	7.6:1
2001	123	101(82)	22(18)	4.6:1
2002	101	83(82)	18(18)	4.6:1
2003	153	120(78)	33(22)	3.6:1
2004	223	155(69.5)	68(30)	2.3:1
2005	182	137(75.3)	45(24.7)	3:1
2006	177	131(76.5)	46(23.5)	2.8:1
2007	125	104(83.2)	21(17)	4.9:1
2008	94	78(83)	16(17)	4.8:1
2009	124	104(84)	20(16)	5.2:1
2010	86	77(90)	9(10)	8.5:1
2011	116	104(90)	12(10)	8.6:1
2012	70	58(82)	12(18)	4.8:1
2103	74	64(86)	10(14)	6.4:1

Age Related Difference

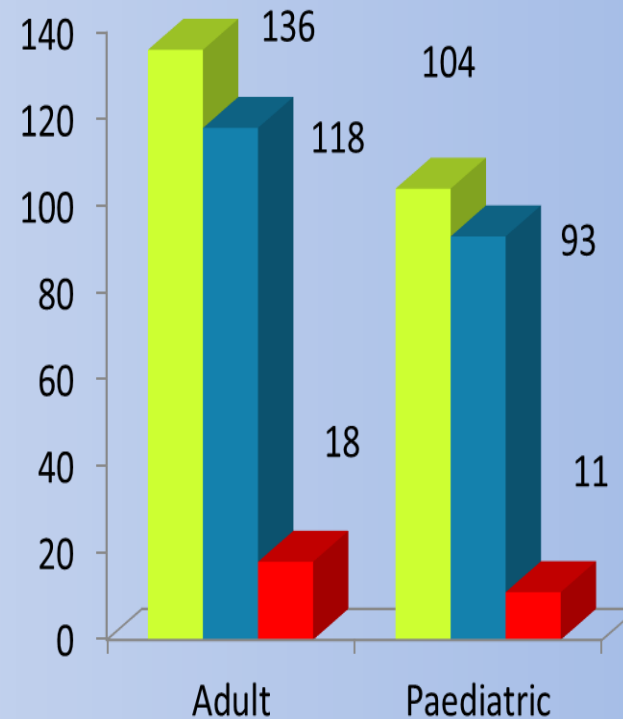


Distribution of serotypes by Out/Inpatient

S Typhi



S Paratyphi A

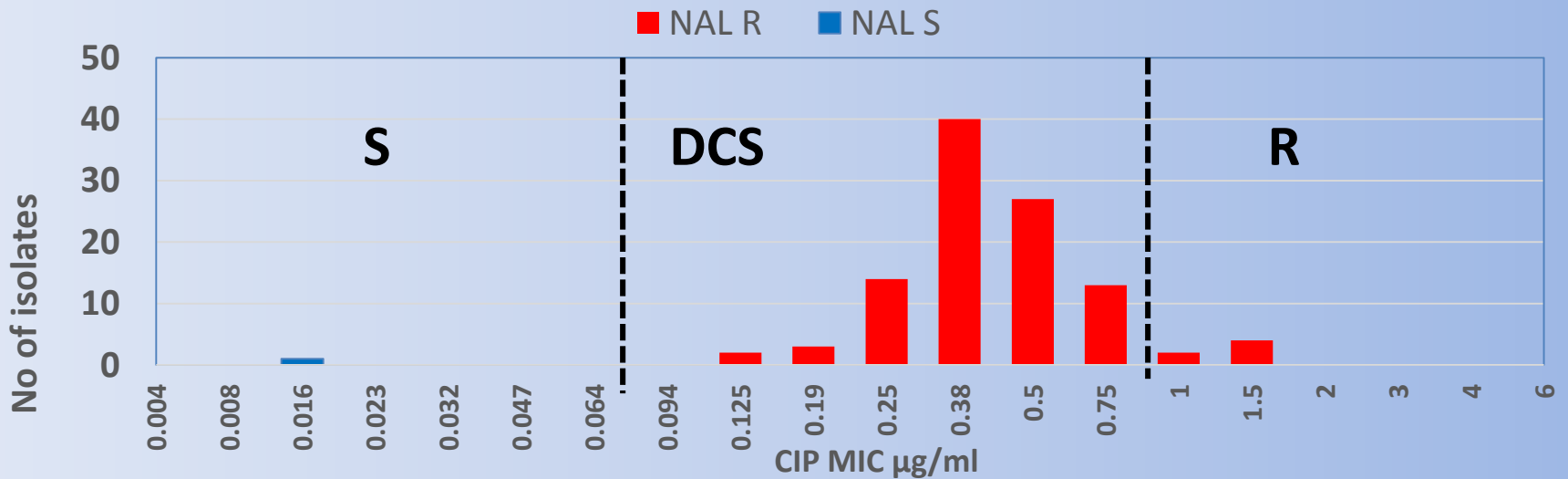
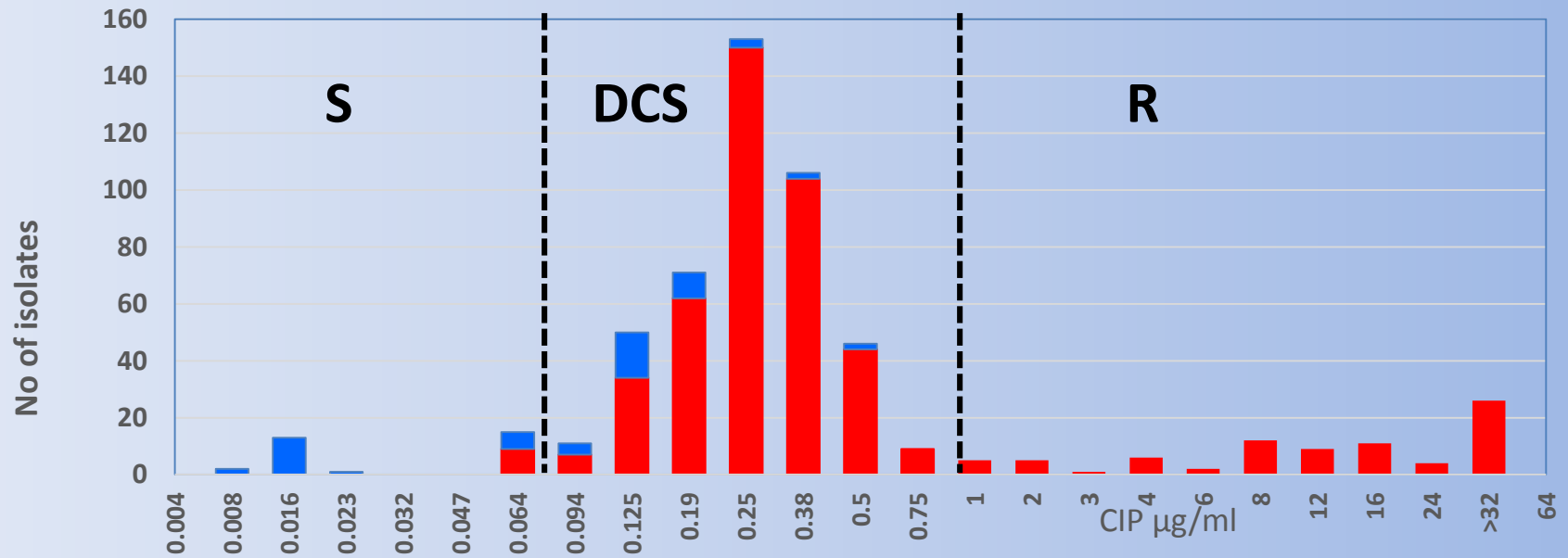


P value < 0.005

Definitions (CLSI 2012)

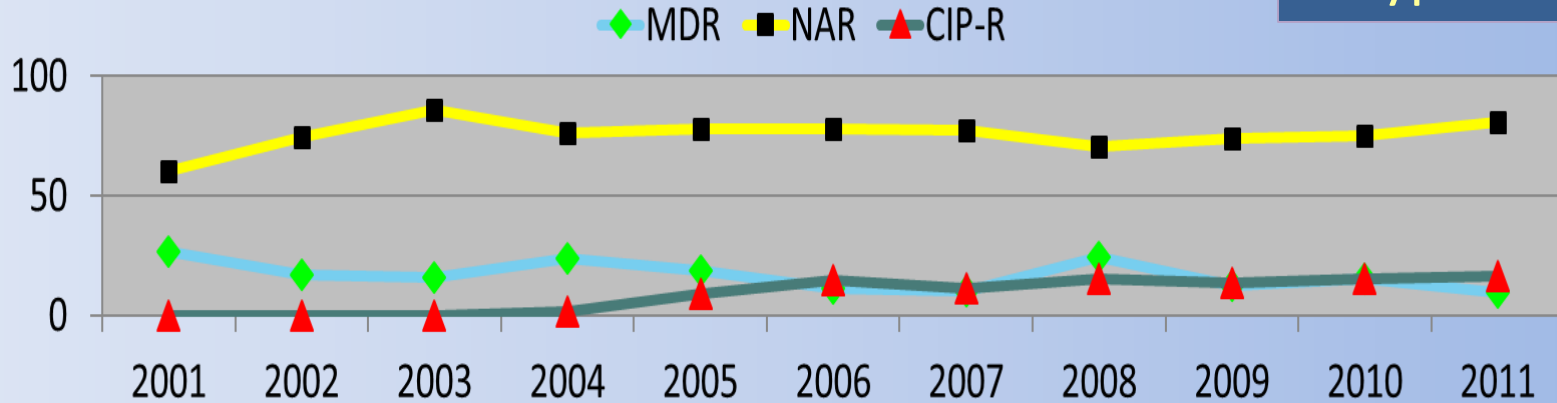
Phenotype	ABBV	MIC ($\mu\text{g/ml}$)
Nalidixic Acid Susceptible	NAL ^S	≤ 16
Nalidixic Acid Resistant	NAL ^R	≥ 32
Ciprofloxacin susceptible	CIP ^S	≤ 0.064
Ciprofloxacin decreased Susceptible	CIP ^{DCS}	0.125-0.5
Ciprofloxacin resistant	CIP ^R	≥ 1
Multidrug resistance	MDR	

Ciprofloacin MIC of S.Typhi and Paratyphi A

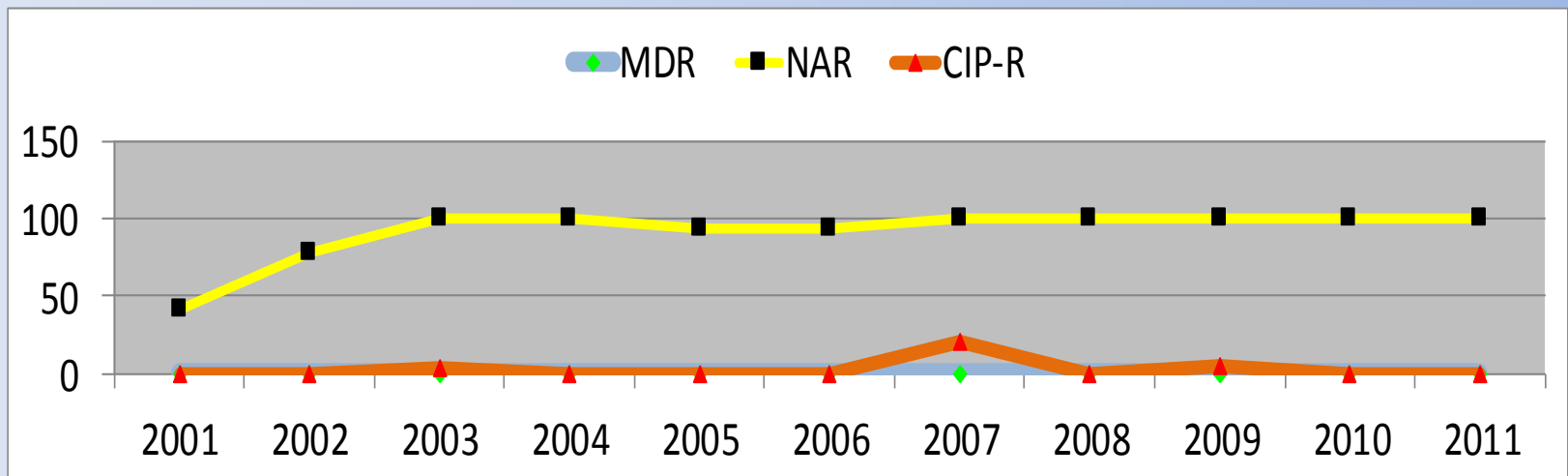


Trends of MDR, NAR & Cip-R

S. Typhi



S. Paratyphi A

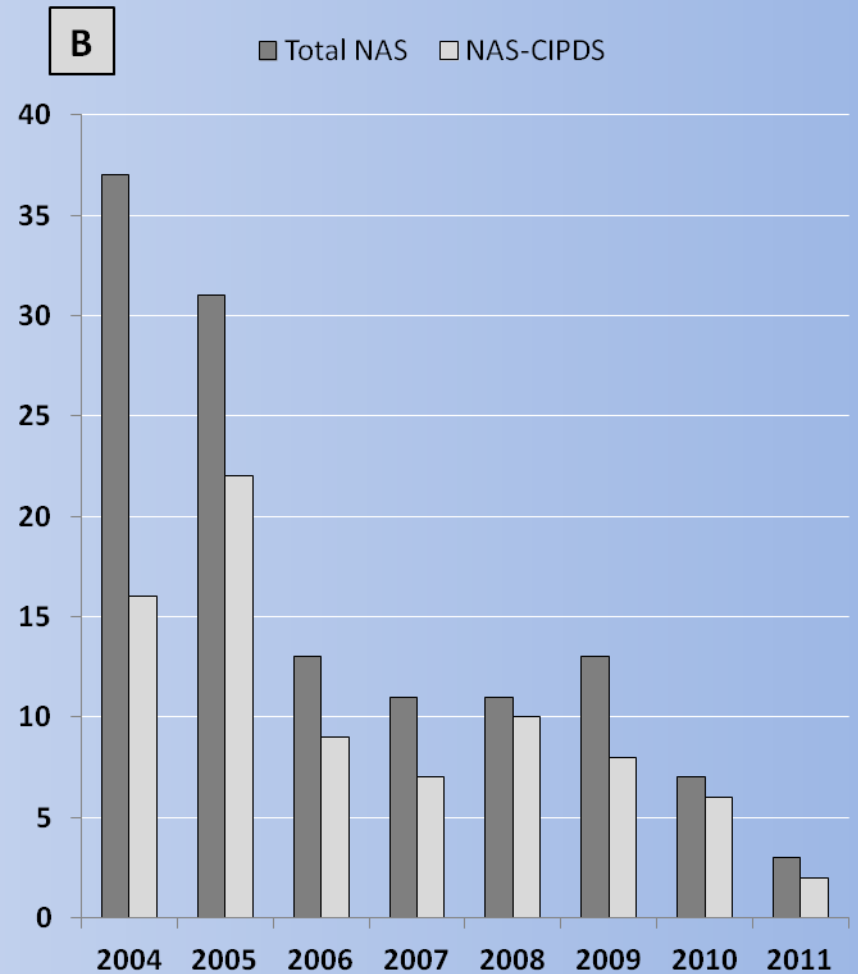
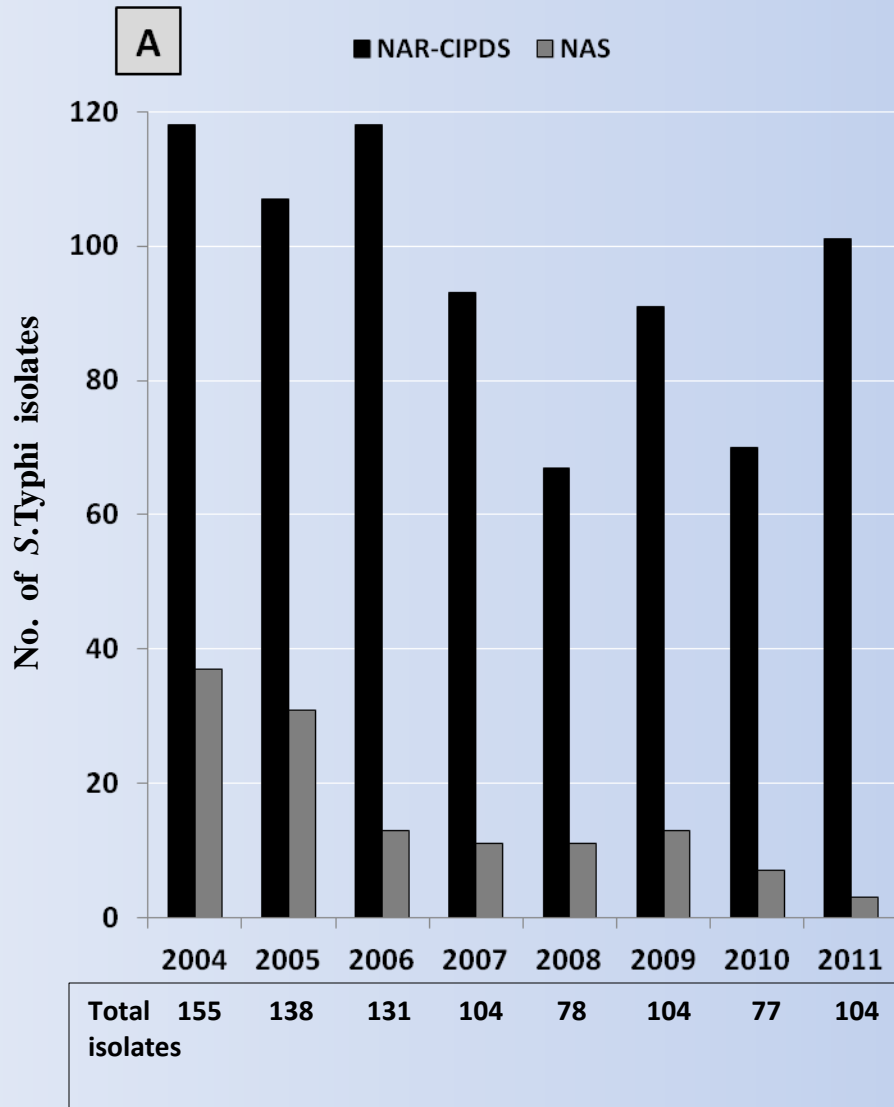


Comparison of phenotypic *S.Typhi* & *ParatyphiA*

Phenotype	<i>S.Typhi</i> (N=558)	<i>S.Paratyphi A</i> (N=106)
Nalidixic acid susceptible (NAL ^S)	58 (10.3%)	3 (2.8%)
Nalidixic acid resistance (NAL ^R)	419 (74.7%)	97 (91.5%)
Ciprofloxacin resistance (CIP ^R)	81 (14.5%)	6 (5.6%)
Multi-Drug-Resistance (MDR)	79 (14%)	0

Fluroquinolone Resistance in *S.Typhi* and *Paratyphi A*

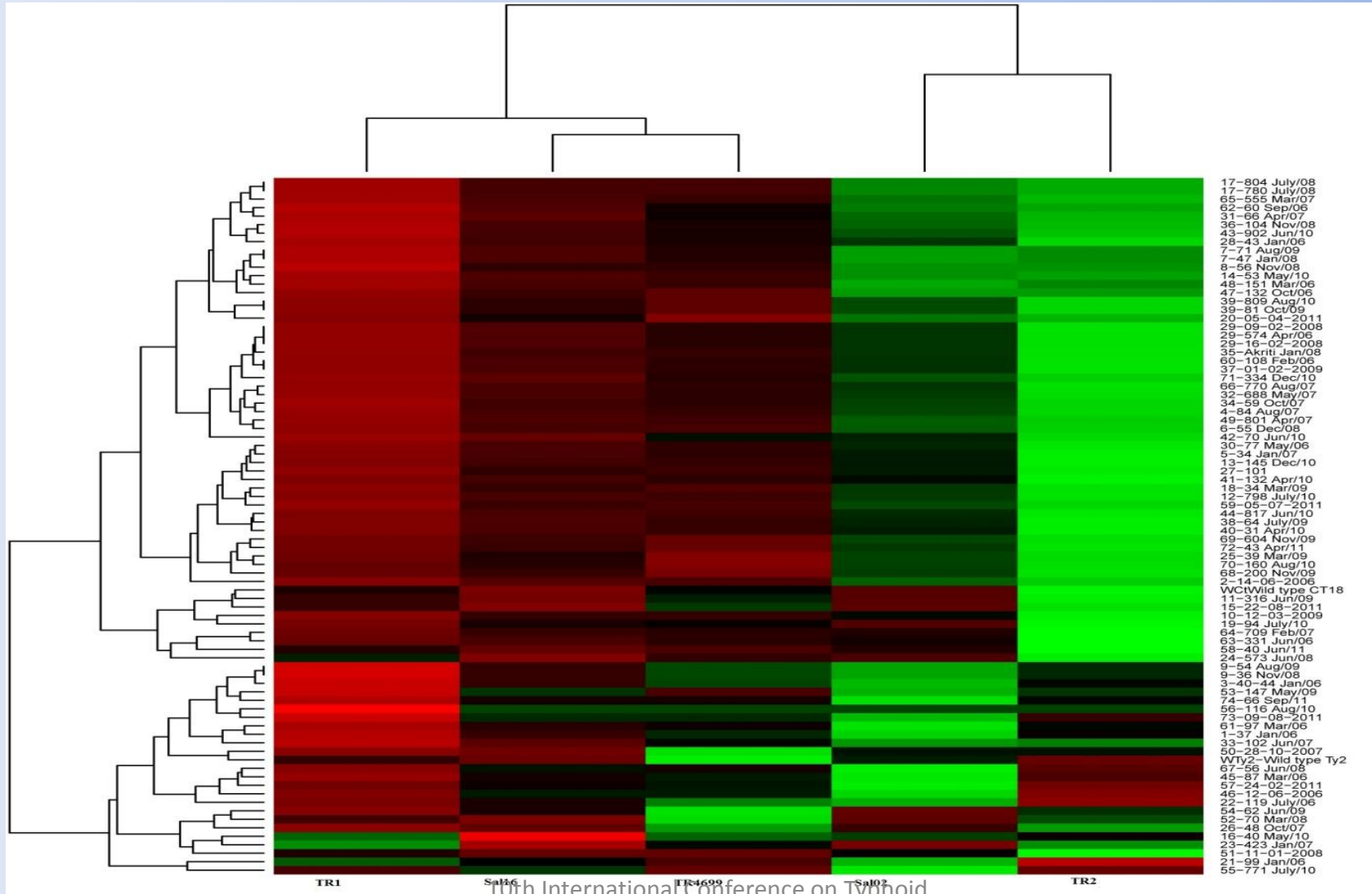
Phenotype	Site of Mutation	<i>Salmonella Typhi</i>				<i>Salmonella Paratyphi A</i>			
		Mutation		MIC Range (µg/ml)		Mutation		MIC Range (µg/ml)	
		Type	No	NAL	CIP	Type	No	NAL	CIP
NAS	<i>gyr A</i> <i>gyrB</i> <i>parC</i>	Nil	16	1.5-3	.006-0.023	Nil	3	3	0.012-0.064
NARDCS	<i>gyr A</i>	S83F/S83Y/ D87N/D87G	57	16-256	0.064-1	S83F/S83Y	40	256	0.38-1.5
NARDCS	<i>gyr A</i> <i>parC</i>	S83F S80I	3	> 256	0.38-0.5				
NAR-S CIP-DCS	<i>gyrB</i>	S83P, Asp87A S83Tyr	36	> 256	2-32				



Other Antibiotics

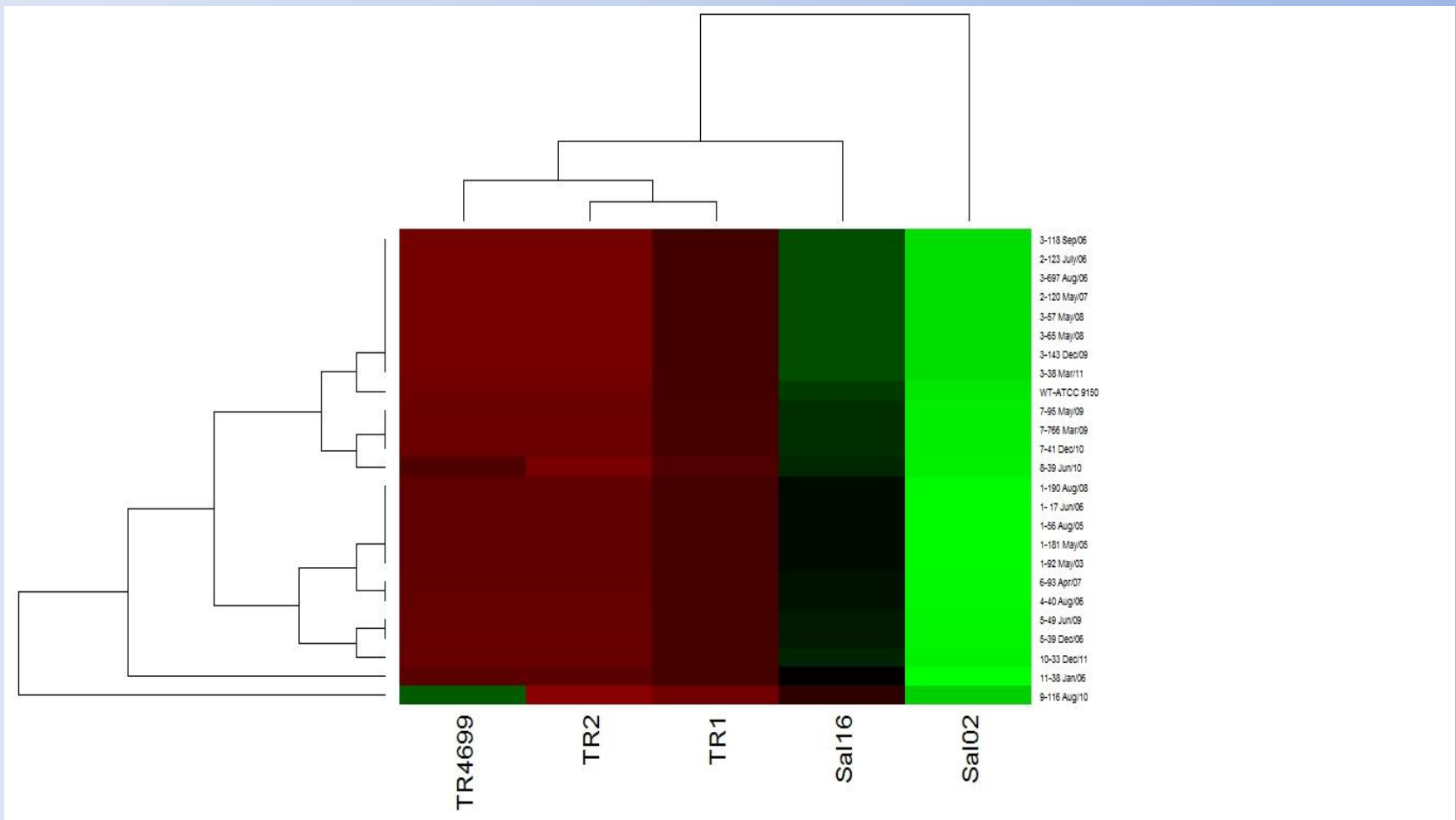
	Azithromycin (MIC $\mu\text{g/ml}$)				Ceftriazone (MIC $\mu\text{g/ml}$)			
	50	90	GM	Range	50	90	GM	Range
S Typhi	6	12	5.3	1.5-32	0.064	0.125	0.076	0.023-0.25
S Paratyphi A	8	24	10	1.5-48	0.125	0.125	0.1	0.047-0.19

VNTR-profile obtained from 82 *S. Typhi* isolates. Ty2 and CT18 *S.Typhi* were used as reference isolates. The dendrogram generated by R- software show the results of cluster analysis on the basis of copy number. The isolates are indicated by MLVA profile /identification no/month year of isolation



4/11/2017

VNTR-profile obtained from 25 *S. ParatyphiA* isolates. Ty2 and CT18 *S.Typhi* were used as reference isolates. The dendrogram generated by R-software show the results of cluster analysis on the basis of copy number. The isolates are indicated by MLVA profile /identification no/month year of isolation



Conclusion

- Epidemiology and clinical presentation of Typhoid and paratyphoid fevers are different
- *S. Paratyphi A* is declining and overall contributes to only approximately 20% of Enteric fever cases
- Antibiotic resistance patterns are different
 - The first line antibiotics can still be used
 - However resistance to fluoroquinolones is higher as 100% isolates are NAR
 - Azithromycin and Ceftriaxone MICs are higher compared to *S. Typhi*
 - Epidemiologically less diversity is seen among *S. Paratyphi A* suggesting limited clones are circulating