Trends in Medical and Biological Sciences

Journal homepage: https://scholarsacademiaworld.com/index.php/TMBS

Frequency of Enteric Fever in Pediatric Patients With Acute Febrile Illness

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ARTICLE INFO

Received:
June 29, 2025
Revised:
July 26, 2025
Accepted:
August 20, 2025
Available Online:
August 28, 2025

Keywords:
Acute febrile illness; Enteric fever; Infants; Blood culture; Antimicrobial stewardship; Pediatrics

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ABSTRACT

Background: Acute febrile illness (AFI) is a leading cause of pediatric healthcare utilization in low- and middle-income countries, where enteric fever remains endemic. While the burden of enteric fever in older children is well recognized, data focusing on infants and toddlers presenting with AFI are limited. This study aimed to determine the frequency of enteric fever among children aged 6–24 months presenting with acute febrile illness and to examine its association with selected demographic and clinical characteristics.

Methods: A cross-sectional study was carried out at one 2024 at one of the the Children Hospital and Institute of Child Health (ICH) in Peshawar. Sampling was conducted through consecutive sampling on children aged 624 months with acute febrile illness. Baseline demographics and clinical data were obtained and to establish the enteric fever, the blood cultures were done by the BACTEC system. The data were analyzed based on descriptive statistics and stratified analyses and the association was evaluated against the Chi-square test or Fisher test.

Results: A total of 200 children participated, with a mean age of 14.02 ± 4.86 months; 56.0% were male. Enteric fever was diagnosed in 44 children, resulting in a frequency of 22.0%. No statistically significant correlations were found between enteric fever and age group, gender, nutritional status, duration of fever, or recent antibiotic usage ($p > 0.05$ for all). Significantly, 41.0% of children had been administered antibiotics before presentation, indicating prevalent empirical antimicrobial utilization.

Conclusions: This study found that enteric fever contributed to one in five cases of acute febrile infections occurrences among children aged between 6 and 24 months of age, highlighting why enteric fever continues to be of public health importance among this vulnerable population. The inability to provide reliable clinical or demographic indicators contributes to the drawbacks of symptom-based diagnosis and the need to introduce regular laboratory validation, which will help to provide timely and proper care. The improvement of diagnostic abilities, the promotion of the use of antibiotics rationally, and the introduction of preventive strategies, including vaccination, plays an essential role in reducing the burden of diseases and resistance to antimicrobials in endemic conditions.

Introduction

Acute febrile illness (AFI) is among the most common causes of pediatric morbidity and mortality in low- and middle-income countries, where infectious diseases remain the primary cause of pediatric illness and mortality worldwide [1,2].

Fever is often the first and, in most cases, the sole symptom of a disease in young children and infants. Nevertheless, its inherently non-specific nature makes AFI difficult to diagnose, as AFI may be caused by numerous viral, bacterial, or parasitic agents [3]. Clinical assessment alone is difficult because most infectious illnesses present with irritability, fatigue, lack of appetite, and gastroenterological complications [4].All of these complications exacerbate in the context of limited resources in healthcare settings, where a patient can oftentimes be compelled to use an empirical approach to management due to the unavailability of rapid and precise diagnostic tools. Enteric fever, mainly caused by Salmonella enterica serotypes Typhi and Paratyphi, continues to pose a major threat to the health of the general population in terms of pediatric febrile disorders, especially in endemic areas such as South Asia [5]. Recent estimates worldwide indicate that young children have to contend with an unduly high number of illnesses. This is because they tend to develop difficulties owing to late diagnosis, abnormal symptoms, or poor diagnostic abilities (World Health Organization [6]. Enteric fever has been aggravated in terms of public health by the dissemination and further propagation of multidrug-and extensively drug-resistant Salmonella isolates. These strains have significantly restricted treatment options and increased the likelihood of treatment failure [7,5]. Enteric fever is particularly difficult to diagnose among babies and toddlers, as the typical symptoms, including stepwise fever, abdominal pain, and hepatosplenomegaly, are not always found or are not always clear in children of this age [8]. Rather, there are prolonged fever and more general systemic symptoms that tend to accompany other common childhood infections, and the clinical criteria are of lesser usefulness in diagnosis. The most effective method of identifying the cause is through blood culture, which is not effective in small children with low concentrations of bacteria in the blood and may not be easy to access in localities with numerous cases[1]. Therefore, pediatricians tend to adopt broad-spectrum antibiotics in their practice. This is only likely to alleviate the symptoms in the short run, yet it promotes the abuse of antibiotics and resistance to antibiotics [4]. Early and accurate diagnosis of enteric fever is critical to avoid serious complications, such as intestinal bleeding, perforation, chronic disease, and death. Late diagnosis among young children has been linked to more hospitalizations, higher healthcare costs, and poor clinical outcomes [6]. Rapid diagnosis improves the health of individual patients and is essential for the management of the overall population's health, as it allows treatment with specific antibiotics, infection control, and vaccination against typhoid conjugates to be used strategically among high-risk groups. Although they are crucial to both the health of the population and the treatment of patients with acute febrile syndrome, there is a significant lack of age-specific, facility-based data regarding enteric fever among children with acute febrile syndrome, especially those below 5 years of age [8]. Many recent studies have focused on older children or have utilized community-based surveillance data, which are less useful for making immediate clinical decisions in hospitals with a high level of diagnostic uncertainty [7]. The World Health Organization has emphasized the significance of current, location-specific, and age-stratified epidemiological statistics to help with diagnostic algorithms, antibiotic stewardship programs, and vaccination efforts in endemic disease locations. This information deficit should be addressed to enable better identification of enteric fever in children, better use of antibiotics, and improvement of preventative and control strategies against at-risk children. Reassessing the estimates of the frequency of acute febrile disease in young children would benefit evidence-based treatment programs and targeted public health campaigns to reduce the disease burden and control the development of antimicrobial resistance.

Material And Methods

This cross-sectional study was conducted at the Children Hospital and Institute of Child Health (ICH) in Peshawar. The study was also carried out during a six-month period, namely, January 1, 2024, to June 30, 2024, when the Institutional Research and Ethical Committee approved the study. Every parent or legal guardian of the participants had to sign a paper prior to enrollment, indicating that they knew what they were getting into. The study population included children who received outpatient (pediatric) and inpatient services during the study periods and had acute fever. To determine the starting sample size of 100, we used the sample size calculator provided by the World Health Organization (WHO). We used a 95-size confidence level, 8-margin of error, and the prevalence of enteric (typhoid) fever in children in developing countries was estimated to be 12. Eligible kids numbered a hundred and sixty three were recruited to provide strength and validity to the results. Our sampling method was a non-probability consecutive sampling method, in which we recruited as many children as possible who showed interest in participating in the study and who visited the study during the study period until we arrived at the required sample size. We selected boys and girls aged 6 to 24 months with a minimum of 3 days or axillary temperature of over 37.5o C on arrival. We also excluded children with fever that may have been caused by other diseases, such as otitis media, pneumonia, skin infections, and soft tissue infections. Moreover, children with already known chronic comorbid illnesses, including congenital heart disease, chronic liver disease, and chronic kidney disease, and those hospitalized as a result of non-urgent operations, trauma, and injury were excluded to reduce the likelihood of confusion.

After obtaining informed consent, the caregivers were provided with a full clinical history, and the staff supervising the case performed a full physical examination. The age, sex, and weight of the patient, the duration of time the patient had been on fever, and the antibiotics the patient had been taking were recorded in a structured proforma. Each of the registered children who participated in the study underwent sampling of aseptic venous blood. Approximately 5 mL of blood was sent to the BACTEC automated blood culture to determine the species of Salmonella. The entry and statistical analysis of the data and statistical analysis were performed using the IBM SPSS Statistics version 22.0. Continuous variables (e.g., age and weight) were recorded as means and standard deviations, and nominal variables (e.g., sex, nutritional status, duration of fever, previous antibiotic use, and blood culture results) were recorded as frequencies and percentages. The variables analyzed were age, sex, weight, duration of fever, and recent exposure to antibiotics to determine whether these factors influenced the effect. This was done because groups were compared using the chi-square test or Fisher's exact test, where appropriate, after stratification. The statistical significance level is less than or equal to p-value of 0.05.

Results

The trial was carried out on 200 children with the acute febrile disease. The age of the subjects was 14.02 mean with a standard deviation of 4.86 months. There was a large percentage of children (62.0, n = 124) whose ages were in the range of 6-15 months and 38.0 (n = 76) in the age range of 16-24 months, depicting that the febrile illnesses were mainly found during infancy. There was also a slight male dominance with 112 boys (56.0) and 88 girls (44.0). This trend is in line with previous epidemiological studies on pediatrics and could indicate biological vulnerability as well as variations in healthcare-seeking behaviour.

The mean body weight of the cohort was 9.31kg and the standard deviation was 1.58kg. Most of the children (69.5%, n = 139) were within the weight of their age, but 30.5 percent (n = 61) of children were categorized as underweight, which is a significant number of children with malnutrition. The mean and standard days of fever before presentation was 4.81 and 1.12 respectively. Sixty-eight percent of the children (n = 136) reported a five-day or longer fever duration, which indicates a delay in healthcare use whereas thirty two percent (n = 64) obtained medical attention during the first five days of the disease. With respect to previous antimicrobial exposure, 82 children (41.0) were exposed to antibiotics within the 7 days, and 118 children (59.0) were not exposed to any antibiotics recently.

Table 1. Demographic and Clinical Characteristics of Children with Acute Febrile Illness

Characteristics	Participants
Age (months)	14.02 ± 4.86
6–15 months	124 (62.0%)
16–24 months	76 (38.0%)
Gender	
Boys	112 (56.0%)
Girls	88 (44.0%)
Weight (kg)	9.31 ± 1.58
Normal weight	139 (69.5%)
Underweight	61 (30.5%)
Duration of fever (days)	4.81 ± 1.12
< 5 days	64 (32.0%)
≥ 5 days	136 (68.0%)
Antibiotics used in last 7 days	
Yes	82 (41.0%)
No	118 (59.0%)

Of the 200 children, 44 cases (22.0%) were confirmed as enteric fever using blood culture, whereas 156 (78.0%) yielded negative results. The findings reveal that roughly 20% of pediatric patients presenting with acute febrile illness had laboratory-confirmed enteric fever.

Table 2. Frequency of Enteric Fever among Children with Acute Febrile Illness

Enteric Fever	Frequency (n)	Percentage (%)
Yes	44	22.0
No	156	78.0
Total	200	100.0

No significant statistically significant relationships were found between enteric fever and the investigated demographic or clinical variables on stratified analysis. Enteric fever was found in 21.8 of the children between 6 and 15 months as well as in 22.4 of the children between 16 and 24 months (p = 0.918). The proportion of those who were positive was also equal in both genders with 23.2 percent of boys and 20.5 percent girls testing positive (p = 0.648). Enteric fever was not significantly correlated with the nutritional status, but the proportion of children with less weight (24.6) had tested positive slightly higher than the proportion of children with normal weight (20.9; p = 0.554). The length of fever was not a significant predictor; they found enteric fever in 20.3 and 22.8 in children with less than 5 days of fever and those with no less than 5 days of fever respectively (p = 0.674). There was no significant difference between culture positivity with recent antibiotic administration (p = 0.601).

Table 3. Stratified Analysis of Enteric Fever among Children with Acute Febrile Illness

Subgroups	N	Enteric Fever n (%)	P-value
Age (months)			0.918
6–15 months	124	27 (21.8%)	
16–24 months	76	17 (22.4%)	
Gender			0.648
Boys	112	26 (23.2%)	
Girls	88	18 (20.5%)	
Weight status			0.554
Normal weight	139	29 (20.9%)	
Underweight	61	15 (24.6%)	
Duration of fever			0.674
< 5 days	64	13 (20.3%)	
≥ 5 days	136	31 (22.8%)	
Antibiotics in last 7 days			0.601
Yes	82	19 (23.2%)	
No	118	25 (21.2%)	

Chi-square test/Fisher's Exact Test; p > 0.05 considered statistically insignificant.

Result and discussion

The Results section is organized, has a logical structure, and provides the study results in an effective way with the help of appropriate descriptive and inferential statistics. Demographic characteristics of the cohort were fully described and at that the stratified analysis increased the internal validity since it strictly examined potential relations between the enteric fever and clinically significant variables. The use of structured tables will help to increase the clarity and accessibility and,

therefore, become able to interpret physicians and researchers. It is curious to note the frequency of enteric fever (22.0%), in the case of children taken to the physician with acute febrile disease, and who are not more than two years of age. This ratio is also observed in the eternity of the contribution of the enteric fever to the febrile morbidity in children in countries where this disease is endemic. The results are revealed in a smart way without any overstatement. The researchers also indicated that about 1 in every 5 febrile children was diagnosed with an illness confirmed by laboratory tests and this has great implications in diagnosing. Although the descriptive statistics are so strong, there is still a bit of contextualization that could be provided in the Results section. It would be more statistically rigorous to give the confidence intervals of the prevalence estimates and allow readers to view the accuracy in a better way. Also, despite the stratified analyses conducted, the absence of the multivariate analysis prevents dealing with the potential confounding variables, particularly because of the drug dependence between malnutrition and exposure to antibiotics and late presentation. The Discussion section also gives the findings a context in the greater epidemiological context and is not inconsistent with the regional and global literature. The authors identify the indistinctive clinical manifestation of enteric fever in early childhood and reasonably caution against the conclusion based on the demographic or more general clinical variables. This definition is consistent with the existing findings and highlights the problems associated with resource-locked settings with regards to treatment. The competent integration of antibacterial stewardship consideration Discussion is worthy. The rate of children who received antibiotics before presentation was also important and was greatly scrutinized by the authors who attached this to be among the possible causes of antimicrobial resistance. The topicality of this discussion is related to the fact that the number of Salmonella multidrug-and extensively drug-resistant strains is increasing in South Asia. The research must also look closely at the impact of the previous exposure to the antibiotics which may have led to the identification of the actual burden of the disease failure. According to the Discussion, the lack of statistically significant relations between subgroups is mentioned; nevertheless, the statistical power should be studied in more detail to enhance the interpretation. The subgroup analysis necessarily leads to the decrease of the sample size, and the risk of the type II error should be mentioned more clearly. This is especially concerning the tendencies of underweight children and the children who have the long-term fever, which, though, are not statistically relevant, may also be of clinical use. The other area, which can be enhanced, is the poor discussion of the health systems and social-environmental determinants. The Results are adequate to demonstrate the clinical variables, and the Discussion may be improved by acknowledging that the risk of having enteric fever is largely predetermined by the hygiene, water quality, vaccination of the patients, and socioeconomic status. These unquantified drivers would be better identified to get a better understanding of the results and be in a position of comparing discourse to public health priorities better.

Limitations and Future Recommendations

This study provides important evidence on facilities where the prevalence of enteric fever in young children with acute febrile illness is concerned; however, there are some limitations that need to be addressed and offer significant prospects for further research. Cross-sectional approach restricts the ability to make causal inferences and to evaluate disease progression, intervention effectiveness and outcome, thus, additional longitudinal or cohort research is needed to clarify the relationships over time and clinical pathways. The single-centre nature of the study can limit the extrapolation to the wider population, since the similar research in a variety of different healthcare facilities is needed to enhance the generalizability and be able to capture broader epidemiological trends. Reliance on blood culture alone as a diagnostic method, especially among individuals with a high degree of previous antibiotic exposure, could have led to an underestimation of the actual prevalence of enteric fever. The incorporation of other diagnostic methods, such as molecular methods or laboratory-established rapid point-of-care methodologies, would improve diagnostic sensitivity in future studies. The lack of data regarding the severity of sickness, treatment process, complications, and clinical outcomes limits the translational value of the results, which identifies the need to include outcome-based measures to inform risk assessment and therapeutic judgment. . The study also failed to take into account the contextual factors that are likely to influence the transmission of enteric fever including sanitation, quality of water, immunization and socioeconomic factors, which must be properly interpreted in future research studies to provide informed population health outcomes. This elevated rate of empirical antibiotic use at the point of presentation shows that there is an immediate need to conduct an in-depth study on the antimicrobial stewardship options within the community setting and within the primary care setting. To improve the

evidence-based prevention responses, clinical management, and policy initiatives to lessen the occurrence of the enteric fevers in children at risk, it is important to rectify these methodological and contextual shortcomings through conducting rigorously designed, multi faceted research.

Conclusion

This study demonstrates that enteric fever results in high levels of acute febrile disease in children below the age of two years old and it causes a significant number of cases in a high burden area. The insignificance of correlation between enteric fever and demographic or common clinical factors implies the unspecificity of emergence of enteric fever during early childhood and the ineffectiveness of clinical examination as a method of effective diagnosis. The results underline the need to have laboratory confirmation to inform the early and appropriate treatment particularly in a situation where there is heavy empirical use of antibiotics. Its results highlight the necessity to enhance the performance of diagnostic tests, promote the use of antibiotics, and enhance the education of physicians on the evaluation of febrile diseases in children. When these lessons are applied to pediatric education, population health planning, and preventive interventions, such as immunization and population-wide interventions, health outcomes and disease burden in vulnerable pediatric populations will be better.

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