



Antibiotic Resistance Patterns in Pediatric Typhoid Cases in Combined Military Hospital Peshawar

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ARTICLE INFO

Keywords: Typhoid fever, Antibiotic resistance pattern, Salmonella typhi, Children.

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Declaration

Authors' Contribution: All authors equally contributed to the study and approved the final manuscript.

Conflict of Interest: No conflict of interest.

Funding: No funding received by the authors.

Article History

Received: 19-03-2025 Revised: 06-06-2025
Accepted: 18-06-2025 Published: 30-06-2025

ABSTRACT

Background and Aim: Poor public health infrastructure and low socioeconomic indicators are the primary contributors to the prevalence of typhoid fever. Currently, Pakistan is facing the challenges of severe outbreak of typhoid fever, resulting in increased rates of illness and fatalities, particularly among the pediatric population. The aim of the current study was to investigate the antibiotic resistant patterns in pediatric typhoid cases. **Patients and Methods:** A cross-sectional study investigated 173 typhoid cases at the Department of Pediatrics, Combined Military Hospital, Peshawar from July 2024 to February 2025. Children aged 1 day to 12 years of either gender with prior history of fever and positively diagnosed typhoid fever were enrolled. A self-structured questionnaire designed for data collection such as age, gender, socioeconomic status, and drinking water status. Symptoms of typhoid fever were recorded. Blood sample taken from each children and tested for antibiotic susceptibility. Data analysis was done using SPSS version 26. **Results:** Out of 173 typhoid cases, there were 106 (61.3%) male and 67 (38.7%) female children. Salmonella typhi was identified in 156 (90.2%) of the patients, while Salmonella paratyphi was found in 17 (8.8%) of the cases. Significant determinants for the acquisition of salmonella infection included youth (68.2%), male sex (61.3%), middle to low socioeconomic status (80.9%), and the intake of untreated water (78%). Moreover, a notable prevalence of extended drug resistance found in 70.5% of the affected individuals. The majority of the isolates demonstrated sensitivity to meropenem and azithromycin, with rates of 95.8% and 94.3%, respectively. Resistance to ceftriaxone was widespread affecting various age groups: 1 day-3 years (96%), 4-7 years (90%), and 8-12 years (100%), with a notable predominance in males (57%). **Conclusion:** The probability of extended drug-resistant typhoid fever increased among children aged 1 day to 3 years, males, and individuals from lower socioeconomic backgrounds. Consumption of untreated water recognized as a significant factor contributing to this issue. It is essential to implement measures across all healthcare levels to ensure the responsible use of antibiotics.

INTRODUCTION

Typhoid fever is a common febrile disease in Pakistan, which has the second highest incidence rate globally, following India [1]. Typhoid fever is associated with paratyphoid fever, and the Salmonella typhi bacterium spreads in the blood and intestine [2]. Contaminated water or food leads to typhoid fever, presents as a viral infection with persistent fever, headache, and nausea, and abdominal pain. Approximately 10% of patients experience recurrence of symptoms after short-term improvement one to two weeks, recurrence increases with antibiotic treatment. Risk factors for this expansion include inadequate water quality, inadequate hygiene practices, and inadequate food hygiene practices [3]. In Pakistan, public health authorities are actively isolating

the typhoid fever potential cases and initiating the campaigns of anti-typhoid in majority affected zone by educational counselling, proper techniques of rinsing and washing hands, and supply of safe water and avoiding hygienic food. Furthermore, there is an urgent need to assess the immune response in isolates of anal meningitis, which is carefully investigated is urgently needed [4]. S. typhi considered as the responsible factor for majority of typhoid cases in Pakistan [5]. The use of antibiotics remains critical; however, treatment options severely limited by emerging resistance to commonly prevented drugs. Ampicillin, chloramphenicol, and trimethoprim are the three antibiotics characterizing the MDR is widespread in Pakistan [6]. Earlier study reported increase antibiotic resistance like ciprofloxacin in Pakistan. There is a

worrying increase in antibiotic resistance, especially with the emergence of MDR strains of Salmonella [7].

An earlier research study involving 452 children with a history of fever persisting for more than a week and confirmed positive blood cultures for Salmonella typhi or S. paratyphi indicated a notable resistance to ceftriaxone, fluoroquinolones, ampicillin, and chloramphenicol. The anticipated resistance rate for ampicillin among Salmonella species reported to be 87.1% [8]. The cultures revealed S. Typhi in 164 patients (92.1%) and S. Paratyphi in 14 patients (7.9%). The highest resistance observed with nalidixic acid at 96.4%, followed by sulphamethoxazole at 65.5%. Conversely, azithromycin showed no resistance (0%), while imipenem (1.8%), piperacillin-tazobactam (1.9%), and meropenem (2%) had minimal resistance. Additionally, minocycline, classified as a tetracycline, exhibited low resistance (12.6%) and prescribed for children [9].

Prior research conducted in Pakistan has indicated a growing resistance to Ciprofloxacin. The prevalence of antibiotic resistance is escalating, particularly with the emergence of multidrug-resistant (MDR) strains of Salmonella. This phenomenon poses a significant challenge to infection control, and our study aims to enhance the understanding of this microbial characteristic. While there have been a limited number of studies focusing on antibiotic resistance in Salmonella among adults in Islamabad and northern Punjab, there has yet to be any investigation into this issue in children. Consequently, the current study initiated to assess antimicrobial drug resistance in typhoid cases at CMH Peshawar.

METHODOLOGY

A cross-sectional study investigated 173 typhoid cases Department of Pediatrics, Combined Military Hospital, Peshawar from July 2024 to February 2025. The study included children from 1 day to 12 years of age, of any gender, who had a fever persisting for over one week and confirmed to have Salmonella typhi or S. paratyphi through positive blood cultures. Conversely, children showing signs of typhoid fever but with negative blood culture results, along with those diagnosed with other infections, were excluded. The sample size (n=173) calculation was done using Open-Epi sample size calculator by taking confidence interval 95%, margin of error 5%, and anticipated proportion of ampicillin resistance against Salmonella species⁸ 87.1%. A self-structured questionnaire designed for data collection such as age, gender, socioeconomic status, and drinking water status. Symptoms of typhoid fever were recorded. Blood sample taken from each children and tested for antibiotic susceptibility.

SPSS version 26 used for data analysis. Quantitative variables expressed as Mean \pm SD or Median (IQR) after checking for normality of data by Shapiro-Wilk test. Qualitative variables such as gender, age groups, Salmonella species, and resistance to antibiotics presented as frequencies and percentages. The effect modifiers including age, gender, and antibiotic resistance pattern controlled by stratification. $P \leq 0.01$ considered statistically significant.

RESULTS

Out of 173 typhoid cases, there were 106 (61.3%) male and 67 (38.7%) female children. Salmonella typhi was identified in 156 (90.2%) of the patients, while Salmonella paratyphi was found in 17 (8.8%) of the cases. Significant determinants for the acquisition of salmonella infection included youth (68.2%), male sex (61.3%), middle to low socioeconomic status (80.9%), and the intake of untreated water (78%). Moreover, a notable prevalence of extended drug resistance found in 70.5% of the affected individuals. The majority of the isolates demonstrated sensitivity to meropenem and azithromycin, with rates of 95.8% and 94.3%, respectively. Resistance to ceftriaxone was widespread affecting various age groups: 1 day-3 years (96%), 4-7 years (90%), and 8-12 years (100%), with a notable predominance in males (57%). Children distribution in different age groups were as follows; 84 (48.6%) 1 day to 3 years, 48 (27.7%) 4-7 years, and 41 (23.7%) 8-12 years as shown in Table 1. Types of water consumed by children depicted in Table 2. Fever for three days, tongue coating, Hepatomegaly, vomiting and abdominal pain were the major symptoms as illustrated in Figure 1. Resistance patterns of first line drugs illustrated in Figure 2. Figure 3 depicts the isolated Salmonella typhi and Salmonella paratyphi among investigated children.

Table 1

Demographic Details of Children (N=173)

Variables	Value [N (%)]	
Age (years)	3.48 \pm 1.2	
Age groups (years)	1 day to 3 years	84 (48.6%)
	4-7	48 (27.7%)
	8-12	41 (23.7%)
Gender	Male	106 (61.3%)
	Female	67 (38.7%)

Table 2

Water Consumed by Children (N=173)

Types of water	N (%)
Boiled	60 (34.7%)
Filtered	53 (30.6%)
Line	60 (34.7%)
Total	173 (100%)

Figure 1

Symptoms (N=173)

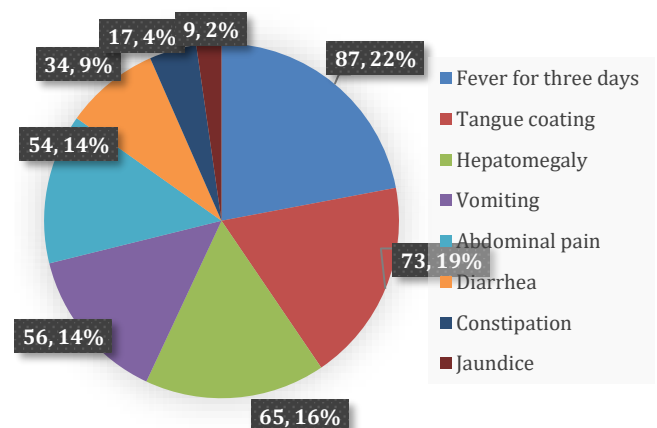


Figure 2
Resistance Pattern of First Line Drugs

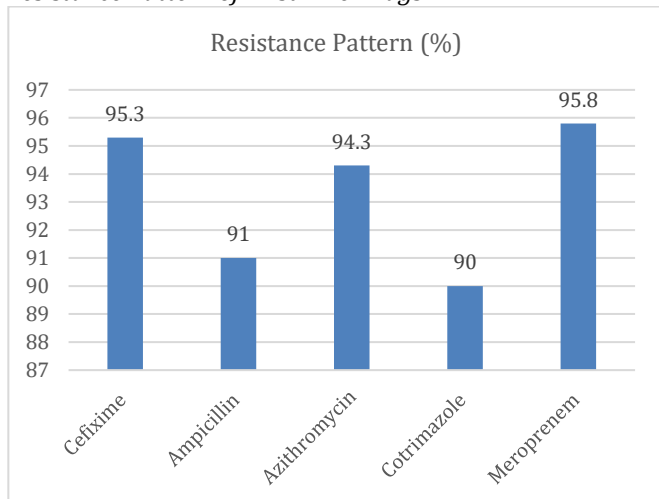
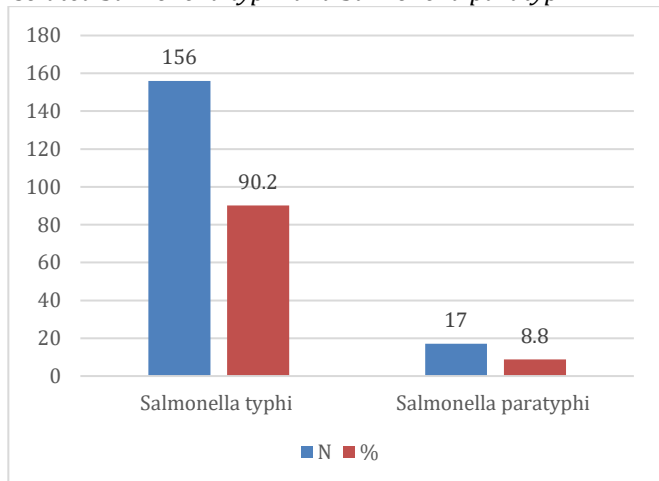


Figure 3
Isolated *Salmonella typhi* and *Salmonella paratyphi*



DISCUSSION

The present study mainly focused on the antibiotic resistance patterns in pediatric typhoid cases and reported that children aged 1 day to 3 years, males, and individuals from lower socioeconomic strata face a greater risk of acquiring extended drug-resistant typhoid fever. The consumption of untreated water is a key factor associated with this health concern. This study revealed a concerning trend of antibiotic resistance in children suffering from typhoid cases. The incidence of enteric fever was notably higher among children (1 day-3 years). A comparable outcome reported in an earlier study [10]. The inadequate dietary practices and increased contaminated food exposure especially among younger results typhoid cases. In this study, typhoid was mainly associated with male individual, tap water consumers, and eating food outside their homes. Previous study identified similar risk factors [11].

A previous study indicated that 92% of ceftriaxone-resistant cases in children under 15 years old documented over the course of one year. In contrast, our research

identified 122 cases (70.5%) of typhoid fever within a six-month timeframe [12]. Prior research conducted in Karachi reported a 96% resistance rate to ceftriaxone among the pediatric population. In children aged 1 day to 3 years, we observed a high incidence of 68.2%, compared to 56% reported in children under 5 years, aligning with findings from studies conducted in Asia [13-15]. Children are particularly susceptible to developing resistance due to their weaker immune responses, the prevalence of empirical treatments, and increased interactions with healthcare providers. Consistent with findings from other regions of the subcontinent, including India, China, Bangladesh, and various areas of Pakistan, a higher prevalence of extended drug-resistant typhoid fever among males [16-20].

Conversely, our observations, along with various reports from other regions of the province, indicate a notable shift in the sensitivity of *Salmonella* towards azithromycin and meropenem, which raises significant concerns [21]. In Pakistan, where antibiotics often misused due to the availability of over-the-counter medications without prescriptions, or where presumed typhoid fever treated with broad-spectrum antibiotics without conducting necessary diagnostic tests like blood cultures, comprehensive treatment for typhoid cases are essential [22].

Children under the age of five, who primarily rely on their parents or caregivers for their needs, represent the most affected demographic group. Therefore, it is essential for healthcare providers to prioritize educating parents and caregivers about the risk factors associated with this serious illness. Research indicates that immunization against typhoid can significantly alleviate the burden of disease, particularly when administered to high-risk age groups in specific geographic locations [23]. Furthermore, vaccination not only diminishes the prevalence of circulating multidrug-resistant strains but also lowers the occurrence of undifferentiated febrile illnesses, which in turn reduces the necessity for empirical antimicrobial treatments [24]. The prevalence of *S. Paratyphi* isolates in our research found to be lower than that reported in other investigations, a variation that can be attributed to regional disparities [24, 25]. Consistent with studies, the resistance to amoxicillin was less pronounced compared to that of ceftriaxone and other first-line antibiotics [24, 25].

CONCLUSION

Children aged 1 day to 3 years, males, and individuals from lower socioeconomic strata face a greater risk of acquiring extended drug-resistant typhoid fever. The consumption of untreated water is a key factor associated with this health concern. This study's findings have the potential to assist pediatricians in the proper management of typhoid cases and in choosing the right antibiotics. Furthermore, they add to the expanding knowledge base on drug resistance and can bolster efforts to mitigate the spread of typhoid.

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