Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v6i2.1551
*Biol. Clin. Sci. Res. J., Volume 6(2), **2025**: 1551*
Original Research Article

Frequency of Extensively Drug Resistant Typhoid Fever in Children Aged 4-16 Years at Pediatrics Unit of Khyber Teaching Hospital

Syeda Aminah Shah, Sabahat Amir

Department of Pediatrics, Khyber Teaching Hospital Peshawar, Pakistan
**Corresponding author`s email address:* aminahshah36@gmail.com

(Received, 02th February 2025, Accepted 25th February 2025, Published 28thFebruary 2025)

Abstract: *Extensively drug-resistant (XDR) enteric fever is a growing public health concern, particularly in pediatric populations. The increasing resistance to multiple antibiotics limits treatment options and complicates disease management. Identifying demographic and clinical factors associated with XDR enteric fever is crucial for improving early diagnosis and intervention strategies.* ***Objectives:*** *This study aimed to determine the frequency of extensively drug-resistant (XDR) enteric fever in pediatric patients and identify associated demographic and clinical factors.* ***Methodology:*** *Over six months, a cross-sectional study was conducted at Khyber Teaching Hospital, Peshawar. Children aged 4–16 years with prolonged fever (>40°C for >1 week), abdominal pain (VAS >3), and malaise were included. Diagnosis was confirmed by positive blood cultures for Salmonella enterica serovar Typhi. XDR enteric fever was defined as resistance to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, ceftriaxone, and fluoroquinolones. Consecutive non-probability sampling was used, and data were analysed using SPSS version 20.* ***Results:*** *Among 136 participants, the mean age was 9.85 ± 3.76 years, and 57.4% were male. XDR enteric fever was identified in 44.9% (n=61) of cases. Males accounted for 68.9% of XDR cases, while females represented 31.1%. Lower socioeconomic status (49.2%) and rural residence (57.4%) were significantly associated with XDR typhoid (p<0.0001). Prolonged fever duration (>15 days) was observed in 55.7% of XDR cases compared to 25.3% of non-XDR cases (p<0.0001).* ***Conclusion:*** *XDR enteric fever is prevalent among pediatric patients, particularly in males, lower socioeconomic groups, and rural residents. Prolonged fever duration is a significant risk factor.*

Keywords: Extensively drug-resistant typhoid, pediatric population, Salmonella Typhi, antibiotic resistance, risk factors

[***How to Cite:*** Shah SA, Amir S. Frequency of extensively drug resistant typhoid fever in children aged 4-16 years at the Khyber Teaching Hospital paediatrics unit. *Biol. Clin. Sci. Res. J.*, **2025;** 6(2): 16-18. doi: https://doi.org/10.54112/bcsrj.v6i2.1551

Introduction

Typhoid fever is a systemic infection resulting from Salmonella Typhi and Paratyphi, representing a significant public health challenge in developing nations (1). The outbreak tends to occur more frequently during the monsoon season, typically resulting from the contamination of water and food sources. Typhoid fever may lead to severe complications in certain patients. The issue continues to be a public health concern, with the most significant prevalence observed in children, leading to higher hospitalisation rates. Antimicrobial agents are the primary treatment to avert complications linked to typhoid fever (2).

Feces acts as the primary medium for the spread of Salmonella typhi organism (3). The gram-negative organism enters the human body by ingesting contaminated water or food. While it passes through the small intestine, it infiltrates the reticuloendothelial system and subsequently enters the bloodstream. The disease presents with a prolonged fever, accompanied by headache, diminished appetite, discomfort in the abdomen, intestinal perforation, and in some rare cases, neurological symptoms (4-6).

Each year, typhoid fever impacts 21.6 million individuals globally, leading to 216,500 fatalities, with a significant portion affecting Asia. There have been rising instances of antibiotic resistance and MDR in the Indian Subcontinent (7). S Typhi, which exhibits resistance to first-line antibiotics such as ampicillin, sulfamethoxazole, and chloramphenicol, was initially classified as multidrug-resistant. There has been a significant report of decreased susceptibility to second-line medications, such as fluoroquinolones, which have become the favored treatment for multidrug-resistant typhoid fever. Ceftriaxone and azithromycin are currently utilised to treat patients with typhoid fever who do not respond to fluoroquinolones and first-line drug therapies (8-10).

Typhoid fever, which has been traditionally managed with antibiotics like ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole, is currently encountering increasing difficulties due to the emergence of XDR strains that have markedly diminished the efficacy of these standard therapies. This study aims to determine the frequency of extensively drug resistant typhoid fever in children aged 4-16 years at the pediatrics unit of the Khyber teaching hospital. This study's findings will assist in developing improved clinical management strategies, shaping public health policies, and highlighting the necessity for enhanced surveillance and antibiotic stewardship programs to address the increasing threat in pediatric populations.

Methodology

The study aimed to determine the frequency of extensively drug-resistant (XDR) enteric fever in pediatric patients at Khyber Teaching Hospital, Peshawar. A cross-sectional design was employed, with data collected from 26-07-2024 to 26-01-2025 following ethical approval. Children aged 4–16 years presenting with prolonged fever (>40°C for >1 week), abdominal pain (VAS >3), and malaise were included. Diagnosis was confirmed by positive blood cultures for Salmonella enterica serovar Typhi. XDR enteric fever was defined as resistance to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, ceftriaxone, and fluoroquinolones.

The sample size was calculated using the WHO sample size calculator, with an anticipated XDR frequency of 54%[11], 95% confidence level, and 8.4% absolute precision, yielding 136 participants. Consecutive non-probability sampling was used. Exclusion criteria included ICU admission, severe sepsis, respiratory infections, or meningitis.

Informed consent was secured from parents or guardians. Demographic data (age, gender, weight, socioeconomic status, residence) were

recorded. Blood samples were collected aseptically and processed using the Bact/Alert automated system. Positive cultures were sub-cultured on Blood and MacConkey agar, and isolates were identified using Gram staining, biochemical tests (VITEK 2 system), and serotyping (Kauffmann and White scheme). Antibiotic susceptibility was determined using AST cards.

Data were analysed using SPSS version 20. Continuous variables (age, weight, fever duration) were summarised as mean ± SD or median (IQR), while categorical variables (gender, XDR status, residence) were expressed as frequencies and percentages. Stratification was performed for age, gender, weight, fever duration, socioeconomic status, and residence. Post-stratification analysis used chi-square or Fisher's exact tests, with significance at $p < 0.05$.

Results

The study included 136 children aged 4 to 16 years, with a mean age of 9.85 ± 3.76 years and an average weight of 33.81 ± 13.84 kg. The duration of fever among participants averaged 13.99 ± 3.70 days. Most of the cohort (55.9%, n=76) fell within the younger age bracket of 4–10 years, while 44.1% (n=60) were adolescents aged 11–16. Males constituted 57.4% (n=78) of the sample, compared to 42.6% (n=58) females. Geographically, 66.2% (n=90) resided in urban areas, and 33.8% (n=46) in rural settings. Socioeconomically, 58.8% (n=80) belonged to the middle class, followed by 22.1% (n=30) lower class and 19.1% (n=26) upper class.

Extensively drug-resistant (XDR) typhoid fever was identified in 44.9% (n=61) of cases, with the remaining 55.1% (n=75) testing negative for XDR strains. Gender disparities were evident, with males exhibiting a significantly higher prevalence of XDR typhoid (68.9% vs. 31.1% in females, p=0.01). Socioeconomic status revealed a striking disparity: 49.2% of XDR cases originated from lower-class households, contrasting sharply with the absence of XDR cases in this group among non-XDR patients (p<0.0001). Middle- and upper-class participants showed lower XDR frequencies (42.6% and 8.2%, respectively).

Residence played a critical role, as rural dwellers accounted for 57.4% of XDR cases compared to only 14.7% in non-XDR cases (p<0.0001). Urban participants, conversely, represented 42.6% of XDR cases versus 85.3% of non-XDR cases. Prolonged fever duration (>15 days) was strongly associated with XDR typhoid, observed in 55.7% of XDR-positive children against 25.3% in non-XDR cases (p<0.0001). These findings underscore the interplay of demographic, socioeconomic, and clinical factors in the epidemiology of XDR typhoid, highlighting vulnerabilities linked to rural residence, prolonged illness, and economic disadvantage. We could not find notable associations between XDR enteric fever and age and weight.

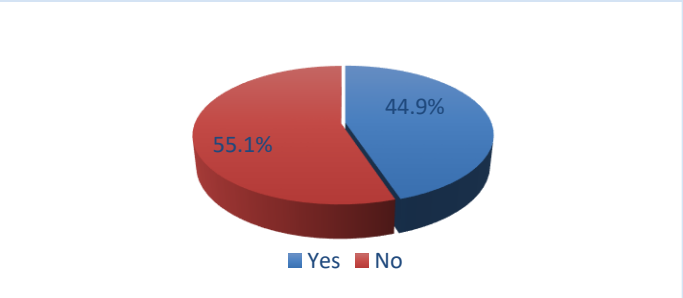

Figure 1 XDR enteric fever

Table 1 Demographic features

Demographic features		N	%
Age distribution (Years)	4 to 10	76	55.9%
	11 to 16	60	44.1%
Gender	Male	78	57.4%
	Female	58	42.6%
Residence	Urban	90	66.2%
	Rural	46	33.8%
Socioeconomic status	Lower class	30	22.1%
	Middle class	80	58.8%
	Upper class	26	19.1%

Table 2 Frequency of extensively drug resistant enteric fever

XDR typhoid fever	Frequency	Percent
Yes	61	44.9
No	75	55.1
Total	136	100.0

Table 3 Stratification of XDR enteric fever with various parameters

Parameters		Extensively drug resistant enteric fever				P value
		Yes		No		
		N	%	N	%	
Gender	Male	42	68.9%	36	48.0%	0.01
	Female	19	31.1%	39	52.0%	
Socioeconomic status	Lower class	30	49.2%	0	0.0%	0.0001
	Middle class	26	42.6%	54	72.0%	
	Upper class	5	8.2%	21	28.0%	
Residence	Urban	26	42.6%	64	85.3%	0.0001
	Rural	35	57.4%	11	14.7%	
Duration of fever (Days)	8 to 15	27	44.3%	56	74.7%	0.0001
	> 15	34	55.7%	19	25.3%	

Discussion

The emergence of extensively drug-resistant (XDR) typhoid fever among children represents a critical public health challenge, particularly in regions plagued by inadequate sanitation and limited healthcare access. This study, conducted among 136 children aged 4–16 years, revealed an XDR typhoid prevalence of 44.9%, reflecting a troubling trend of antibiotic resistance in pediatric populations. These findings align with recent reports from Pakistan, a retrospective cohort study in Karachi documented an XDR prevalence of 54% among children with typhoid fever. In comparison, another investigation was conducted on strains in 92.9% of Salmonella Typhi isolates (11,12). Though our study reports a comparatively lower prevalence, the results remain alarming, suggesting regional variations in resistance patterns or differences in healthcare-seeking behavior. Such disparities underscore the need for localised surveillance to tailor interventions effectively.

A closer examination of demographic variables reveals parallels with existing literature. The mean age of participants in this study was 9.85 ± 3.76 years, with 55.9% of the cohort aged 4–10 years. This aligns with findings from Memon et al., who identified children under eight as the most vulnerable cohort, attributing this susceptibility to behavioral factors like consumption of contaminated street food and limited hygiene

practices (13). The predominance of males (57.4%) in the current study mirrors observations from Vighio et al., where males constituted 53% of the cases (14). This gender disparity may reflect cultural norms, such as boys having greater outdoor exposure or families prioritising healthcare access for male children.

Socioeconomic status emerged as a pivotal determinant of XDR typhoid in this cohort. Nearly half (49.2%) of XDR-positive children belonged to lower-class households, compared to 42.6% from the middle class and 8.2% from the upper class. This gradient mirrors findings from Vighio et al, where low-income families faced a higher risk of XDR typhoid due to reliance on contaminated piped water and inability to afford typhoid vaccines (14). The absence of XDR cases among lower-class non-typhoid patients in our study underscores the compounding effects of poverty, where malnutrition and crowded living conditions exacerbate susceptibility to severe, resistant infections.

Geographic residence further influenced disease outcomes, with 57.4% of XDR cases residing in rural areas compared to 42.6% in urban settings. The rural predominance observed here may reflect unique challenges, such as limited access to diagnostic facilities and higher reliance on untreated groundwater.

Clinical factors, particularly fever duration, played a significant role in XDR susceptibility. Children with fever lasting >15 days constituted 55.7% of XDR cases, compared to 25.3% of non-XDR cases. This aligns with Memon et al., who identified prolonged fever as a hallmark of delayed diagnosis and inappropriate antibiotic use (13). In Pakistan, where over-the-counter antibiotic sales are rampant, extended illness often leads to self-medication with subtherapeutic doses of antimicrobials, practices that fuel resistance by applying selective pressure on bacterial populations (16).

Conclusion

In conclusion, the frequency of XDR enteric fever in our study was 44.9%, this study illuminates the multifaceted drivers of XDR typhoid in pediatric populations, emphasising the interplay of socioeconomic, geographic, and clinical factors. Tackling this crisis demands a holistic approach: scaling up vaccination coverage, improving water and sanitation infrastructure, and enforcing antibiotic stewardship. By prioritising these measures, policymakers can disrupt the cycle of resistance and safeguard the health of vulnerable children.

Declarations

Data Availability statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (IREB-571/DME/KMC)

Consent for publication

Approved

Funding

Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

SAS (Post Graduate Resident)
Manuscript drafting, Study Design, Data Acquisition, Review of Literature, Data entry, Data analysis, and Drafting article.
SA (Professor)
Critical Input, and Supervision
All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

References

1. Pitzer VE, Meiring J, Martineau FP, Watson CH, Kang G, Basnyat B, et al. The invisible burden: diagnosing and combatting typhoid fever in Asia and Africa. Clin Infect Dis. 2019; 69(5):395-401.
2. Petersiel N, Shresta S, Tamrakar R, Koju R, Madhup S, Shresta S, et al. The epidemiology of typhoid fever in Dhulikhel, Nepal: A prospective cohort study. PLoS One. 2018;13(9):e0204479
3. Crump JA. Progress in typhoid fever epidemiology. Clinical Infectious Diseases. 2019; 68(1):4-9.
4. Antillón M, Warren JL, Crawford FW, Weinberger DM, Kürüm E, Pak GD, et al. The burden of typhoid fever in low- and middle-income countries: A meta-regression approach. PLoS Negl Trop Dis. 2017; 11(2):e0005376.
5. Anwar T, Rais H, Jamil MF, Safdar S, Amir MR, Altaf A, et al. Extended drug resistance in children with typhoid fever. Professional Med J. 2020; 27(3):581-7.
6. Shahid S, Mahesar M, Ghouri N, Noreen S. A review of clinical profile, complications and antibiotic susceptibility pattern of extensively drug-resistant (XDR) Salmonella Typhi isolates in children in Karachi. Infect Dis. 2021; 21:1-9.
7. Chandane P, Gandhi A, Bowalekar S. Study of antibiotic susceptibility pattern of Salmonella typhi in children suffering from enteric fever. Ann Trop Med Int Health. 2017; 10(2).
8. Crump JA, Sjölund-Karlsson M, Gordon MA, Parry CM. Epidemiology, clinical presentation, laboratory diagnosis, antimicrobial resistance, and antimicrobial management of invasive Salmonella infections. Clin Microbiol Rev. 2015; 28(4):901-37.
9. Tack B, Vanaenrode J, Verbakel JY, Toelen J, Jacobs J. Invasive non-typhoidal Salmonella infections in sub-Saharan Africa: a systematic review on antimicrobial resistance and treatment. Medicine. 2020; 18(1):1-22.
10. Lamichhane B, Mawad AM, Saleh M, Kelley WG, Harrington PJ, Lovestad CW, et al. Salmonellosis: An Overview of Epidemiology, Pathogenesis, and Innovative Approaches to Mitigate the Antimicrobial Resistant Infections. Antibiotics. 2024; 13(1):76.
11. Batool A, Yunus N, Yaqoob AS, Lone DS, Khalid A, Ejaz HA, et al. Prevalence of Multi-Drug Resistant and Extensively Drug-Resistant Salmonella enterica Serovar Typhi Recovered from Pediatrics' Septicemia Patients in Lahore. Pak J Med Sci. 2021; 15(4):843-5.
12. Khan, M. & Tu-Zahra, F. & Gul, A. & Saleem, M.Z. & Riaz, M. & Gul, W. Extensively Drug-Resistant Salmonella enterica serovar Typhi in Pediatric population during COVID-19 Pandemic. International Journal of Infectious Diseases. 2022; 116. S4.
13. Memon H, Saeed F, Iqbal M, Saboohi E, Hanif S, Mallick AHH. Association of extensively drug-resistant Salmonella infection in children with typhoid fever. Pak J Med Sci. 2022; 38(7):1864–9.
14. Vighio A, Syed MA, Hussain I, Zia SM, Fatima M, Masood N, et al. Risk factors of extensively drug-resistant typhoid fever among children in Karachi: case-control study. JMIR Public Health Surveill. 2021; 7(5):e27276.
15. Yousafzai MT, Qamar FN, Shakoor S, Saleem K, Lohana H, Karim S, et al. Ceftriaxone-resistant Salmonella Typhi outbreak in Hyderabad city of Sindh, Pakistan: high time for the introduction of typhoid conjugate vaccine. Clin Infect Dis. 2019; 68(Suppl 1): S16 –21.
16. Qamar FN, Yousafzai MT, Khalid M, Kazi AM, Lohana H, Karim S, et al. Outbreak investigation of ceftriaxone-resistant Salmonella enterica serotype Typhi and its risk factors among the general population in Hyderabad, Pakistan: a matched case-control study. Lancet Infect Dis. 2018; 18(12):1368–76.