

# Antibiotic Sensitivity Pattern in Blood Culture Positive Typhoid Fever

Antibiotic Sensitivity in Blood Culture Positive Typhoid

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## ABSTRACT

**Objective:** To assess the antibiogram assay for the typhoid culture positive samples

**Study Design:** A observational study

**Place and Duration of Study:** This study was conducted at the Pediatric Department of Divisional Headquarters Teaching Hospital, Mirpur, Azad Kashmir from April 2022 to April 2023.

**Materials and Methods:** All the patients from both in and outdoor were enrolled in our study. The Kirby-Bauer disk diffusion technique was used to assess the antibiotic susceptibility of Salmonella isolates by using Mueller-Hinton agar. All the analysis of data was done by employing IBM SPSS version 24.

**Results:** In our study, a total of 180 children participated. The male children were 99 (55%) whereas female children were 81 (45%). Amongst the salmonella spp isolates, sensitive cases of typhoid were 16 (29.63%); cases of MDR 35 (66.67%), whereas cases of XDR were 3(5.56%). Amongst the 54 isolates of salmonella spp, 11 (20.37%) isolates were sensitive to Ampicillin while 43 (79.63%) isolates were resistant. 9 (16.67%) isolates were sensitive to Chloramphenicol whereas 45 (83.33%) isolates were resistant. Ceftriaxone was sensitive in 22 (40.74%) isolates while 32 (59.26%) isolates were resistant to Ceftriaxone. Ciprofloxacin was sensitive in 18 (33.33%) isolates while it was resistant in 36 (66.67%) isolates. Amongst the 54 isolates, Azithromycin was sensitive in 52 (96.30%) isolates while it was resistant in 2 (3.70%) isolates. Meropenem was the most efficient antibiotic in the current study. All the isolates 100% (n=54) were sensitive to Meropenem.

**Conclusion:** Our study concludes that meropenem and azithromycin are the most sensitive antibiotics against the Salmonella spp isolates. Enteric fever MDR and XDR strains are becoming more prevalent, and they have very high resistance to the most widely used antibiotics. The usage of antibiotics without prescription must be avoided, and prescribing procedures must be changed.

**Key Words:** Antibiotic sensitivity pattern; Blood culture; Typhoid fever

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## INTRODUCTION

Typhoid fever caused by *Salmonella typhi* is a potentially fatal systemic illness that mostly affects underdeveloped nations and is still a significant public health concern.<sup>1,2</sup> *Salmonella enterica* serovars Paratyphi A, B, and C are responsible for causing paratyphoid fever.<sup>3</sup> Typhoid and paratyphoid fever are both categorized as enteric fever.<sup>1</sup>

It is estimated that there are 17 million cases globally with 178,000,000 fatalities per year.<sup>4</sup> According to reports, the illness affects 1600 persons out of every 100,000 people in various regions of South Asia.<sup>1</sup> It is regrettable that Pakistan is one of the nations where this illness is persistent and has a significant disease burden. In Pakistan, the prevalence of the illness for children aged 2 to 15 is estimated to be 451.7/1000/year.<sup>5</sup>

First-line antibiotic resistance has been seen across South Asia and was associated with a number of outbreaks between the end of the 1980s and the beginning of the 1990s.<sup>6</sup> After 2010, complete fluoroquinolone resistance, including resistance to the advanced generation fluoroquinolone gatifloxacin, appeared and has been linked to persistent fever and therapeutic failures.<sup>6</sup> Fluoroquinolone-resistant *Salmonella enterica* was listed as one of the top microorganisms for the development and research on novel antibiotics by the WHO in 2017.<sup>4</sup> More than 50% of the *Salmonella typhi* in Pakistan were multidrug resistant, and 90% of the isolates of *Salmonella typhi* and *Salmonella Paratyphi* were fluoroquinolone resistant, as per data from the Surveillance for Enteric Fever in Asia Project (SEAP).<sup>6</sup>

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In uncomplicated typhoid fever, azithromycin is being regarded as a substitute medication because it has a lower risk of negative clinical outcomes, a shorter hospital stay compared to fluoroquinolones, and a lower rate of deterioration compared to ceftriaxone when used to treat enteric fever. The use of this medication, yet, is still relatively new.<sup>7</sup> Enteric fever complications and death must be prevented with appropriate and prompt antibiotic treatment. This research was conducted to look at the antibiogram assay of *Salmonella typhi* amongst the pediatric population attending a tertiary care hospital since there is very little information accessible about this issue in our setting.

## MATERIALS AND METHODS

The current study was observational study carried out at the Pediatric Department of Divisional Headquarters Teaching Hospital, Mirpur, Azad Kashmir. The duration of our study was one years from April 2022 to April 2023. Before the sampling, the study was approved by the institution ethical and research review board (IERB). The calculated sample size for the current research on the basis of WHO sample size calculator was 180. The inclusion criteria for our study were all the children of both the gender and age range of 2-12 years, diagnosed with typhoid on culture and willing to take part in this study. The exclusion criteria were all the children who were on antibiotic treatment within seven days and children whose parents/guardian were not willing to participate in the current study. Informed consent was taken from the parents/guardian of all the enrolled children.

A clinically confirmed case of enteric fever was described as having a temperature of 38 degrees Celsius or higher for 3 days or longer, as well as Gastrointestinal tract symptoms such vomiting, nausea, constipation, diarrhea, or prostration, and being typhidot IgM/IgG positive.<sup>12</sup> A suspected or likely case of MDR enteric fever is one that is "laboratorially confirmed by the isolation of *S. typhi* from blood, bone marrow, stool, urine, or any other material and is resistant to three or more first-line drugs, such as quinolones. Ampicillin chloramphenicol and trimethoprim / sulfamethoxazole are first-line medications".<sup>12</sup> It was determined that XDR enteric fever is the kind of enteric fever that is caused by strains of *S. typhi* or *S. paratyphi* A, B, or C that are resistant to all antibiotics that are indicated for treatment.<sup>12</sup> After a maximum of 7 days of the incubation period patients were considered culture-positive if their blood cultures showed growth of *Salmonella typhi* or *Paratyphi* ( $\geq 1$  colonies). All the patients from both in and outdoor were enrolled in our study.

On a pre-made questionnaire, demographic and socioeconomic information was gathered. Blood was taken immediately and sent to Excel Lab for culture and

sensitivity. Inoculation of the blood was done in 40–45 cc of brain–heart infusion broth. The incubation temperature was 37 degrees for all the blood culture samples. The Kirby-Bauer disk diffusion technique was used to assess the antibiotic susceptibility of *Salmonella* isolates by using Mueller-Hinton agar. Antimicrobial susceptibility testing was done for the antibiotics including amoxicillin, azithromycin, ampicillin, chloramphenicol, cefixime, cefotaxime, ceftriaxone, ciprofloxacin, and meropenem. To categorize the organism in either sensitive, resistant, or intermediate sensitivity group to the specific antibiotic, the diameter of the inhibitory zone of each antibiotic disc was measure for each isolate of *Salmonella* and then compared with the standard chart advised by The European Committee on Antimicrobial Susceptibility Testing.<sup>13</sup> According to the operational definition, instances of cultural positivity and sensitivity patterns were documented. All the analysis of data was done by employing IBM SPSS version 24. Variables like age were determined as mean and standard deviation while the variables like gender, antibiotic sensitivity, XDR and MDR were determined as frequency and percentages.

## RESULTS

In our study, a total of 180 children participated. The male children were 99 (55%) whereas female children were 81 (45%). (Figure 1) The mean age (SD) of the enrolled children was 9 (2.11) years. Out of 180 blood cultures, 54 (30%) blood culture were positive. Amongst 54 blood cultures, 51 (94.44%) cultures were positive for *Salmonella Typhi* while only 3 (5.56%) were positive for *S. paratyphi*. (Figure 2) Amongst the salmonella spp isolates, sensitive cases of typhoid were 16 (29.63%); cases of MDR 35 (66.67%), whereas cases of XDR were 3(5.56%). (Figure 3) Amongst the 54 isolates of salmonella spp, 11 (20.37%) isolates were sensitive to Ampicillin while 43 (79.63%) isolates were resistant. 9 (16.67%) isolates were sensitive to Chloramphenicol whereas 45 (83.33%) isolates were resistant. Amongst the 54 isolates, Cefixime was sensitive in 18 (33.34%) isolates and resistance was observed in 36(66.67%) isolates. Ceftriaxone was sensitive in 22 (40.74%) isolates while 32 (59.26%) isolates were resistant to Ceftriaxone. Trimethoprim / Sulfamethoxazole was sensitive in 14 (25.93%) isolates while resistant in 40 (74.07%) isolates. Amoxicillin was sensitive in 36 (66.67%) while resistant in 18 (33.33%) isolates. Ciprofloxacin was sensitive in 18 (33.33%) isolates while it was resistant in 36 (66.67%) isolates. Amongst the 54 isolates, Azithromycin was sensitive in 52 (96.30%) isolates while it was resistant in 2 (3.70%) isolates. Meropenem was the most efficient antibiotic in the current study. All the isolates 100% (n=54) were sensitive to Meropenem. (Table 1)

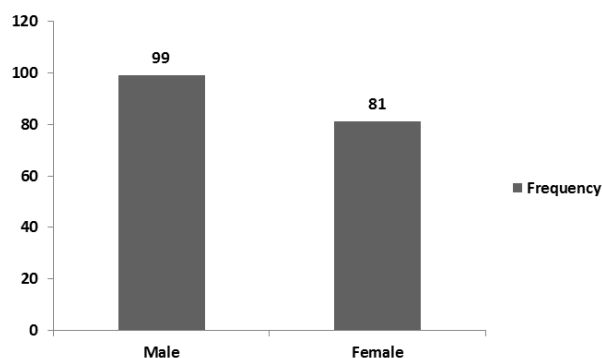


Figure No. 1: Distribution of children enrolled in the current study

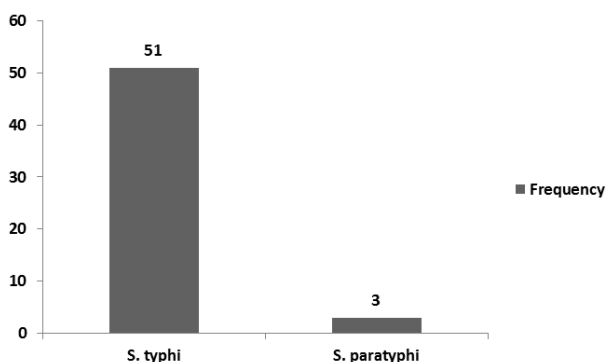


Figure No. 2: Frequency of S. typhi and S. paratyphi amongst 54 isolates

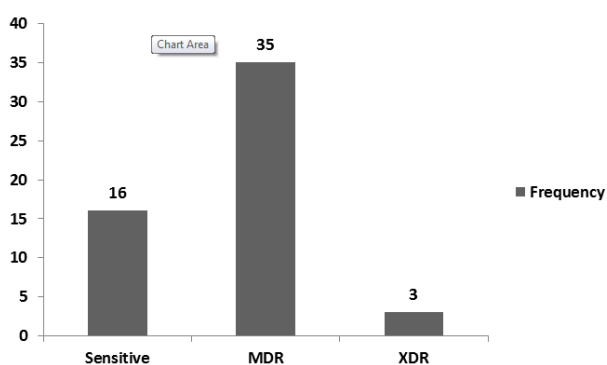


Figure No. 3: Frequency of sensitive, XDR and MDR amongst 54 isolates

Table No. 1: Antibiogram assay of salmonella isolates

Antibiotic name	Frequency of sensitive	Frequency of resistant
Ampicillin	11 (20.37%)	43 (79.63%)
Chloramphenicol	9 (16.67%)	45 (83.33%)
Cefixime	18 (33.34%)	36(66.67%)
Ceftriaxone	22 (40.74%)	32 (59.26%)
Trimethoprim / Sulfamethoxazole	14 (25.93%)	40 (74.07%)
Amoxicillin	36 (66.67%)	18 (33.33%)
Amoxicillin	18 (33.33%)	36 (66.67%)
Azithromycin	52 (96.30%)	2 (3.70%)
Meropenem	54 (100%)	00 (00%)

## DISCUSSION

Infections caused by antibiotic resistant bacteria are a major cause of medical anxiety due to the risk that they present to human health. The high rates of typhoid fever-related mortality and morbidity may be partially ascribed to drug resistance. For many years, the first-line medicines for enteric fever were fluoroquinolones and third-generation cephalosporins. However, they have often been used in human medicine without getting adequate investigation prior to use due to their wide antibacterial action, cheap cost, and ease of accessibility.<sup>8</sup> In our study, a total of 180 children participated. The male children were 99 (55%) whereas female children were 81 (45%). The mean age (SD) of the enrolled children was 9 (2.11) years. An earlier study carried out by Sumaira Hassan et al. reported comparable findings to our study. They reported male children predominance in their findings. The mean age (SD) of children in their study was 6.15 ( $\pm$  3.37) years.<sup>9</sup> Out of 180 blood cultures, 54 (30%) blood culture were positive. These findings are comparable with the study done by Mubashir A et al. who reported 25.2% culture positive cases.<sup>10</sup> Comparable findings were found in a large hospital-based research carried out in Karachi city of Pakistan, which revealed a 22% culture positive rate.<sup>11</sup>

Amongst 54 blood cultures, 51 (94.44%) cultures were positive for Salmonella Typhi while only 3 (5.56%) were positive for S. paratyphi. These findings are comparable with the study done by Mubashir A et al. who reported that 93.54% isolates were S.typhi whereas 6.46% cases were S. paratyphi.<sup>10</sup> Amongst the salmonella spp isolates, sensitive cases of typhoid were 16 (29.63%); cases of MDR 35 (66.67%), whereas cases of XDR were 3(5.56%). These findings are also similar with the findings of the Mubashir A et al. who reported 32.3% sensitive cases, 64.5% MDR cases while XDR was reported only in 3.2% cases.<sup>10</sup> In developing and resource-constrained nations like Pakistan, enteric fever brought on by resistant strains is becoming an increasingly serious issue. Its prevalence across South-East Asia, particularly Pakistan, India, Nepal, and Bangladesh is extensively reported in the literature.<sup>12</sup> Resistance to first-line antibiotics including chloramphenicol, amoxicillin and TMP/SMX has become a significant issue in recent years. The increasing number of instances of MDR and XDR typhoid may be attributed to unwise use of over-the-counter medications as well as, to some degree, excessive medicine prescriptions by unlicensed medical professionals. According to research, 23% of MDR cases are found in Asian nations. According to a research, the frequency of MDR surged from 34.2% to 48.5% between 2001 and 2006.<sup>13</sup> A total of 14,360 cases of XDR enteric fever have been documented in Karachi between January 2017 and June 2021,

according to a weekly epidemiological report by the National Institute of Health Islamabad. While, totally 5741 instances of XDR enteric were recorded across the remaining parts of Sindh over the same time period, with Hyderabad having the highest percentage of cases, 69.5 percent. Since XDR enteric is a new variant, its precise frequency is not yet mentioned in the literature. The first outbreak was documented in Karachi in November 2016.<sup>14</sup> Amongst the 54 isolates of salmonella spp, 11 (20.37%) isolates were sensitive to Ampicillin while 43 (79.63%) isolates were resistant. 9 (16.67%) isolates were sensitive to Chloramphenicol whereas 45 (83.33%) isolates were resistant. Amongst the 54 isolates, Cefixime was sensitive in 18 (33.34%) isolates and resistance was observed in 36(66.67%) isolates. Ceftriaxone was sensitive in 22 (40.74%) isolates while 32 (59.26%) isolates were resistant to Ceftriaxone. A previous research from central Asia reported 100% sensitivity of Salmonella SPP isolates to Ceftriaxone.<sup>15</sup> Trimethoprim / Sulfamethoxazole was sensitive in 14 (25.93%) isolates while resistant in 40 (74.07%) isolates. Amoxicillin was sensitive in 36 (66.67%) while resistant in 18 (33.33%) isolates. Ciprofloxacin was sensitive in 18 (33.33%) isolates while it was resistant in 36 (66.67%) isolates. Amongst the 54 isolates, Azithromycin was sensitive in 52 (96.30%) isolates while it was resistant in 2 (3.70%) isolates. Meropenem was the most efficient antibiotic in the current study. All the isolates 100% (n=54) were sensitive to Meropenem. In accordance with our study another study done previously by Mubashir A et al. reported comparable results to our findings. They also reported Azithromycin and Meropenem as the effective antibiotics against all the isolates.<sup>10</sup> The same results were found in other Pakistani research as well: in a study by Qamar et al.<sup>16</sup> 91.7% of typhoid fever patients exhibited quinolone resistance. For more than 20 years, fluoroquinolones were the choice antibiotic for treating enteric fever, but large levels of drug resistance to these medications have recently been identified from all over the globe, particularly from South Asia.<sup>17</sup> Before it's too late, it's imperative to take some significant actions to address this public health issue. Typhoid fever vaccination, proper cleanliness, halting the overuse of antibiotics, evaluating blood cultures of patients with probable typhoid fever before beginning antibiotics, and taking antibiotics for typhoid fever for a sufficient amount of time are a few actions that should be performed right away.

## CONCLUSION

Our study concludes that meropenem and azithromycin are the most sensitive antibiotics against the Salmonella spp isolates. Enteric fever MDR and XDR strains are becoming more prevalent, and they have very high resistance to the most widely used antibiotics. The usage of antibiotics without prescription must be

avoided, and prescribing procedures must be changed. We also suggest enhancing public sanitation and hygiene facilities and expanding the availability of potable water.

### Author's Contribution:

Concept & Design of Study: Ammara Manzoor  
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 Data Analysis: Jawad Khalid  
 Revisiting Critically: Ammara Manzoor,  
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**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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