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Frequency of Enteric Fever among Children with Acute Febrile Illness

Dr. Kareema Zulfiqar*
Postgraduate Resident Paediatrics, Central Park Teaching Hospital, Lahore
Email: Zakariyafun@gmail.com

Dr. Fakhar Ul Zaman
Professor, HOD Paediatrics Department, Central Park Teaching Hospital, Lahore

Dr. Farya Bashir
Postgraduate Resident Paediatrics, Central Park Teaching Hospital, Lahore

Dr. Sara Niazi
Postgraduate Resident Paediatrics, Services Hospital, Lahore

Author Details

Corresponding E-mail & Author*:
Dr. Kareema Zulfiqar*
Postgraduate Resident Paediatrics, Services Hospital, Lahore
Email: Zakariyafun@gmail.com

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Abstract

Background: Enteric fever is a widespread cause of acute febrile disease in children, especially in areas with low sanitation and less accessibility to clean water. The timely detection of the problem is the key to its successful management and prevention of complications.

Objective: To assess the prevalence of enteric fever in children presenting with acute febrile illness.

Methods: This was a descriptive cross sectional study was conducted at Central Park Teaching Hospital, Lahore, within a period of six months from January 2024 to June 2024. Children who had a minimum three-day history of fever and had an initial temperature greater than 38 ^{o}C were enrolled. Culture was done on blood to confirm enteric fever. The information regarding demographic details, clinical presentation, and laboratory parameters were noted. Mean + SD or median (IQR) were used in summarizing continuous variables based on the distribution, and frequencies and percentages were used in summarizing categorical variables. Chi-square test was used to analyze associations with $p \leq 0.05$ considered significant.

Results: **The culture-positive rate of enteric fever was found to be 34(22.7%).** Culture-confirmed cases were significantly related to older age, prolonged fever, and hepatosplenomegaly ($p \leq 0.05$). There was no strong relationship with gender or place of residence. Most of the children showed up with abdominal pain, vomiting, or diarrhea.

Conclusion: Enteric fever was a significant proportion of acute febrile disease in children. Clinical predictors included older age, prolonged duration of fever, and hepatosplenomegaly. Early diagnosis, lab diagnosis, and focused treatment should be used in order to decrease morbidity.

Introduction

One of the most frequent causes of childhood hospitalization and admission at the pediatric level in developing countries is acute febrile illness (AFI).[1] Children are especially susceptible because their immunity lacks maturity, they are poorly nourished, sanitation is inadequate, and their living conditions are overcrowded.[2] Enteric fever is one of the most significant public health challenges, particularly in South Asia and sub-Saharan Africa, which harbor a large number of infectious causes of fever. Salmonella enterica serovars Typhi and Paratyphi are the two principal etiological agents of enteric fever, and the disease is spread by contaminated water, food, and substandard hygienic practices.[3] Enteric fever remains a significant cause of childhood morbidity despite the advancement in diagnostic modalities and vaccination strategies to deal with it.[4]

The enteric fever cases are reported annually, and millions of them are reported globally, with the majority of the burden being reported among school-aged children and adolescents.[5] This disease is common in presentation and manifests as persistent fever, malaise, abdominal pain, hepatosplenomegaly, and gastrointestinal disorders that tend to mix with other febrile conditions like malaria, dengue fever, and respiratory infections.[6] Such an indiscriminate clinical picture complicates the prompt diagnosis of this disease in the bipolar world with limited resources due to the lack of laboratory facilities and the widespread use of the empirical antibiotic approach. The problem of delayed or missed diagnosis can result in severe complications such as intestinal perforation, hemorrhage, septicemia, and death.

Blood culture has been the gold standard of diagnosis in most areas, though the sensitivity is compromised by prior antibiotic use and the volume of the sample.[7] Widal test and rapid serological assays are popular despite being weak in accuracy. The current increasing trend of antimicrobial resistance, especially to fluoroquinolones and the third-generation cephalosporins, has also complicated treatment outcomes.[8] Determining the actual disease burden of enteric fever in children with acute febrile disease is thus essential in making empirical treatment decisions, enhancing surveillance, and providing preventative measures of vaccination and community health efforts.

Despite the fact that a number of studies have reported the prevalence of enteric fever in general pediatric populations, little local evidence has been done to determine the frequency of enteric fever in children who present with acute febrile illness within our setting.[8-10] Knowledge about this frequency will assist clinicians in focusing more on diagnostic testing, preventing the use of unnecessary antibiotics, and enhancing clinical outcomes. Due to the burden of febrile diseases in children, as well as the similar presentation of enteric fever with other infectious diseases, it is necessary to identify the prevalence of enteric fever in children who present with acute febrile illness in our population. This will help in the early diagnosis, correct use of antimicrobial therapy, and proper resource distribution within a pediatric care environment. The present study aimed to determine the prevalence of enteric fever in children with acute febrile illness.

Methodology

This research was carried out as descriptive cross-sectional research to establish the prevalence of enteric fever in children with acute febrile illness. The reason to select the cross-sectional design was that it allowed for the measurement of the prevalence of enteric fever at a given time among the eligible children who were in the pediatric outpatient and emergency departments. The study was conducted at Central Park Teaching Hospital, Lahore, within a period of six months from January 2024 to June

2024, to enable sufficient enrollment over seasons to detect differences in febrile presentation.

The openEpi software was used to estimate a single proportion to determine the sample size. The minimum required sample size was estimated assuming an expected prevalence (P) of enteric fever of 22.7% in a prior study of children who presented with acute febrile illness, a 95% confidence level (Z = 1.96), and a margin of error (d) of 5%.[11] The overall sample was estimated to be 150 children after taking into consideration a 10% non-response rate.

The study included children of both sexes between the ages of 1 and 12 years with the following characteristics: acute febrile illness, that is, the presence of documented fever ≥ 38 °C (≥ 100.4°F) during at least 3 consecutive days without an apparent focus of infection at the time of admission. Written informed consent was given by parents or other legal persons before enrolment. Children were not included when they had a documented history of malaria, tuberculosis, or diarrhea in the last two weeks, when they had been given antibiotic therapy in the current illness, or had underlying systemic conditions such as congenital heart disease, atmospheric suppressive disorders, or recent steroid therapy, which would confound clinical examination.

At the time of admission, demographic (age, gender, residence), clinical history (duration of fever, its symptoms), and physical examination results were recorded with the aid of a structured proforma. Each of the participants was sampled under aseptic conditions by drawing 5 ml of blood, with 2–3 ml being taken as the blood culture using standard microbiological methods to identify Salmonella Typhi or Paratyphi, and the rest of the sample was subjected to routine laboratory examination, including complete blood count and inflammatory markers. The microbiology laboratory in the hospital performed all laboratory procedures based on the standardized protocols. Enteric fever was declared confirmed when blood culture produced Salmonella Typhi or Paratyphi.

The Statistical Package of the Social Sciences version 25 was used to enter and analyze data. The study variables were as follows: continuous variables (age in years), length of fever in days, hemoglobin level (g/dL), and total leukocyte count (x 109 /L and categorical variables (gender, residence (urban/rural), age group (≤5 years / >5 years), presence of abdominal pain, vomiting, diarrhea, hepatosplenomegaly and enteric fever (culture-positive / culture-negative). The Shapiro-Wilk test of normality was used to test the distribution of continuous variables. Mean ± (SD) was used to report the normally distributed variables like age and hemoglobin level, and median with interquartile range (IQR) was used to summarize the variables with non-normal distribution like duration of fever and total leukocyte count.

Frequencies and percentages were used to describe categorical variables, which include enteric fever status, as determined by blood culture results. The prevalence of enteric fever in children with acute febrile disease was computed as the percentage of the total number of study participants. The Chi-square test was used to determine the associations between enteric fever and categorical independent variables, which include gender, age group, residence, period of fever category, and hepatosplenomegaly, and Fisher's exact test was used where the number of cells was less than five on the expected cells. A p-value ≤0.05 was regarded as significant.

Results

The age and levels of hemoglobin were normally distributed and were expressed as mean ± SD, whilst duration of fever and total leukocyte count were non-normally distributed and were presented as median with interquartile range. These descriptive

trends gave a picture of the clinical and hematological picture of children presenting with acute febrile illness (Table 1).

Categorical characteristics were described by frequencies and percentages to distribute them. The proportion of the older age group was higher, and males represented a slightly higher proportion than females. The majority of children lived in the urban setting, and the most common related symptom was abdominal pain, with other common symptoms being vomiting and diarrhea, with a smaller percentage developing hepatosplenomegaly during the examination. Such results indicated the general demographic and clinical trends of the study population (Table 2).

Enteric fever frequency was ascertained based on the outcomes of blood culture. A significant percentage of children who reported with acute febrile disease were observed to have culture-positive enteric fever, and the rest of the majority had no record of Salmonella growth in culture. Therefore, enteric fever was a significant burden on children with undifferentiated febrile disease assessed in the study environment (Table 3).

There was a statistically significant relationship between age group, fever duration, and hepatosplenomegaly, and a lack of statistical significance between gender and place of residence. These results showed that older age, extended fever, and the presence of hepatosplenomegaly were more indicated among the culture-positive cases than culture-negative children (Table 4).

Table 1. Demographic and Clinical Characteristics of Children with Acute Febrile Illness (n = 150)

Variable	**Mean ± SD / Median (IQR)**
Age (years)*	6.2 ± 2.8
Duration of fever (days)**	6 (4–9)
Hemoglobin (g/dL)*	10.5 ± 1.6
Total leukocyte count (×10⁹/L)**	9.8 (7.2–12.4)
* Normally distributed variables presented as Mean ± SD (Based on the Shapiro–Wilk test) ** Non-normal variables presented as Median (IQR)	

Table 2. Distribution of Categorical Characteristics of Study Participants (n = 150)

Variable	**Categories**	**Frequency (n)**	**Percentage (%)**
Gender	Male	82	54.7%
	Female	68	45.3%
Residence	Urban	91	60.7%
	Rural	59	39.3%
Age Group	≤5 years	63	42.0%
	>5 years	87	58.0%
Associated Symptoms	Abdominal pain	72	48.0%
	Vomiting	56	37.3%
	Diarrhea	39	26.0%
	Hepatosplenomegaly	28	18.7%

Table 3. Frequency of Enteric Fever among Children with Acute Febrile Illness (n = 150)

Enteric Fever Status (Blood Culture)	**Frequency (n)**	**Percentage (%)**
Culture-positive enteric fever	34	22.7%
Culture-negative cases	116	77.3%

Total	150	100.0%
Overall frequency of enteric fever was 22.7%.		

Table 4. Association of Enteric Fever with Demographic and Clinical Factors (n = 150)

Variable	Categories	Enteric Fever Positive n (%)	Enteric Fever Negative n (%)	p-value
Gender	Male	21 (25.6%)	61 (74.4%)	0.36
	Female	13 (19.1%)	55 (80.9%)	
Age Group	≤5 years	8 (12.7%)	55 (87.3%)	0.03*
	>5 years	26 (29.9%)	61 (70.1%)	
Duration of fever	≤5 days	9 (13.6%)	57 (86.4%)	0.04*
	>5 days	25 (29.4%)	60 (70.6%)	
Residence	Urban	17 (18.7%)	74 (81.3%)	0.18
	Rural	17 (28.8%)	42 (71.2%)	
Hepatosplenomegaly	Present	13 (46.4%)	15 (53.6%)	0.002*
	Absent	21 (17.1%)	101 (82.9%)	
* Statistically significant ($p \leq 0.05$)				

Discussion

Enteric fever has been detected in a significant number of children with the case of acute febrile illness in the current study, and notable associations were observed with older age, prolonged duration of fever, and hepatosplenomegaly. This prevalence is similar to the current regional data; a cross-sectional study in Lahore gave a similar prevalence of culture-confirmed enteric fever in young children with acute febrile illness, which supports the high rate of enteric fever in children with febrile presentations in Pakistan.[12]

We have found that enteric fever is associated with older ages, which is in line with the general epidemiological patterns in South Asia. The North Indian cohort study established the highest incidence of enteric fever in older children and adolescents, indicating that there may be age related increase in susceptibility, probably because of exposure to contaminated food and environment.[13] The age-related distribution supports our results, although the Indian study did not emphasize frequency, but focused on incidence rates in acute febrile illnesses.

Our result showed that hepatosplenomegaly was strongly linked with enteric fever, but other researchers have underscored the diverse clinical presentation of the disease. A study in tertiary centers in Kashmir indicated that hepatomegaly and splenomegaly were frequent clinical manifestations in the pediatric cases of enteric fever despite showing mixed cultures of Salmonella Typhi and Paratyphi.[14] This supports the value of close clinical assessment in suspected cases, even though the signs may not be discriminatory enough without laboratory confirmation.

Contrary to findings of other studies that show no significant demographic predictor, including gender and duration of fever, other large-scale surveillance studies in Asia have established that enteric fever is still largely a childhood disease regardless of gender, although there are also mixed associations with symptom duration. As an example, the Surveillance for Enteric Fever in Asia Project revealed widespread culture-confirmed cases in children of all ages, of typhoid as compared to paratyphoid, and little variation in gender, although antimicrobial resistance patterns differed across geographic areas.[15] The clinical usefulness of prolonged fever as a risk predictor of endemic environments is supported by our association with a longer duration of fever.

In comparison to the studies that have explicitly assessed the cohorts of acute febrile illnesses, our findings differ by geographic area. The similar frequency (22.7%) of enteric fever in children with acute fever was reported in a recent facility-based study in Gujrat, which supports the endemicity and uniform burden of enteric fever in the various regions of Pakistan.[11] A different study in Ethiopia, not directly relevant to children, investigated and found that the prevalence of typhoid among clinically febrile patients was high and that laboratory confirmation, in addition to demographic information, remained significant.[16]

Others have focused on such epidemiological trends instead of prevalence. The burden of disease estimates show that every year, global enteric fever cases are in the millions, especially among children in low- and middle-income countries, which justifies the applicability of our findings locally worldwide.[17] These international patterns indicate that there is continued transmission because of a constant water and sanitation problem, a major determinant of the spread of enteric fever.

Recent research on antimicrobial resistance has also put enteric fever into context in treatment problems that could affect clinical outcomes. The prevalence of drug-resistant Salmonella Typhi has been emphasized by research showing that a high percentage of the pediatric isolates are resistant to drugs, raising doubts that, in addition to prevalence, the patterns of resistance complicate treatment and possibly may be associated with clinical manifestation and duration of illness.[18] Though our present study did not measure antimicrobial resistance, the problem is also extremely important in terms of interpreting disease burden and treatment efficacy in a similar environment.

The results of the study have significant implications for pediatric clinical practice and community health in endemic areas of typhoid. The finding that a significant rate of children presenting with acute febrile illness had culture-confirmed enteric fever underscores the importance of clinicians having a high index of suspicion to consider when considering undifferentiated fever (especially in older children and those with prolonged fevers and hepatosplenomegaly). These findings highlight the need to use early diagnostic tests, such as blood cultures, instead of basing treatment on empirical evidence or clinical observations. Increasing microbiology laboratory capacity and timely culture testing could help to improve accurate diagnosis, rational antibiotic prescription, and decrease inappropriate antimicrobial use. On a larger scale, the results are in favor of the promotion of preventive interventions, including enhancement of the levels of water, sanitation, and hygiene, and increasing coverage of the typhoid conjugate vaccination among high-risk pediatric groups.

Limitations

Some limitations of this study must be taken into account when interpreting the results. The research was cross-sectional in nature; thus, no causal associations between clinical variables and enteric fever were possible. The sample size used was that of one tertiary-care hospital, and this might not well represent community or rural settings. The diagnostic criterion was blood culture, and though it is regarded as reliable, its sensitivity can be compromised by previous exposure to antibiotics and low bacteremia levels, which can result in underestimation of the actual enteric fever burden. Patients were not analyzed in terms of antimicrobial resistance patterns, serotype distribution, and dietary or environmental exposure factors, which would have given additional clinical and epidemiological information. Nevertheless, the research offers valuable and context-specific evidence on the burden and trends of enteric fever among children with acute febrile illness.

Conclusion

Enteric fever was a large percentage of children presenting with acute febrile illness, and there was a large association with older age, an extended period of febrile illness, and hepatosplenomegaly. The results show that enteric fever is a significant differential diagnosis when febrile in children in endemic areas. Regular attention to enteric fever in both protracted and unexplained fevers, coupled with prompt laboratory diagnosis, can enhance the accuracy of diagnosis and the provision of the right clinical care. The research highlights the necessity to enhance diagnostic services, rational use of antibiotics, and fortification of preventive community-based health solutions in order to decrease the burden of enteric fever in children.

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