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Original Article

Frequency of Enteric Fever Among Children Presenting with Acute Febrile Illness at Capital Development Authority Hospital Islamabad

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ABSTRACT

Background: Enteric (typhoid/paratyphoid) fever is a common cause of acute febrile illness (AFI) in children in South Asia. The emergence of widely drug-resistant Salmonella Typhi in Pakistan makes empiric therapy more difficult, highlighting the importance of local, culture-based estimates to inform diagnostics, stewardship, and vaccination plans.

Objectives: To identify the prevalence of culture-confirmed enteric fever in children who present with AFI at a tertiary hospital in Islamabad and to evaluate the correlation with age, sex, length of fever, and weight.

Methodology: A cross sectional study was carried out in a period of six months in the Department of Paediatrics, Capital Development Authority (CDA) Hospital, Islamabad from Jan-June 2025. After obtaining ethical approval and parental consent, consecutive children aged 1 8 years with AFI (recorded temperature over 101 F during the last four days) and no antibiotic use in the last two weeks were enrolled (n=150). About 5 mL of the venous blood was cultured according to the hospital protocol (Wilson and Blair bismuth sulphite agar). Demographic and clinical information were noted. Associations were tested with χ^2 (α=0.05).

Results: Mean age was 4.6 ± 2.1 years; 54.0% were boys. Median fever duration at presentation was 5 days (IQR 4–6). Blood culture yielded *S. Typhi* in 18/150 children (12.0%; 95% CI 7.3–18.3); no *S. Paratyphi* was isolated. Culture positivity did not differ by sex (boys 12.3% vs girls 11.6%; χ^2=0.03, p=0.86) or weight tertiles (χ^2=0.39, p=0.82). By age, positivity was 7.7% (6/78) in 1–4 years versus 16.7% (12/72) in 5–8 years (χ^2=3.01, p=0.083). Fever ≥5 days was significantly associated with culture positivity (17.9% [15/84] vs 4.5% [3/66]; χ^2=6.09, p=0.014). Median time-to-positivity among confirmed cases was 36 hours (IQR 30–44). No procedure-related adverse events occurred.

Conclusions: Culture-confirmed typhoid accounted for 12% of pediatric AFI presentations at a tertiary center in Islamabad. Prolonged fever (≥5 days) significantly increased the likelihood of a positive blood culture, while sex and weight were not associated; there was a non-significant trend toward higher yield in children aged 5–8 years.

Keywords: enteric fever; typhoid; acute febrile illness; children; blood culture; *Salmonella Typhi*; antimicrobial resistance.

Introduction

In low- and middle-income nations with inadequate access to clean water and sanitary facilities, typhoid fever caused by Salmonella enterica serovar Typhi continues to pose a serious threat to children. [1,2] With episodic surges and persistent community transmission that put a strain on diagnostic and treatment pathways, South Asia bears a disproportionate burden. [3, 4] The advent and spread of extensively drug-resistant (XDR) S. Typhi in Pakistan have made empirical treatment more difficult and highlighted the necessity of accurate, timely diagnosis to maintain the efficacy of antibiotics. [5,6] Without microbiological testing, bedside discrimination is unreliable because enteric fever often manifests in children as undifferentiated acute febrile illness (AFI), which can overlap with viral syndromes, malaria, and other invasive bacterial diseases. [7–9], The bone-marrow culture, more sensitive yet not feasible in routine care, still makes the blood culture the reference standard, but with low-grade bacteremia, prior exposure to antibiotics, and inappropriate blood volumes in children with lower ages. [11–14] These limitations underline the need for context-specific data to inform empirical management and stewardship and contribute to the significant variation in reported AFI etiologies across settings. [7–9,4]

Using standardized clinical criteria and blood culture as the main diagnostic technique, we seek to ascertain the prevalence of culture-confirmed enteric (typhoid/paratyphoid) fever among children ages 1–8 who present with AFI at a tertiary hospital in Islamabad. [11–14] In the midst of XDR circulation, accurate local estimates can help improve diagnostic algorithms, guide empirical antibiotic decisions, and serve as a baseline for assessing vaccine and diagnostic interventions in Pakistan. [1–6, 15] In pediatric AFI pathways, stratified analyses by weight, age, sex, and duration of fever will further elucidate risk profiles and lower diagnostic uncertainty. [7–10,4]

Methodology

This descriptive cross-sectional study was carried out in the pediatric medicine department of the Capital Development Authority (CDA) Hospital in Islamabad for duration of six months from Jan-June 2025. Children who presented with acute febrile illness (AFI) were screened using non-probability consecutive sampling until the desired sample size of 150 participants was reached. This sample size was calculated with a 95% confidence level, a 5% margin of error, and an estimated 10.3% frequency of enteric fever. AFI was defined as a temperature recorded by thermometer, during the previous four days that was greater than 101°F. According to hospital laboratory protocol, enteric fever was defined as Salmonella enterica serovar Typhi culture-confirmed on standard media (Wilson & Blair bismuth sulphite agar) exhibiting jet-black colonies with a metallic sheen. Children of either sex between the ages of 1 and 8 who satisfied the AFI definition and had not taken antibiotics in the preceding two weeks were eligible to participate; children with a recorded medical history of diarrhea, malaria, or tuberculosis within the previous two weeks were excluded.

Following written informed consent from a parent or guardian, eligible children were enrolled one after the other after approvals by the CPSP Research Department and the institutional ethics committee; confidentiality was guaranteed and participation did not come with any additional risk or expense. Five milliliters of blood were aseptically extracted and sent to the hospital lab for blood culture; enteric fever cases were defined as those with positive cultures for S. Typhi.

The laboratory findings and clinical and demographic information (weight, age, sex, and length of fever) were recorded on a structured proforma. The data were entered and analyzed with SPSS v25.0; the qualitative variables (sex, enteric fever) were summarized into frequencies and percentages, and the quantitative variables (age, weight, and duration of fever) were summarized as the mean and the standard deviation. Stratification by age, sex, weight, and duration of fever was done to control potential effect modification. Post-stratification Chi-square tests were used to evaluate associations, with $p \leq 0.05$ taken as statistically significant.

Results

A total of 150 children presenting with acute febrile illness (AFI) were included in the study. The baseline characteristics of the study participants are summarized in Table I. More than half of the children belonged to the 1–4 years age group (n=78, 52.0%), while 72 (48.0%) were aged 5–8 years. There was a slight male predominance, with 81 (54.0%) boys and 69 (46.0%) girls. In terms of clinical presentation, 84 (56.0) children had a duration of fever 5 days and above, and 66 (44.0) children had a duration of less than 5 days. The distribution across weight categories was equal, with 50 (33.3%) children in each tertile.

Table I: Baseline Characteristics of Study Participants (n = 150)

Variable	Category	(n)	(%)
Age Group	1–4 years	78	52.0
	5–8 years	72	48.0
Sex	Boys	81	54.0
	Girls	69	46.0
Fever Duration	<5 days	66	44.0
	≥5 days	84	56.0
Weight Categories	≤12.5 kg	50	33.3
	12.6–18.0 kg	50	33.3
	>18.0 kg	50	33.3

Table II shows the distribution of culture-confirmed enteric fever by different subgroups. The total number of culture positive children was 18 out of 150 giving a frequency of (12.0%). A higher proportion of culture positivity was observed in children aged 5–8 years (16.7%) compared to those aged 1–4 years (7.7%). In terms of gender, culture positivity was similar between boys (12.3) and girls (11.6). Notably, children with fever duration ≥5 days had a markedly higher proportion of positive cultures (17.9%) compared to those with fever duration <5 days (4.5%). Culture positivity was relatively similar across weight categories, ranging from 10.0% to 14.0%.

The association between culture positivity and selected demographic and clinical variables is shown in Table 3. Fever duration was the only variable significantly associated with culture-confirmed enteric fever, with children presenting after ≥5 days of fever having a significantly higher positivity rate ($\chi^2 = 6.09$, $p = 0.014$). Although a higher proportion of cases was observed in the 5–8 years age group, the association was not statistically significant ($\chi^2 = 3.01$, $p = 0.083$). Similarly, no significant associations were found with sex ($\chi^2 = 0.03$, $p = 0.860$) or weight tertiles ($\chi^2 = 0.39$, $p = 0.820$).

Table 2: Distribution of Culture-Confirmed Enteric Fever by Subgroups (n = 150)				
Variable	Category	Total (n)	Culture Positive (n)	(%)
Age Group	1–4 years	78	6	7.7
	5–8 years	72	12	16.7
Sex	Boys	81	10	12.3
	Girls	69	8	11.6
Fever Duration	<5 days	66	3	4.5
	≥5 days	84	15	17.9
Weight Categories	≤12.5 kg	50	5	10.0
	12.6–18.0 kg	50	7	14.0
	>18.0 kg	50	6	12.0

Table III: Association of Culture Positivity with Demographic and Clinical Variables. (n = 150)				
Variable	Category	Culture Positive n (%)	χ^2	p-value
Overall		18 (12.0)		
Age Group	1–4 years	6 (7.7)	3.01	0.083
	5–8 years	12 (16.7)		
Sex	Boys	10 (12.3)	0.03	0.860
	Girls	8 (11.6)		
Fever Duration	<5 days	3 (4.5)	6.09	0.014
	≥5 days	15 (17.9)		
Weight Tertiles	≤12.5 kg	5 (10.0)	0.39	0.820
	12.6–18.0 kg	7 (14.0)		
	>18.0 kg	6 (12.0)		

Discussion

We observed a 12% frequency of culture-confirmed typhoid in this single-center cohort of children with acute febrile illness at a tertiary hospital in Islamabad. This is consistent with regional surveillance from South Asia, which shows a significant pediatric burden and sustained transmission. [16, 17] Our age-stratified signal, which shows a higher yield among children aged 5–8 as opposed to 1-4 years, is consistent with multi-country estimates that indicate increased exposure in Pakistan's early school-age strata and geographic heterogeneity. [16, 18] When clinical features are otherwise non-specific, the practical bedside heuristic of prioritizing blood cultures is provided by the significant correlation between fever duration ≥5 days and culture positivity. [19, 20] Given the dynamics of bacteremia and the performance limitations of blood culture in pediatrics, where sensitivity is heavily influenced by blood volume and previous antibiotics, this pattern is biologically conceivable. [19] Under program conditions, routine blood-culture sensitivity for typhoid is about 60%, according to meta-analytic work, highlighting the possibility of false negatives in younger children with smaller blood volumes. [19] Given the prevalence of drug-resistant Salmonella Typhi that has been reported from Pakistan, resistance-aware empirical therapy is crucial while awaiting culture results. Once susceptibilities are known, de-escalation should be initiated promptly. [21, 22] Contemporary guidance and case series favor azithromycin and, where warranted by severity or local patterns, a carbapenem for suspected XDR disease, with stewardship-driven narrowing as soon as feasible. [21, 22,23] Our results support the case for long-term typhoid conjugate vaccine (TCV) implementation at the population level. [16] Programmatic data from Karachi shows that TCV is highly effective in the real world against drug-resistant typhoid, while randomized evidence from Nepal indicates that it is highly effective against culture-confirmed disease. [16, 17] The argument for integrated strategies that combine vaccination with advancements in water, sanitation, and hygiene is further supported by modeling, which indicates that high coverage can result in significant incidence reductions in Pakistan. [18, 24] Our study has limitations, including the potential to attenuate associations and underestimate true burden due to its single-center design and reliance on an imperfect reference standard. [19]. Children who have recently been exposed to antibiotics are excluded, which improves internal validity for culture yield but may limit generalizability to outpatient settings where pre-treatment is prevalent. To enhance case identification and treatment regimens, subsequent studies in similar settings must normalize blood volumes, time-to-positivity, and next-generation diagnostics beyond culture. [19, 20] In the meantime, our evidence suggests a pragmatic strategy prioritizing culture in protracted fever, applying empiric regimens based on local resistance patterns, and expediting the adoption of TCV to reduce the morbidity of typhoid in children. [21,22,17,24]

Conclusion

The culture-confirmed typhoid included 12% of AFI cases; positivity was more prevalent when the fever lasted 5 days or more. These data can justify the priority of blood cultures in the prolonged fever and the application of the empiric therapy based on the local resistance and maintaining the TCV coverage

Limitations: Single-center, six-month window limits generalizability and seasonality assessment. Blood-culture sensitivity in children and exclusion of recent antibiotic users may underestimate true burden and real-world applicability

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