

Prevalence of multidrug-resistant and extensively drug-resistant *Salmonella enterica* serovars Typhi and Paratyphi in blood cultures in a tertiary care hospital

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ABSTRACT

Objective: To find out the frequency of multidrug-resistant (MDR) and extensively drug-resistant (XDR) *Salmonella enterica* serovars Typhi and Paratyphi in blood cultures in a tertiary care hospital.

Material and Methods: This prospective study was conducted at Department of Microbiology, SIUT Hospital, Karachi over a period of one year from October 30, 2020, to October 29, 2021. A required sample size was 116 patients. Blood samples were collected for culture. Pus, urine and stool specimens of those received with blood cultures were also processed accordingly. Colonies giving biochemical reactions suggestive of *Salmonellae* were confirmed serologically with specific O and H antisera (BD Laboratories). Antimicrobial susceptibilities for seven antimicrobial agents were performed. For XDR isolates, Meropenem (10µg) and Azithromycin (15µg) discs were used additionally. Descriptive statistics were calculated. Stratification was done and Post-stratification Chi-square test was applied. P-value ≤0.05 was considered as significant.

Results: There were 94.8% male and 5.2% female patients. Mean age was 21.51±12.11 years. Blood cultures alone were done for 87.9% patients. Total 72.4% of patients were *Salmonella enterica* serovars Typhi positive and 27.6% were *Salmonella enterica* serovars Paratyphi positive with 37.5% type-A, 46.9% type-B, and 15.6% type-C. Further, MDR pattern was observed in 8.6% patients, while MDR+quinolone resistance was observed in 7.8% patients and XDR resistance was observed in 61.2% patients.

Conclusion: In our study, XDR pattern was observed more as compared to MDR. Cefixime and Ceftriaxone were found sensitive to MDR. Among XDR, Azithromycin and Meropenem were found sensitive.

Keywords: Blood cultures, Enteric fever, Multi-drug resistance, *Salmonella enterica* serovar Typhi.

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INTRODUCTION

Enteric fever is a globally prevalent infection caused by *Salmonella enterica* [1]. Due to high costs of surveillance, prevention, and treatment, infections caused by this pathogen continue to impose a significant burden on both public health systems and the economy [2].

The endemic nature of enteric fever in Pakistan continues to make it a significant public health concern [3]. It is responsible for between 128 000 and 161 000 fatalities each year. Pakistan has the third highest typhoid rate of any country in the world [4].

Pakistan has been at the forefront of the emergence

of multi drug-resistant (MDR) and extensive drug-resistant (XDR) *Salmonella* Typhi, so this study holds a great deal of significance. *Salmonella* Typhi, *Salmonella* Paratyphi A and B, and in some cases, *Salmonella* Paratyphi C, are the bacteria that are responsible for enteric fever, which is a severe bacterial infection that is typically transmitted by consumption of contaminated food and drink [5].

This is owing to the fact that the abuse of antibiotics in underdeveloped countries has led to the development and spread of multidrug-resistant and extensively resistant enteric fever. According to the findings of a study that was carried out in Karachi, Pakistan, the consumption of contaminated food and the use of antibiotics that were not essential led to an increase in the number of cases of enteric fever [6]. Most of South Asia currently has a lot of multidrug-resistant (MDR) enteric fever. In India, the number of cases is up to 13%, and in Pakistan, it's up to 44% [7]. This caused Fluoroquinolones to be used a lot to treat enteric fever. According to the Asian project for surveillance of enteric fever, the fluoroquinolones resistance in Pakistan was 90% for *S. Typhi* [8].

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There is an increasing concern on a global scale regarding antibiotic resistance, which is estimated to be responsible for more than 700,000 fatalities annually across the globe. It is anticipated that antimicrobial resistance will be responsible for the loss of ten million lives by the year 2050 if suitable measures are not implemented to halt its progression [9]. Since 2016, Sindh Province, Pakistan has been experiencing a significant outbreak of extensively drug-resistant (XDR) typhoid fever (TF), which has been connected to contaminated water. This outbreak is still ongoing today [10]. Infections with XDR Typhi have been recorded all over the world among travellers who have travelled to or from Pakistan [11]. At present azithromycin is the sole oral antibiotic that is sensitive in all isolates in Pakistan but there have been reports of some strains that are resistant to azithromycin in South Asia, and there is a good likelihood that the increased usage of this azilide will also lead to an increase in the appearance of resistance to this antibiotic worldwide [12].

Consequently, the available antibiotics would consist of costly antimicrobials that are provided intravenously. These include carbapenems (imipenem-cilastatin combination, meropenem, and ertapenem) and tigecycline (aglycylcycline). The price of these medications would make them prohibitive for routine usage as first-line treatments in the treatment of typhoid fever cases in underdeveloped nations, despite the fact that they are options for treating patients in wealthy countries. We are rapidly approaching a situation in which the acquisition of one more resistance (to azithromycin) might result in a *S. Typhi* pathogen that is, in practical terms, nearly untreatable in the majority of developing countries. The outbreak of enteric fever in Pakistan, which was caused by an XDR H58 strain of *S. Typhi*, should be considered as a clear and loud message that alerted public health authorities worldwide. This would bring impoverished countries where typhoid fever is endemic back to the situation that existed prior to 1948, when around fifteen percent of cases of typhoid fever resulted in death.

Multidrug-resistant *Salmonella enterica* strains are not only difficult to treat, but they also contribute to the spread of antibiotic resistance. Furthermore, because the patterns of antibiotic resistance that they exhibit are always changing, there is a need for continuous antimicrobial sensitivity surveillance.

While XDR strains have understandably drawn global attention, MDR and other resistance phenotypes, such as quinolone resistance, continue to circulate in the community and contribute to treatment failures,

their persistence alongside XDR strains highlights the complex and evolving landscape of antimicrobial resistance in typhoidal *Salmonella*. Comprehensive local surveillance data capturing not only MDR but also other clinically relevant resistance patterns are therefore essential for guiding empirical therapy, informing public health policy, and supporting antimicrobial Stewardship efforts.

MATERIAL AND METHODS

This prospective study was conducted in the Department of Microbiology at Sindh Institute of Urology and Transplantation, over a period of one year from October 30, 2020, to October 29, 2021, following approval from the institutional ethical committee (IRB-2021-913-SIMS dated 3rd December 2019). The estimated proportion of MDR *Salmonella enterica* serovars Typhi and Paratyphi in previous studies was observed to be 62.6% [13], which was utilized to calculate an appropriate sample size. Given a 10% margin of error and a 95% confidence level, a sample size of 92 was determined. However, 116 patients were included in the study. The study utilized a non-probability consecutive sampling technique, ensuring inclusion of all eligible blood culture isolates that met the predefined selection criteria.

Blood cultures included in the study were those that tested positive for *Salmonella enterica* serovars Typhi and Paratyphi, irrespective of patient age and gender. Identification was performed using standardized microbiological methods to maintain consistency and accuracy in diagnostic procedures. Blood cultures that did not yield *Salmonella enterica* serovars Typhi or Paratyphi, multiple positive cultures from the same patient, or cultures with no bacterial growth were excluded. Pus, urine and stool specimens of those received with blood cultures were also processed accordingly.

Multidrug-resistant (MDR) *Salmonella enterica* was defined as resistant to all conventional first-line antityphoid agents, namely chloramphenicol, ampicillin, and cotrimoxazole. Quinolone resistance was determined by assessing the sensitivity to ciprofloxacin, whereas extensively drug-resistant (XDR) isolates were identified based on their resistance to first-line antityphoid agents, fluoroquinolones, and third-generation cephalosporins.

Blood samples were collected from patients and inoculated into enriched soybean-casein digest broth using BACTEC (Becton-Dickinson, New Jersey, USA) bottles. Growth detection was performed using

the automated BACTEC system. Upon positive indication, Gram staining was conducted to confirm the presence of Gram-negative bacilli, which were subsequently sub-cultured onto blood agar and MacConkey agar plates. Colonies exhibiting biochemical reactions suggestive of *Salmonella* underwent serological confirmation using specific O and H antisera (BD Laboratories).

Antimicrobial susceptibility was performed using Kirby-Bauer disk diffusion method on standard Muller-Hinton agar, with measurements strictly adhering to the Clinical and Laboratory Standards Institute (CLSI-M100, 30th edition, 2020) breakpoint zone sizes. Quality Control ATCC strains (e.g. *E.coli* ATCC 25922, *P.aeruginosa* ATCC 27853 for carbapenems, *S. aureus* ATCC 25923 for azithromycin) were used for validating antimicrobial susceptibility results. The antibiotic panel included ampicillin (10 µg), chloramphenicol (30 µg), trimethoprim/ sulfamethoxazole (1.25/23.75 µg), cefixime (5 µg), ceftriaxone (30 µg), and ciprofloxacin (5 µg), and

in cases of suspected XDR, additional disks for meropenem (10 µg) and azithromycin (15 µg) were utilized. This comprehensive approach allowed for accurate classification and facilitated comparisons with resistance profiles reported in earlier studies.

Data regarding patient demographics, isolate type, and antibiotic susceptibility profiles were meticulously recorded using structured proformas to facilitate subsequent analysis. Patient confidentiality was strictly maintained through anonymization of personal identifiers. The collected data were systematically entered and analyzed using SPSS version 22. Continuous variables such as patient ages were presented as mean and standard deviation (SD), while categorical variables including gender distribution, drug susceptibility profiles, and resistance patterns were reported as frequencies and percentages. Stratification was done with regards to gender, age, test done, organism and patient status to see the effect of these modifiers on resistance by using chi square/fisher exact test (as appropriate). A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

Among 116 patients, 110(94.8%) were male and 6(5.2%) were female. The overall mean age was 21.51 ± 12.11 years. The age was further stratified in groups. Among all study patients, blood C/S was done and among them blood C/S alone was positive in 102(87.9%) patients, however blood C/S with urine

C/S was positive for 7(6%) of patients, blood C/S with stool C/S was positive for 4(3.4%) of patients and blood C/S with pus C/S was positive for 3(2.6%) of patients. 84(72.4%) of patients were found with *Salmonella enterica* serovar Typhi and 32(27.6%) with *Salmonella enterica* serovars Paratyphi. Among patients with *Salmonella enterica* serovars Paratyphi, 12(37.5%) were found with type A, 15(46.9%) with type B, and 5(15.6%) with type C. 80(69%) were inpatients and 36(31%) were outpatients. These results are also presented in table-I.

Susceptibility pattern tabulated in table-II. (MDR+XDR). It was observed that 80 (69%) isolates were resistant to ampicillin, 73 (62.9%) to trimethoprim/ sulfamethoxazole, 82 (70.7%) to chloramphenicol, 110 (94.8%) to ciprofloxacin, 71(61.2%) to ceftriaxone, and 71(61.2%) were resistant to Cefixime.

The table-III identified a high prevalence of Extended Drug-Resistant (XDR) *Salmonella enterica* serovars Typhi and Paratyphi in blood cultures, with 71(61.2%) of isolates exhibiting resistance. Multidrug-Resistant (MDR) strains were detected in 10(8.6%) of cases, while an additional 9(7.8%) of isolates displayed resistance to both MDR-associated drugs and quinolones. Notably, 35(30.2%) of isolates were classified as non-MDR/ non-XDR, demonstrating susceptibility to standard antimicrobial regimens.

In table-IV, All MDR isolates exhibited complete resistance to Ampicillin, Trimethoprim/ Sulfamethoxazole, and Chloramphenicol, while Ciprofloxacin resistance was noted in 9(90%) of cases. However, MDR strains remained fully susceptible to third-generation cephalosporins, Ceftriaxone and Cefixime. Among XDR isolates, all were resistant to Ampicillin 71(100%), Trimethoprim/ Sulfamethoxazole 71(100%), Chloramphenicol 71(100%), and Ciprofloxacin 71(100%). Despite extensive resistance, all XDR isolates remained sensitive to Azithromycin and Meropenem, suggesting their continued effectiveness in managing such infections. MDR isolates with additional quinolone resistance showed an identical resistance pattern, with all isolates exhibiting complete resistance to Ciprofloxacin alongside Ampicillin, Trimethoprim/ Sulfamethoxazole, and Chloramphenicol. However, sensitivity to Ceftriaxone and Cefixime was preserved in all cases. Among non-MDR/ non-XDR isolates, the majority remained susceptible to Ampicillin 34(97.1%), Trimethoprim/ Sulfamethoxazole 35(100%), and Chloramphenicol 34(97.1%). However, all isolates in this group displayed resistance to Ciprofloxacin, emphasizing

the widespread quinolone resistance observed in this study. Sensitivity to third-generation cephalosporins remained intact.

The table-V showed distribution of antimicrobial resistance among *Salmonella enterica* serovars Typhi and Paratyphi isolates demonstrates notable trends across different demographic and clinical parameters. For XDR, we found significant association of resistance with test done ($p=0.001$), organism ($p=0.000$). For MDR, there was significant association of resistance with test done ($p=0.016$). For MDR+Quinolone Resistance, there was significant association of resistance with age($p=0.023$), test done ($p=0.028$) and patient status ($p=0.025$). Further it was observed that among XDR isolates, resistance was observed in 67(60.9%) of male patients and 4(66.7%) of female patients ($p=1.000$). Age-related differences revealed a higher resistance rate in the 19–35-year age group 32(69.6) compared to younger 31(58.5%) and older 8(47.1%) individuals ($p=0.229$). Resistance was significantly more prevalent in blood culture isolates 68(66.7%) ($p=0.001$) and *Salmonella enterica* serovar Typhi

isolates 67(79.8%) ($p=0.000$) compared to other culture sources and serovars.

For MDR isolates, resistance was found in 10(9.1%) of males, while no female cases exhibited MDR resistance ($p=1.000$). Age-wise distribution indicated a higher resistance rate in patients older than 35 years 4(23.5%) compared to younger individuals ($p=0.070$). Resistance was significantly associated with blood culture isolates 5(5.9%) ($p=0.016$), whereas urine 3(42.9%) and stool cultures 1(25%) had comparatively higher resistance rates. Serovar Typhi isolates exhibited a lower MDR resistance rate 5(6%) than serovar Paratyphi 5(15.6%) ($p=0.136$). In MDR isolates with additional quinolone resistance, a similar resistance trend was observed, with males exhibiting 9(8.2%) resistance rate and no resistance detected in female patients ($p=1.000$). Age-related differences showed the highest resistance in individuals older than 35 years 4(23.5%) ($p=0.023$). Blood culture isolates showed a significantly higher resistance rate ($p=0.028$), whereas serovar Paratyphi exhibited a lower resistance rate 4(12.5%) compared to serovar Typhi 5(6%) ($p=0.258$).

Table-I: Descriptive statistics of demographic and laboratory parameters.

Gender^a	
Male	110 (94.8)
Female	6 (5.2)
Age	
Age ^b	21.51±12.11
≤18 years ^a	53 (45.7)
19-35 years ^a	46 (39.6)
>35 years ^a	17 (14.7)
Test Done^a	
Blood C/S	102 (87.9)
Blood C/S + Urine C/S	7 (6)
Blood C/S + Stool C/S	4 (3.4)
Blood C/S + Pus C/S	3 (2.6)
Organism^a	
<i>Salmonella enterica</i> Serovars Typhi	84 (72.4)
<i>Salmonella enterica</i> Serovars Paratyphi	32 (27.6)
<i>Salmonella enterica</i> Serovars Paratyphi Type^a	
A	12 (37.5)
B	15 (46.9)
C	5 (15.6)
Patient Status^a	
In-Patient	80 (69)
Out-Patient	36 (31)

a= n(%) , b= (mean ± SD), SD; Standard deviation

Table-II: Frequency distribution of overall susceptibility pattern.

Antibiotics	Resistant	Sensitive
Ampicillin	80(69)	36(31)
Trimethoprim/Sulfomethoxazole	73(62.9)	43(37.1)
Chloramphenicol	82(70.7)	34(29.3)
Ciprofloxacin	110(94.8)	6(5.2)
Ceftriaxone	71(61.2)	45(38.8)
Cefixime	71(61.2)	45(38.8)
Azithromycin	-	71(61.2)
Meropenem	-	45(38.8)

Table-III: Frequency distribution of isolates resistance.

	Yes	No
Extended Drug Resistant (XDR)	71(61.2)	45(38.8)
Multidrug Resistant (MDR)	10(8.6)	106(91.4)
MDR + Quinolone Resistant	9(7.8)	107(92.2)
Non MDR+XDR	35(30.2)	81(69.8)

Table-IV: Frequency distribution of antibiotic resistance according to isolates.

	Resistant	Sensitive
FOR MDR		
Ampicillin	10(100)	0(0)
Trimethoprim/ Sulfomethoxazole	10(100)	0(0)
Chloramphenicol	10(100)	0(0)
Ciprofloxacin	9(90)	1(10)
Ceftriaxone	0(0)	10(100)
Cefixime	0(0)	10(100)
Azithromycin	NG	NG
Meropenem	NG	NG
FOR XDR		
Ampicillin	71(100)	0(0)
Trimethoprim/ Sulfomethoxazole	71(100)	0(0)
Chloramphenicol	71(100)	0(0)
Ciprofloxacin	71(100)	0(0)
Ceftriaxone	71(100)	0(0)
Cefixime	71(100)	0(0)
Azithromycin	0(0)	71(100)
Meropenem	0(0)	71(100)
MDR + QUINOLONE RESISTANT		
Ampicillin	9(100)	0(0)
Trimethoprim/ Sulfomethoxazole	9(100)	0(0)
Chloramphenicol	9(100)	0(0)
Ciprofloxacin	9(100)	0(0)
Ceftriaxone	0(0)	9(100)
Cefixime	0(0)	9(100)
Azithromycin	NG	NG
Meropenem	NG	NG
NON MDR + NON-XDR		
Ampicillin	1(2.9)	34(97.1)
Trimethoprim/ Sulfomethoxazole	0(0)	35(100)
Chloramphenicol	1(2.9)	34(97.1)
Ciprofloxacin	35(100)	0(0)
Ceftriaxone	0(0)	35(100)
Cefixime	0(0)	35(100)
Azithromycin	NG	NG
Meropenem	NG	NG

NG = Not Given

Table-V: Association of isolates of *Salmonella enterica* serovars typhi and paratyphi in blood cultures with demographic and clinical parameters.

Demographic and clinical parameters:				
	Resistant			P-value
	Yes	No	Total	
FOR XDR				
Male	67(60.9)	43(39.1)	110	1.000
Female	4(66.7)	2(33.3)	6	
≤18 years	31(58.5)	22(41.5)	53	0.229**
19-35 years	32(69.6)	14(30.4)	46	
>35 years	8(47.1)	9(52.9)	17	
Blood C/S	68(66.7)	34(33.3)	102	0.001*
Blood C/S + Urine C/S	1(14.3)	6(85.7)	7	
Blood C/S + Stool C/S	0(0)	4(100)	4	
Blood C/S + Pus C/S	2(66.7)	1(33.3)	3	
<i>Salmonella enterica</i> Serovars Typhi	67(79.8)	17(20.2)	84	0.000*
<i>Salmonella enterica</i> Serovars Paratyphi	4(12.5)	28(87.5)	32	
FOR MDR				
Male	10(9.1)	100(90.9)	110	1.000**
Female	0(0)	6(100)	6	

≤18 years	4(7.5)	49(92.5)	53	0.070**
19-35 years	2(4.3)	44(95.7)	46	
>35 years	4(23.5)	13(76.5)	17	
Blood C/S	6(5.9)	96(94.1)	102	0.016*
Blood C/S + Urine C/S	3(42.9)	4(57.1)	7	
Blood C/S + Stool C/S	1(25)	3(75)	4	
Blood C/S + Pus C/S	0(0)	3(100)	3	
<i>Salmonella enterica</i> Serovars Typhi	5(6)	79(94)	84	0.136**
<i>Salmonella enterica</i> Serovars Paratyphi	5(15.6)	27(84.4)	32	
FOR MDR+ QUINOLONE RESISTANT				
Male	9(8.2)	101(91.8)	110	1.000**
Female	0(0)	6(100)	6	
≤18 years	4(7.5)	49(92.5)	53	0.023**
19-35 years	1(2.2)	45(97.8)	46	
>35 years	4(23.5)	13(76.5)	17	
Blood C/S	6(5.9)	96(94.1)	102	0.028*
Blood C/S + Urine C/S	3(42.9)	4(57.1)	7	
Blood C/S + Stool C/S	0(0)	4(100)	4	
Blood C/S + Pus C/S	0(0)	3(100)	3	
<i>Salmonella enterica</i> Serovars Typhi	5(6)	79(94)	84	0.258**
<i>Salmonella enterica</i> Serovars Paratyphi	4(12.5)	28(87.5)	32	

Chi-square/fisher exact test was applied.

P-value less than 0.05 considered as significant.

* Significant at 0.05 level. ** Not Significant at 0.05 level.

DISCUSSION

In Pakistan, the treatment of enteric fever is significantly impacted by the high prevalence of antibiotic resistance to first-line antibiotics [14]. These drug resistances have important ramifications [8].

Nalidixic acid, in instance, had the highest resistance rate, which was 92% for *S. typhi* and 91% for *S. paratyphi*, according to the findings of a study. This indicates that it is mostly ineffectual for empirical therapy in the region. When it comes to the treatment of enteric fever, ciprofloxacin had been an essential antibiotic for a considerable amount of time. However, the high resistance rates to ciprofloxacin, which are 64 percent for *S. typhi* and 51 percent for *S. paratyphi*, are particularly alarming. As a result of the appearance of MDR and XDR strains of *Salmonella*, the entire treatment landscape has become more complicated. As opposed to XDR *S. typhi*, which was discovered in 25% of patients, MDR *S. typhi* was detected in 29% of cases investigated. There was a reduced prevalence of MDR and XDR for *S. paratyphi*, with 9% and 2%, respectively, of the cases diagnosed [8].

During the course of another trial, 25.2% of patients had positive results for *Salmonella* in their blood culture [1]. A hospital-based study that was carried, revealed 22% culture positive rate. This is comparable to the findings revealed by that study [15]. Blood culture positivity rates in febrile cases were reported to be approximately 8.5%, 5%, and 4.2%, respectively, according to data acquired from population-based studies [16].

According to the findings of a systematic review and meta-analysis, out of 10,355 confirmed instances of gastrointestinal illness, 2,719 (26.3%) of those cases reported complications. The average duration of fever was 6.90 days, with a standard deviation of 2.571 days. Fever can last anywhere from three to fourteen days, but the average length of time that fever lasts was nine days, according to a study that was carried out in India [17].

In another study, the incidence of multidrug-resistant typhoid fever was found to be 64.5%, while the incidence of XDR typhoid fever was found to be 3.2% [1]. In underdeveloped nations with inadequate resources, such as Pakistan, enteric fever caused by resistant strains is becoming an increasingly prevalent concern because of its prevalence. According to the available research, it is endemic in South-East Asian countries such as Pakistan, Nepal, Bangladesh, and India. This is widely established in the literature [18].

It is possible that the increasing number of cases of multidrug-resistant and extensively drug-resistant typhoid fever can be attributed to the irresponsible use of over-the-counter medications that are readily available, as well as, to some extent, the excessive prescription of medication by medical professionals who are not trained. The frequency of MDR in Asian countries is found to be 23%, according to research data [1]. Between January 2017 and June 2021, Karachi reported a total of 14,360 cases of XDR enteric fever, as documented in a weekly epidemiological report by the National Institute of Health (NIH) Islamabad. During the same timeframe,

Sindh recorded a total of 5,741 cases of XDR enteric, with the district of Hyderabad accounting for 69.5% of these cases, marking it as the district with the highest incidence [19].

Lahore, Pakistan, was the location of one of the investigations that found that the prevalence of XDR enteric fever was 3.2%. Based on the findings of this investigation, ciprofloxacin was shown to be resistant in 27.3% of the cases. According to findings of another research, chloramphenicol was resistant 80.6% cases [1]. This high resistance stands in contrast to the findings of previous research that was carried out in Karachi, Pakistan, which demonstrated that forty-one percent of the cases were chloramphenicol-sensitive isolates [20].

In a prior study [1], the proportion of isolates that were susceptible to ceftriaxone was 38.7%. This finding stands in contrast to the findings of another investigation from central Asia, which revealed a sensitivity of up to 100% to ceftriaxone [21]. The antibiotic azithromycin is among the most effective oral medications for treating enteric fever. It continues to be the only oral antibiotic that is highly efficient in treating enteric fever, and the isolates that were used in this study shown sensitivity in as much as 96.7% of the cases, while resistance was only observed in 3.3% of the isolates. Meropenem was shown to be sensitive in every single instance, and it continues to be the sole antibiotic that exhibits no signs of resistance to date [1].

Among the limitations of this study is the fact that the sample size is small and scope of this investigation was restricted to a single location. Prior to the formulation of general guidelines for the prescription of antibiotics, it is necessary to conduct further comprehensive multicentric research in addition to population-based studies.

This study highlights the need for improved sanitation, safe water practices, strict regulation of antibiotics use in agriculture and use of mass vaccination with effective typhoid conjugate vaccines especially in high-risk areas to control outbreaks.

Future plans and tackling XDR *Salmonella* focus on a multi-dimensional strategy that includes preserving the few remaining effective antibiotics, developing new therapies (like efflux pump inhibitors, drug repurposing and combination therapies and genomic surveillance) and implementing comprehensive public measures.

CONCLUSION

Our study results showed that *Salmonella enterica* serovars typhi was more prevalent as compared to

Salmonella enterica serovars paratyphi. Among paratyphi types, type-B was observed more followed by type-A and type-C. XDR was observed more compared to MDR. Cefixime and Ceftriaxone were found sensitive to MDR. Ceftriaxone, and Cefixime were found sensitive to MDR+Quinolone. While among XDR, Azithromycin and Meropenem were found sensitive.

Thus, treatment of enteric fever should be supported with antimicrobial susceptibility test mainly in patients having a history of Enteric fever infection.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHORS CONTRIBUTION

Yousra Muhammad Pervaiz: Study design, conceptualization, data curation, visualization, and writing of the original draft, final approval, accountable for all aspects of publication.

Sana Jamil: Data curation, statistical analysis, supervision, writing the original draft, and methodology, final approval, accountable for all aspects of publication.

Anoosha Jameel: Data curation, literature review, writing original draft, and methodology, final approval, accountable for all aspects of publication.

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