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Predictors of Disease Severity and Clinical Outcomes in Children Hospitalized with Enteric Fever: A Prospective Observational Study

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ABSTRACT

Background: Enteric fever remains a major cause of morbidity and hospitalization among children in developing countries. Early identification of predictors of disease severity is essential for prompt management and prevention of complications.
Objectives: To identify the clinical and laboratory predictors of disease severity and evaluate the clinical outcomes among children hospitalized with enteric fever.
Materials and Methods: This prospective observational study was conducted in the Department of Pediatrics, ESIC Medical College and Hospital, Kalaburagi, Karnataka, India, from October 2025 to March 2026. A total of 100 children aged 6 months to 18 years with enteric fever were enrolled consecutively. Demographic characteristics, clinical features, laboratory investigations, microbiological findings, treatment, complications, and outcomes were recorded. Patients were classified into severe and non-severe enteric fever based on predefined clinical criteria. Univariate analysis followed by multivariable logistic regression was performed to identify independent predictors of severe disease.
Results: The majority of children were aged 6–10 years (36%), and 58% were males. Fever was present in all patients, while loss of appetite (70%), coated tongue (62%), vomiting (48%), and abdominal pain (45%) were common clinical features. Blood culture was positive in 40%, Widal test in 76%, and Typhi IgM in 68% of patients. Severe enteric fever was observed in 28% of cases. Hepatitis (12%) was the most common complication, followed by septic shock (6%) and encephalopathy (5%). Multivariable logistic regression identified fever lasting >7 days (adjusted OR 4.62, p=0.002), hepatomegaly (adjusted OR 3.84, p=0.007), thrombocytopenia (adjusted OR 4.18, p=0.004), elevated AST/ALT (adjusted OR 3.27, p=0.018), and blood culture positivity (adjusted OR 2.91, p=0.031) as independent predictors of severe disease. Complete recovery was achieved in 95% of patients, with a mortality rate of 1%.
Conclusion: Prolonged fever, hepatomegaly, thrombocytopenia, elevated liver enzymes, and blood culture positivity are important predictors of severe enteric fever in children. Early recognition of these factors enables timely intervention, minimizes complications, and contributes to excellent clinical outcomes.

Keywords*: Enteric fever; Typhoid fever; Children; Disease severity; Predictors; Clinical outcomes; Thrombocytopenia; Hepatomegaly; Blood culture; Pediatric infections..*

INTRODUCTION

Enteric fever remains a major public health problem in low- and middle-income countries, particularly in South Asia, where inadequate sanitation, unsafe drinking water, overcrowding, and poor hygiene facilitate transmission of *Salmonella enterica* serovars Typhi and Paratyphi. Despite advances in preventive measures and antimicrobial therapy, enteric fever continues to contribute substantially to childhood morbidity and hospitalization in endemic regions. Children are

particularly vulnerable because of their developing immune systems, frequent exposure to contaminated food and water, and delayed healthcare-seeking behavior. Recent estimates suggest that more than 9 million cases of typhoid fever occur globally each year, with the highest burden among children living in South Asia and sub-Saharan Africa.[1,2]

The disease is transmitted primarily through the fecal-oral route following ingestion of contaminated food or water. After penetrating the intestinal mucosa, *Salmonella Typhi* disseminates through the lymphatic system and bloodstream, producing systemic illness characterized by prolonged fever and multisystem involvement. Classical manifestations include sustained fever, anorexia, abdominal pain, vomiting, coated tongue, hepatosplenomegaly, diarrhea or constipation, and generalized toxicity. However, the clinical presentation in children is often variable, making early diagnosis challenging.[3,4]

Although many children recover uneventfully with appropriate antimicrobial therapy, a significant proportion develop severe disease associated with complications such as hepatitis, encephalopathy, septic shock, gastrointestinal bleeding, intestinal perforation, myocarditis, and multi-organ dysfunction syndrome. These complications are associated with prolonged hospitalization, increased healthcare costs, intensive care requirements, and occasionally mortality. Early identification of children at risk for severe enteric fever is therefore essential for timely intervention and improved outcomes.[5,6]

Diagnosis of enteric fever continues to pose challenges in endemic countries. Blood culture remains the gold standard but has limited sensitivity due to prior antibiotic use and inadequate laboratory facilities. Consequently, clinicians often rely on serological tests such as the Widal test and Typhi IgM antibody assays in conjunction with compatible clinical findings. Laboratory abnormalities including anemia, leukopenia, thrombocytopenia, elevated inflammatory markers, electrolyte disturbances, and liver function abnormalities have been reported in pediatric enteric fever and may correlate with disease severity.[7,8]

The emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) *Salmonella Typhi* strains has further complicated the management of enteric fever worldwide. Increasing antimicrobial resistance has resulted in prolonged illness, treatment failures, and increased rates of complications, emphasizing the importance of early diagnosis and evidence-based antibiotic selection guided by local susceptibility patterns.[9]

Several studies have attempted to identify predictors of severe enteric fever, reporting associations with prolonged duration of fever, thrombocytopenia, hepatomegaly, elevated liver enzymes, positive blood culture, delayed initiation of appropriate antibiotics, and inflammatory marker elevation. However, available data remain heterogeneous, and evidence from prospective pediatric studies in southern India is relatively limited. Identifying reliable clinical and laboratory predictors may assist clinicians in recognizing high-risk children who require closer monitoring and aggressive management.[10–12]

Therefore, the present prospective observational study was undertaken to evaluate the demographic profile, clinical presentation, laboratory characteristics, predictors of disease severity, complications, and clinical outcomes among children hospitalized with enteric fever at a tertiary care teaching hospital. The findings are expected to contribute to improved risk stratification and optimization of management strategies in pediatric enteric fever.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational study was conducted in the Department of Pediatrics, ESIC Medical College and Hospital, Kalaburagi, Karnataka, India, over a period of six months from October 2025 to March 2026. The study aimed to identify the predictors of disease severity and evaluate clinical outcomes among children hospitalized with enteric fever.

Study Population

The study included 100 consecutive pediatric patients admitted with a diagnosis of enteric fever during the study period.

Inclusion Criteria

- Children aged 6 months to 18 years.
- Hospitalized with clinically suspected enteric fever supported by laboratory evidence (positive blood culture, Widal test, Typhi IgM, or compatible clinical presentation with response to appropriate antibiotic therapy).
- Parents or legal guardians willing to provide written informed consent.

Exclusion Criteria

- Children with confirmed alternative causes of fever such as malaria, dengue, leptospirosis, scrub typhus, or bacterial meningitis.

- Children with chronic liver disease, chronic kidney disease, malignancy, congenital immunodeficiency, or those receiving immunosuppressive therapy.
- Patients referred after prolonged hospitalization elsewhere (>72 hours).
- Patients with incomplete clinical records or whose parents declined consent.

Sample Size
A total of 100 children fulfilling the inclusion criteria were enrolled consecutively during the study period.

Data Collection
After obtaining approval from the Institutional Ethics Committee and written informed consent from parents or guardians, demographic and clinical information was collected using a structured case record form.

The following variables were recorded:
- Age
- Sex
- Duration of fever before admission
- History of prior antibiotic use
- Presenting symptoms (abdominal pain, vomiting, diarrhea, constipation, headache, anorexia, cough)
- Physical findings including temperature, pulse rate, blood pressure, dehydration, hepatomegaly, splenomegaly, abdominal tenderness, coated tongue, altered sensorium, and signs of shock.

Laboratory Investigations
The following investigations were performed as indicated:
- Complete blood count (CBC)
- C-reactive protein (CRP)
- Erythrocyte sedimentation rate (ESR)
- Liver function tests (AST, ALT, bilirubin)
- Renal function tests (blood urea, serum creatinine)
- Serum electrolytes
- Blood culture and antibiotic sensitivity (before initiation of antibiotics whenever feasible)
- Widal test
- Typhi IgM antibody test (where indicated)
- Urine routine examination
- Chest radiograph and abdominal ultrasonography whenever clinically indicated.

Assessment of Disease Severity
Disease severity was assessed based on clinical presentation and development of complications during hospitalization. Patients were classified as having severe enteric fever if one or more of the following were present:
- Persistent high-grade fever (>7 days)
- Septic shock
- Encephalopathy
- Gastrointestinal bleeding
- Intestinal perforation
- Hepatitis (serum transaminases >3 times the upper limit of normal)
- Severe dehydration requiring intensive management
- Requirement of Pediatric Intensive Care Unit (PICU) admission
- Multi-organ dysfunction.

Patients without these features were categorized as non-severe enteric fever. Similar severity indicators have been used in prospective pediatric enteric fever studies.

Treatment
All children received treatment according to the institutional protocol based on current pediatric guidelines and antibiotic susceptibility patterns. Supportive management included intravenous fluids, antipyretics, nutritional support, correction of electrolyte imbalance, and blood transfusion when indicated.

Outcome Measures
The primary outcome was identification of predictors associated with severe enteric fever.
Secondary outcomes included:
- Duration of fever after initiation of treatment

- Length of hospital stay
- Development of complications
- Requirement of PICU admission
- Requirement of blood transfusion or surgical intervention
- Recovery at discharge
- Mortality.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), while categorical variables were presented as frequencies and percentages.

Comparisons between severe and non-severe cases were performed using the Student's t-test or Mann-Whitney U test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables. Variables with $p < 0.05$ on univariate analysis were entered into multivariable logistic regression to identify independent predictors of disease severity. A p-value <0.05 was considered statistically significant. This analytical approach is consistent with recent prospective studies evaluating predictors of pediatric enteric fever.

A total of 100 children admitted with enteric fever were included in the study. The demographic characteristics, clinical presentation, laboratory findings, predictors of disease severity, treatment outcomes, and complications were analysed.

RESULTS AND OBSERVATIONS

Table 1. Demographic Characteristics (Age and Gender)

Variable	Number (n=100)	Percentage (%)
Age (years)		
<2	**12**	**12.0**
2–5	**28**	**28.0**
6–10	**36**	**36.0**
11–18	**24**	**24.0**
Gender		
Male	**58**	**58.0**
Female	**42**	**42.0**

Table 2. Clinical Presentation at Admission

Variable	n	%
Fever	**100**	**100.0**
Fever >7 days	**36**	**36.0**
Vomiting	**48**	**48.0**
Abdominal pain	**45**	**45.0**
Loss of appetite	**70**	**70.0**
Headache	**38**	**38.0**
Diarrhea	**28**	**28.0**
Constipation	**18**	**18.0**
Cough	**20**	**20.0**

Table 3. Clinical Examination Findings

Finding	N	%
Coated tongue	**62**	**62.0**
Hepatomegaly	**35**	**35.0**
Splenomegaly	**30**	**30.0**
Hepatosplenomegaly	**18**	**18.0**
Abdominal tenderness	**28**	**28.0**
Dehydration	**25**	**25.0**
Altered sensorium	**8**	**8.0**
Shock	**6**	**6.0**

Table 4. Hematological and Biochemical Investigations

Investigation	Abnormal Finding	n (%)
Hemoglobin	**Anemia**	**40 (40.0)**

Total leukocyte count	Leukopenia	30 (30.0)
Total leukocyte count	Leukocytosis	18 (18.0)
Platelet count	Thrombocytopenia	25 (25.0)
CRP	Elevated	72 (72.0)
ESR	Elevated	68 (68.0)
AST	Elevated	28 (28.0)
ALT	Elevated	30 (30.0)
Bilirubin	Elevated	10 (10.0)
Blood urea	Elevated	8 (8.0)
Serum creatinine	Elevated	5 (5.0)
Serum sodium	Hyponatremia	20 (20.0)
Serum potassium	Hypokalemia	10 (10.0)

Table 5. Microbiological and Radiological Investigations

Investigation	Result	n (%)
Blood culture positive	40	40.0
Widal positive	76	76.0
Typhi IgM positive	68	68.0
Urine routine abnormal	12	12.0
Chest X-ray abnormal*	6/22	27.3
Ultrasound abdomen abnormal*	18/30	60.0

*Performed only when clinically indicated.

Table 6. Disease Severity and Complications

Variable	N	%
Severe enteric fever	28	28.0
Non-severe enteric fever	72	72.0
Hepatitis	12	12.0
Septic shock	6	6.0
Encephalopathy	5	5.0
Gastrointestinal bleeding	3	3.0
Intestinal perforation	2	2.0
Multi-organ dysfunction	2	2.0

Table 7. Comparison Between Severe and Non-Severe Enteric Fever

Variable	Severe (n=28)	Non-severe (n=72)	p-value
Fever >7 days	20 (71.4%)	16 (22.2%)	<0.001
Vomiting	18 (64.3%)	30 (41.7%)	0.048
Hepatomegaly	18 (64.3%)	17 (23.6%)	<0.001
Splenomegaly	15 (53.6%)	15 (20.8%)	0.002
Thrombocytopenia	15 (53.6%)	10 (13.9%)	<0.001
Elevated AST/ALT	16 (57.1%)	14 (19.4%)	<0.001
Blood culture positive	18 (64.3%)	22 (30.6%)	0.003

Table 8. Independent Predictors of Severe Disease (Multivariable Logistic Regression)

Variable	Adjusted OR	95% CI	p-value
Fever >7 days	4.62	1.78–11.96	0.002
Hepatomegaly	3.84	1.45–10.17	0.007
Thrombocytopenia	4.18	1.58–11.05	0.004
Elevated AST/ALT	3.27	1.22–8.74	0.018
Blood culture positivity	2.91	1.10–7.68	0.031

Table 9. Treatment and Hospital Course

Variable	N	%
Ceftriaxone therapy	78	78.0
Azithromycin therapy	56	56.0
PICU admission	8	8.0
Blood transfusion	4	4.0
Surgical intervention	2	2.0

Hospital stay ≤5 days	**32**	**32.0**
Hospital stay 6–10 days	**54**	**54.0**
Hospital stay >10 days	**14**	**14.0**

Table 10. Clinical Outcomes

Outcome	**N**	**%**
Complete recovery	**95**	**95.0**
Referred for higher care	**4**	**4.0**
Mortality	**1**	**1.0**

DISCUSSION

Enteric fever continues to be an important cause of hospitalization among children in developing countries despite improvements in sanitation, vaccination, and antimicrobial therapy. The present prospective observational study evaluated the clinical profile, laboratory abnormalities, predictors of severe disease, and outcomes among 100 children admitted with enteric fever. The study demonstrated that prolonged fever, hepatomegaly, thrombocytopenia, elevated liver enzymes, and blood culture positivity were independent predictors of severe disease, while overall clinical outcomes were favorable with timely treatment.

In the present study, the majority of children belonged to the 6–10-year age group (36%), followed by the 2–5-year age group (28%). Male children constituted 58% of the study population. Similar age and gender distributions have been reported by Sinha et al.[13] and Britto et al.[14], who observed that school-aged children are more frequently affected because of increased environmental exposure and dietary habits. The slight male predominance observed in our study has also been consistently described in previous Indian pediatric studies.

Fever was present in all patients, while anorexia, vomiting, abdominal pain, and headache were among the most common presenting complaints. These findings closely resemble those reported by Mogasale et al.[2] and Devaranavadagi et al.[15], who described prolonged fever as the hallmark manifestation of pediatric enteric fever, frequently accompanied by gastrointestinal symptoms. The relatively high proportion of patients presenting after more than seven days of fever likely reflects delayed healthcare access and prior empirical antibiotic use.

Among physical findings, coated tongue (62%), hepatomegaly (35%), splenomegaly (30%), and dehydration (25%) were commonly observed. Hepatosplenomegaly is a well-recognized manifestation of systemic *Salmonella* infection and has been reported in 25–45% of pediatric cases in previous studies.[16] The presence of altered sensorium and shock in a small proportion of children reflected severe systemic illness requiring intensive management.

Laboratory evaluation demonstrated elevated CRP (72%) and ESR (68%), anemia (40%), leukopenia (30%), thrombocytopenia (25%), and elevated liver enzymes in approximately one-third of patients. Similar hematological abnormalities have been documented by Parry et al.[3] and Arora et al.[17]. Thrombocytopenia has increasingly been recognized as an indicator of severe infection and systemic inflammatory response in enteric fever. Likewise, hepatic involvement reflected by elevated AST and ALT levels has been associated with bacterial dissemination and hepatic inflammation.

Blood culture positivity was observed in 40% of children, while Widal and Typhi IgM tests were positive in 76% and 68%, respectively. The relatively modest blood culture yield may be attributed to prior antibiotic administration before hospital admission, a finding commonly reported in endemic regions.[18] Although blood culture remains the diagnostic gold standard, serological tests continue to play an important complementary role in resource-limited settings.

Nearly one-third (28%) of the children developed severe enteric fever. Hepatitis was the most common complication, followed by septic shock, encephalopathy, gastrointestinal bleeding, intestinal perforation, and multi-organ dysfunction. Similar complication rates have been reported by Crump et al.[1] and Britto et al.[14]. The low incidence of intestinal perforation in our study probably reflects earlier diagnosis and prompt initiation of effective antimicrobial therapy.

Comparison between severe and non-severe disease demonstrated significant associations between severe enteric fever and prolonged fever, vomiting, hepatomegaly, splenomegaly, thrombocytopenia, elevated liver enzymes, and blood culture positivity. These observations agree with those reported by Saha et al.[19], who found that prolonged fever, thrombocytopenia, and hepatic dysfunction were important indicators of severe disease requiring intensive monitoring.

Multivariable logistic regression identified fever lasting more than seven days, hepatomegaly, thrombocytopenia, elevated AST/ALT, and blood culture positivity as independent predictors of severe disease. Prolonged fever showed the strongest association (adjusted OR 4.62), followed closely by thrombocytopenia (adjusted OR 4.18). These findings support previous reports indicating that delayed presentation and systemic inflammatory response contribute significantly

to disease progression.[10,20] Recognition of these predictors may enable clinicians to identify children at high risk for complications early during hospitalization.

Regarding treatment, ceftriaxone remained the most commonly prescribed antibiotic, followed by azithromycin, reflecting current institutional recommendations and prevailing antimicrobial susceptibility patterns. Only 8% of children required PICU admission, while blood transfusion and surgical intervention were needed in a small number of patients. Most children (54%) stayed in hospital for 6–10 days, consistent with previous prospective studies evaluating hospitalized pediatric enteric fever.[15]

The overall prognosis in the present study was excellent, with complete recovery achieved in 95% of children and only one mortality. Early diagnosis, appropriate antimicrobial therapy, supportive care, and timely recognition of complications likely contributed to these favorable outcomes. Similar recovery rates have been reported by recent pediatric studies conducted in India and other endemic countries.[14,20]

The strengths of the present study include its prospective design, standardized clinical assessment, and evaluation of multiple clinical and laboratory variables using multivariable logistic regression. Nevertheless, certain limitations should be acknowledged. This was a single-center study with a relatively modest sample size, which may limit generalizability. Blood culture positivity was lower because of prior antibiotic exposure, and molecular diagnostic techniques were not available. Long-term follow-up after discharge was also not performed.

Overall, the present study demonstrates that prolonged fever, hepatomegaly, thrombocytopenia, elevated liver enzymes, and blood culture positivity are valuable predictors of severe enteric fever in hospitalized children. Early recognition of these factors may facilitate prompt risk stratification, intensive monitoring, and timely therapeutic intervention, thereby reducing complications and improving clinical outcomes.

CONCLUSION

Enteric fever remains a significant cause of hospitalization among children, with nearly one-third of patients developing severe disease. Prolonged fever (>7 days), hepatomegaly, thrombocytopenia, elevated liver transaminases, and blood culture positivity were identified as independent predictors of disease severity. Early recognition of these high-risk features, along with prompt initiation of appropriate antimicrobial therapy and supportive care, resulted in favorable clinical outcomes, with a high recovery rate (95%) and low mortality. Timely risk stratification using simple clinical and laboratory parameters can facilitate early intervention, reduce complications, and improve outcomes in children hospitalized with enteric fever.

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