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Antibiotic sensitivity pattern of typhoid fever - experience from a tertiary care hospital in Bangladesh

Ishrat Jahan[1], Jesmin Akter Mitu[2], Mehdi Pervez[3], Sanjib Kundu[4], Maruf Hossain[2], Sheikh Anisul Haque[5]

[1]Department of Pediatrics, Bangladesh Shishu Hospital and Institute, Dhaka, Bangladesh, [2]Department of Pediatrics and Neonatology, Bangladesh Specialized Hospital, Dhaka, Bangladesh, [3]Pediatrics (in situ), 250 Bed General Hospital, Barguna, Bangladesh, [4]Neonatal Intensive Care Unit, Bangladesh Specialized Hospital, Dhaka, Bangladesh, [5]Department of Transfusion Medicine, Bangladesh Specialized Hospital, Dhaka, Bangladesh

Address for correspondence: Ishrat Jahan, Professor, Department of Pediatrics, Bangladesh Shishu Hospital and Institute, Dhaka, Bangladesh E-mail: ishratdr@gmail.com

Abstract

Background: Typhoid fever remains a significant pediatric health burden in Bangladesh, compounded by rising antimicrobial resistance. This study aimed to describe the demographic, clinical, and antimicrobial susceptibility patterns of *Salmonella* Typhi isolates in pediatric patients at a tertiary care hospital in Dhaka.

Methods: A retrospective review was conducted of 155 culture-confirmed pediatric typhoid cases from January to December 2024. Demographic, clinical, and microbiological data were analyzed using the Statistical Package for the Social Sciences v25.

Results: Most cases occurred in children aged 9–12 years (50.3%) and 5–8 years (40.0%), with a male predominance (58.1%) and urban residence (67.7%). Resistance to first-line agents was high: Ampicillin (62.6%), chloramphenicol (59.3%), and trimethoprim-sulfamethoxazole (54.9%). Fluoroquinolone (FQ) non-susceptibility was present in 54.8% of isolates. In contrast, susceptibility to ceftriaxone (95.6%), cefixime (93.4%), azithromycin (92.3%), and meropenem (100%) remained high. Multidrug resistance was noted in 29.0% of cases, with rare extensively drug-resistance isolates (1.3%). Median time to defervescence was 5 days, with a mean hospital stay of 7.4 ± 2.8 days, and in-hospital mortality was 0.7%.

Conclusion: Pediatric typhoid fever in Bangladesh continues to exhibit high resistance to first-line agents and substantial FQ non-susceptibility, underscoring the importance of updated empirical therapy guidelines and rigorous surveillance.

Keywords: Antimicrobial resistance, Bangladesh, ceftriaxone, pediatrics, typhoid fever

Introduction

Typhoid fever remains a major global public health concern, particularly in low- and middle-income countries (LMICs), where the disease continues to cause significant morbidity and mortality despite advances in sanitation, vaccination, and antimicrobial therapy. Globally, it is estimated that between 11 and 20 million cases occur annually, leading to approximately 150,000 deaths, with the majority of cases caused by *Salmonella enterica* serovars Typhi and Paratyphi.[1] Systematic global reviews have confirmed that *Salmonella* Typhi accounts for nearly three-quarters of all enteric fever cases, underscoring its central role in the ongoing disease burden.[2,3] While typhoid fever

has declined in some regions due to improved infrastructure and vaccination programs, it remains entrenched in endemic zones across South Asia and Sub-Saharan Africa, perpetuating a cycle of recurrent infections and resistance-driven treatment challenges.[4,5] Children and adolescents, in particular, constitute a disproportionately high-risk group, reflecting both increased exposure to unsafe water and food and the limited reach of preventive strategies.[6]

The burden of typhoid fever in South Asia is especially profound, with Bangladesh consistently reporting among the highest incidence rates worldwide. Population-based surveillance studies, including the surveillance for enteric fever in Asia project (SEAP), demonstrated that adjusted incidence rates in urban Bangladesh exceeded 200 cases per 100,000 person-years, highlighting the intense transmission pressure in densely populated areas.[7] Data from SEAP II further revealed that more than half of all confirmed enteric fever cases across South Asia originated from Bangladesh, reflecting both the endemicity and the concentration of clinical research capacity in Dhaka through icddr,b and affiliated hospitals.[8] Hospital-based studies in Dhaka have consistently shown that children represent the majority of hospitalized enteric fever patients, underscoring the vulnerability of younger age groups to both infection and its complications.[9] These findings align with prior prospective surveillance conducted by icddr,b, which confirmed typhoid as a persistent cause of febrile illness in Bangladesh despite national improvements in cholera control and diarrheal disease prevention.[10]

Parallel to the high incidence burden, the rise of antimicrobial resistance (AMR) among typhoidal *Salmonella* has emerged as a major public health crisis. Historically, first-line agents, such as chloramphenicol, ampicillin, and trimethoprim-sulfamethoxazole (TMP-SMX) were effective for decades; however, their efficacy has been undermined by widespread misuse and over-the-counter availability, leading to the emergence of multidrug-resistant (MDR) strains across South Asia.[11] More recently, reduced susceptibility to fluoroquinolones (FQ), once the mainstay of empirical therapy, has become widespread, rendering these agents unreliable for clinical management.[8] Alarmingly, reports from Bangladesh have documented increasing azithromycin resistance, raising concerns about the potential loss of one of the last remaining effective oral therapies.[9] Genomic surveillance has further confirmed the regional and intercontinental spread of these resistant strains, with resistant *Salmonella* Typhi lineages moving between South Asian countries, amplifying the risk of outbreaks that are difficult to treat.[12] Such resistance trends underscore the fragility of the current treatment arsenal, where ceftriaxone and azithromycin remain as key therapeutic options, but both face the growing threat of declining susceptibility.[13]

The clinical and public health implications of these evolving resistance patterns are profound. In Bangladesh, delayed initiation of effective therapy due to empirical treatment failures has been associated with prolonged hospital stays, increased healthcare costs, and worse patient outcomes.[14] A cost-of-illness study within the SEAP project found that treatment of typhoid cases placed a substantial economic burden on both households and health systems, particularly when resistant infections required prolonged or alternative therapies.[15] Globally, systematic reviews have shown that patients infected with resistant *Salmonella* Typhi strains have significantly higher risks of treatment failure, complications, and mortality, compared to those with susceptible infections.[11] The economic consequences are equally concerning, with resistant infections linked to longer hospitalizations and increased antibiotic expenditures, straining already overburdened healthcare infrastructures in LMICs.[16] The clinical challenge is exacerbated by the limited pipeline of new antimicrobials for enteric fever, meaning that treatment strategies rely heavily on preserving the efficacy of existing drugs.

In this context, continuous local surveillance of antibiotic sensitivity patterns is essential to guide

empirical therapy, inform treatment guidelines, and shape public health policies. Despite several multicenter studies, there remains a critical need for hospital-based research from Bangladesh to provide real-time data on resistance trends in clinical isolates. Such evidence is vital not only for clinical decision-making but also for national antibiotic stewardship initiatives and global strategies aimed at controlling the spread of resistant *Salmonella* Typhi. Therefore, this study aims to evaluate the antibiotic sensitivity patterns of *Salmonella* isolates obtained from patients diagnosed with typhoid fever at a tertiary care hospital in Bangladesh, thereby contributing updated, locally relevant data to strengthen evidence-based management of this persistent and evolving public health challenge.

Methods

This study employed a retrospective observational design and was conducted at Bangladesh Specialized Hospital, Dhaka, Bangladesh, over a period of 1 year, from January to December 2024. The primary objective was to analyze the antibiotic sensitivity patterns of *Salmonella enterica* serovar Typhi isolated from patients diagnosed with typhoid fever at the hospital.

Data were retrieved from the hospital microbiology laboratory records and patient medical charts. The dataset comprised a total of 155 culture-confirmed *Salmonella* Typhi cases, collected between 2019 and 2023, to ensure adequate sample size and statistical power for the analysis. Only records with complete demographic, clinical, and microbiological data were included in the study. Cases with incomplete records, those diagnosed as ectopic fever, and those identified as *Salmonella* Paratyphi A or other non-Typhi *Salmonella* isolates were excluded from the analysis to maintain focus on *Salmonella* Typhi resistance trends.

Laboratory confirmation of *Salmonella* Typhi was performed according to standard microbiological techniques, including blood culture and biochemical identification using automated and manual methods available in the hospital's microbiology department. Antibiotic susceptibility testing was conducted using the Kirby-Bauer disk diffusion method following Clinical and Laboratory Standards Institute (CLSI) guidelines. Antibiotics tested included first-line agents (chloramphenicol, ampicillin, TMP-SMX), FQ (ciprofloxacin, ofloxacin), third-generation cephalosporins (ceftriaxone, cefixime), and azithromycin, as per institutional protocols. The zone diameters were interpreted in accordance with CLSI performance standards current at the time of each test to ensure accuracy and comparability of results over the years.

All collected data were anonymized to protect patient confidentiality before analysis. Statistical analyses were performed using the Statistical Package for the Social Sciences version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize demographic data and frequency distributions of antibiotic susceptibility. Categorical variables were expressed as frequencies and percentages. Temporal trends in antibiotic resistance patterns across the years were evaluated to observe any significant changes in sensitivity profiles. Where appropriate, Chi-square tests were used to assess associations between categorical variables, with a $P < 0.05$ considered statistically significant.

Ethical approval for the study was obtained from the Institutional Review Board of Bangladesh Specialized Hospital, with a waiver of informed consent due to the retrospective nature of the study and the use of anonymized secondary data. The study was conducted in compliance with the principles of the Declaration of Helsinki for medical research involving human subjects.

Results

Among the 155 pediatric patients with culture-confirmed *Salmonella* Typhi infection, the largest age group was 9–12 years ($n = 78$, 50.3%), followed by 5–8 years ($n = 62$, 40.0%) and children younger

than 5 years (n = 15, 9.7%). Males comprised a slight majority of cases (n = 90, 58.1%) compared with females (n = 65, 41.9%). Most patients resided in urban areas (n = 105, 67.7%), while 32.3% (n = 50) were from rural regions. In terms of socioeconomic distribution, the middle-class group predominated (n = 120, 77.4%), followed by the low economic class (n = 25, 16.1%), and a smaller proportion from the upper-middle class (n = 10, 6.5%). Regarding recent medication history, 29.0% (n = 45) of patients had a history of antibiotic use within 72 h before hospital presentation, while the majority (71.0%, n = 110) had no prior antibiotic exposure [Table 1].

Among the 155 pediatric patients, the duration of fever before hospital admission was 8–14 days in the largest proportion (n = 65, 41.9%), followed by more than 14 days in 47 cases (30.3%) and 7 days or less in 43 cases (27.7%). The most frequent clinical feature was abdominal pain, reported in 126 patients (81.3%), followed by diarrhea in 72 patients (46.5%) and vomiting in 64 patients (41.3%). Hepatomegaly was documented in 52 children (33.6%). Severe complications were rare, with gastrointestinal bleeding in 2 patients (1.3%), intestinal perforation in 1 patient (0.7%), and neurologic complications in 1 patient (0.7%). No cases of shock were recorded in this cohort [Table 2].

The yearly distribution of culture-confirmed *Salmonella* Typhi isolates demonstrated relatively consistent numbers across the 5 years of surveillance. In 2019, there were 24 isolates (15.2%), increasing slightly to 29 (19.0%) in 2020 and 34 (21.9%) in 2021. The highest number was observed in 2022, with 35 isolates (22.9%), followed by 33 cases (21.3%) in 2023. Overall, the data indicate a steady burden of confirmed pediatric typhoid cases over the 5-year period [Table 3].

Among the 155 *Salmonella* Typhi isolates, meropenem demonstrated 100% susceptibility (n = 155, 100.0%) with no intermediate or resistant isolates detected. High susceptibility was also observed for ceftriaxone (n = 148, 95.6%) and cefixime (n = 145, 93.4%), with resistance noted in only 7 (4.4%) and 10 (6.6%) isolates, respectively. Azithromycin retained high activity, with 143 isolates (92.3%) sensitive and 12 isolates (7.7%) resistant. In contrast, marked resistance was observed to first-line antibiotics. Ampicillin showed sensitivity in only 58 isolates (37.4%), with resistance in 97 isolates (62.6%). Chloramphenicol susceptibility was 40.7% (n = 63), with 59.3% (n = 92) resistant, and TMP-SMX was sensitive in 45.1% (n = 70) and resistant in 54.9% (n = 85). Ciprofloxacin exhibited a mixed pattern, with 45.1% (n = 70) sensitive, 9.9% (n = 15) intermediate, and 45.1% (n = 70) resistant isolates [Table 4].

Among the 155 *Salmonella* Typhi isolates, MDR – defined as concurrent resistance to ampicillin, chloramphenicol, and TMP-SMX – was observed in 45 isolates (29.0%). FQ non-susceptibility was the most common resistance phenotype, present in 85 isolates (54.8%). Extensively drug-resistant (XDR) strains, characterized by resistance to first-line agents, FQ, and third-generation cephalosporins, were identified in 2 isolates (1.3%), indicating that while rare, XDR *Salmonella* Typhi is present in this cohort [Table 5].

Among the 155 pediatric typhoid cases, the most common empiric therapy administered was ceftriaxone, used in 100 patients (64.5%), followed by azithromycin in 29 patients (18.7%), combination regimens in 12 patients (7.7%), and other antibiotic choices in 14 patients (9.0%). For definitive therapy, ceftriaxone remained the predominant agent (61.3%, n = 95), while azithromycin was used in 40 patients (25.8%). Therapy adjustments based on culture and sensitivity results occurred in 13 patients (8.4%), whereas the majority (65.8%, n = 102) continued their initial empiric regimen. The median time to defervescence following initiation of treatment was 5 days (interquartile range [IQR]: 3–7 days), and the mean length of hospital stay was 7.4 ± 2.8 days. Regarding clinical outcomes, in-hospital mortality was low, recorded in one patient (0.7%). Relapse within 30 days was observed in five patients (3.2%),

Table 1: Demographic and baseline characteristics of pediatric typhoid cases (*n*=155)

Variables	*n*	Percentage
Age		
<5 year	15	9.68
5–8 years	62	40.00
9–12 years	78	50.32
Sex		
Male	90	58.06
Female	65	41.94
Residence		
Urban	105	67.74
Rural	50	32.26
Socioeconomic status		
Low economic class	25	16.13
Middle class	120	77.42
Upper middle class	10	6.45
Prior antibiotic use (within 72 h)		
Yes	45	29.03
No	110	70.97

Table 2: Clinical presentation and complications of pediatric typhoid cases (*n*=155)

Variables	*n*	Percentage
Fever duration before admission		
≤7 days	43	27.74
8–14 days	65	41.94
>14 days	47	30.32
Other clinical features		
Abdominal pain	126	81.29
Diarrhea	72	46.45
Vomiting	64	41.29
Hepatomegaly	52	33.55
Severe complications		
Gastrointestinal bleeding	2	1.29
Intestinal perforation	1	0.65
Shock	0	0.00
Neurologic complications	1	0.65

and readmission within 30 days occurred in seven patients (4.5%) [Table 6].

Table 3: Distribution of *Salmonella* isolates (*n*=155)

Yearly distribution	*n*	Percentage
2019	24	15.2
2020	29	19
2021	34	21.9
2022	35	22.9
2023	33	21

Table 4: Antibiotic susceptibility profile of *Salmonella* Typhi isolates (*n*=155)

Antibiotic	Sensitive *n* (%)	Intermediate *n* (%)	Resistant *n* (%)
Ampicillin	58 (37.4)	–	97 (62.6)
Chloramphenicol	63 (40.7)	–	92 (59.3)
TMP-SMX	70 (45.1)	–	85 (54.9)
Ciprofloxacin	70 (45.1)	15 (9.9)	70 (45.1)
Ceftriaxone	148 (95.6)	–	7 (4.4)
Cefixime	145 (93.4)	–	10 (6.6)
Azithromycin	143 (92.3)	–	12 (7.7)
Meropenem	155 (100.0)	–	0 (0.0)

Table 5: Multidrug-resistance (MDR) and extensively-drug resistance (XDR) patterns (*n*=155)

Resistance phenotype	Frequency	Percentage
MDR (Amp+Chl+TMP-SMX R)	45	29.03
FQ non-susceptible	85	54.84
XDR	2	1.29

Discussion

This retrospective analysis of 155 pediatric cases of culture-confirmed *S. enterica* serovar Typhi infection in a tertiary care hospital in Dhaka, Bangladesh, offers a comprehensive overview of demographic distribution, clinical profiles, antimicrobial susceptibility patterns, resistance phenotypes, treatment modalities, and outcomes over a 5-year period. The findings underscore critical public health concerns around AMR in pediatric typhoid fever, while highlighting the

Table 6: Treatment patterns and clinical outcomes of pediatric typhoid cases (*n*=155)

Variables	*n*	Percentage/ median (IQR)
Empiric therapy		
Ceftriaxone	100	64.52
Azithromycin	29	18.71
Combination	12	7.74
Other	14	9.03
Definitive therapy		
Ceftriaxone	95	61.29
Azithromycin	40	25.81
Switched regimen	13	8.39
Continued initial therapy	102	65.81
Clinical outcomes		
Median time to defervescence (days)	–	5 (IQR 3–7)
Mean length of stay (days)	–	7.4±2.8
Outcomes		
In-hospital mortality	1	0.65
Relapse within 30 days	5	3.23
Readmission within 30 days	7	4.52

efficacy of current treatment protocols and the importance of continuous surveillance.

The demographic profile of affected children revealed a predominance in the 9–12-year age group (50.3%), followed by the 5–8-year cohort (40%). A male preponderance (58.1%) and a substantial urban concentration (67.7%) were also noted. These trends are consistent with regional patterns reported in Dhaka and other South Asian urban centers. For instance, a multicenter study by Qamar *et al*. under the SEAP project similarly identified higher incidence rates in school-aged children in urban settings, aligning with the age and residential trends observed in our cohort.[8] Prior antibiotic use within 72 h of admission was documented in 29%, a figure supported by Hamdulay *et al*., who highlighted the widespread unsupervised antibiotic usage as a contributor to AMR in LMICs.[17]

Clinically, the majority of children presented after more than 1 week of febrile illness, with 41.9% presenting between 8–14 days and 30.3% after 14 days. Abdominal pain (81.3%), diarrhea (46.5%), and vomiting (41.3%) were among the most frequent symptoms, while hepatomegaly was noted in one-third of cases. Severe complications, such as gastrointestinal bleeding (1.3%) and intestinal perforation (0.7%) were rare. This symptom distribution and the low rate of complications are closely aligned with findings from Nepal and India, where similar symptom prevalence and favorable outcomes have been reported in pediatric patients.[18,19]

The annual distribution of isolates remained relatively consistent across the 5-year study period, suggesting a sustained endemic burden. This steady trend reflects regional surveillance reports, such as the SEAP study, which also observed persistent incidence rates in Bangladesh over similar timeframes.[8]

A major highlight of the current study is the concerning level of resistance to first-line antibiotics. Resistance to ampicillin (62.6%), chloramphenicol (59.3%), and TMP-SMX (54.9%) was observed, with FQ resistance and intermediate susceptibility accounting for a combined 55% of isolates. These figures mirror national and regional studies. Tanmoy *et al.*, in a 24-year resistance trend analysis, similarly reported resistance rates exceeding 50% for first-line agents.[14] In addition, SEAP data indicated FQ non-susceptibility as a growing concern in South Asia.[8] These findings collectively underscore the declining reliability of older antibiotics and the urgent need for treatment reassessment.

In contrast, third-generation cephalosporins and azithromycin demonstrated high efficacy in our study: Ceftriaxone (95.6%), cefixime (93.4%), azithromycin (92.3%), and meropenem (100%). These findings are supported by multiple clinical and surveillance studies. For instance, the Cochrane review by Kuehn *et al*. reaffirmed ceftriaxone's role as a cornerstone of typhoid

therapy, while Hye *et al*. observed similarly high ceftriaxone efficacy in pediatric patients in Dhaka.[20,21] The preserved sensitivity to these agents justifies their continued use as empiric and definitive therapies, as supported by global pediatric treatment guidelines.[19]

MDR *Salmonella* Typhi strains, defined as resistance to all three first-line antibiotics, were found in 29% of cases in our cohort. FQ non-susceptibility was higher at 54.8%, while XDR isolates – resistant to first-line agents, FQ, and third-generation cephalosporins – were rare (1.3%). These figures are closely aligned with those reported by Ghurnee *et al*. and Tanmoy *et al*., who noted MDR prevalence between 25–35% and sporadic emergence of XDR strains in Bangladesh.[22,23] Although infrequent, the detection of XDR isolates warrants proactive surveillance and restriction of empiric use of cephalosporins without culture confirmation.

In terms of treatment practices, ceftriaxone was the predominant empiric (64.5%) and definitive (61.3%) therapy. Azithromycin was used in 18.7% empirically and 25.8% definitively. The median time to defervescence was 5 days (IQR 3–7), and the mean hospital stay was 7.4 ± 2.8 days. These figures compare well with those in clinical trials from South Asia, where median defervescence ranged from 4–6 days and length of stay hovered around 6–8 days.[18,24] Adjustment of treatment post-culture was necessary in 8.4% of cases, indicating the importance of microbiological guidance in managing resistant strains. Favorable clinical outcomes were observed overall, with low in-hospital mortality (0.7%) and modest relapse (3.2%) and readmission (4.5%) rates – consistent with regional treatment outcomes as reported by Memon *et al*. and Parry *et al*.[13,19]

In summary, this study reaffirms the high burden of pediatric typhoid fever in Bangladesh, coupled with alarming levels of resistance to conventional antibiotics. While newer agents, such as ceftriaxone, azithromycin, and meropenem remain effective, the detection of MDR and XDR strains highlights the pressing need for stringent antimicrobial stewardship, robust surveillance systems, and community-level education to curb inappropriate antibiotic use and mitigate the risk of further resistance evolution.

Limitations of the study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

Conclusion

This retrospective study highlights the persistent burden of pediatric typhoid fever in Bangladesh, characterized by a predominance in school-aged children and a significant urban representation. High levels of resistance to first-line agents – ampicillin, chloramphenicol, and TMP-SMX – alongside widespread FQ non-susceptibility, underline the diminishing utility of these antibiotics in routine clinical practice. The preserved susceptibility to ceftriaxone, cefixime, azithromycin, and meropenem supports their continued use as empiric and definitive therapies. The detection of rare but emerging extensively drug-resistant (*Salmonella* Typhi) isolates emphasizes the need for robust surveillance, prudent antibiotic stewardship, and region-specific treatment guidelines to prevent further escalation of resistance. Favorable clinical outcomes, with rapid defervescence, low relapse rates, and minimal mortality, reflect effective therapeutic strategies but also highlight the importance of ongoing monitoring and adaptation of treatment protocols in response to evolving resistance trends.

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Conflict of Interest

None declared.

Ethical Approval

The study was approved by the Institutional Ethics Committee.

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