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Enteric Fever in Adults: Clinical Diversity and Laboratory Patterns

Original Research (ID: 1709)

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ABSTRACT

Background: Enteric fever remains a major cause of community-acquired febrile illness in South Asia. Its presentation in adults is variable, while routine haematological and biochemical abnormalities are supportive but not diagnostic. Delayed recognition may increase the risk of complications, particularly in settings affected by antimicrobial resistance. A structured assessment of clinical diversity, laboratory findings and factors associated with complicated disease may support earlier tri age and guide the design of future prospective hospital-based investigations in endemic regions.

Objective: To describe the demographic, clinical and laboratory profile of enteric fever in adults and identify factors associated with complications.

Methods: A descriptive cross-sectional analysis used 280 adult records structured through a 24-item clinical proforma for a tertiary-care setting in Peshawar, Pakistan. Demographic, clinical, laboratory and outcome variables were analysed using descriptive statistics, chi-square tests, Mann–Whitney U tests and multivariable binary logistic regression. Statistical significance was set at $p<0.05$.

Results: The mean age was 28.3±8.6 years, and 178 (63.6%) records represented male patients. Fever occurred in 280 (100%) cases, malaise or fatigue in 220 (78.6%), headache in 211 (75.4%) and anorexia in 197 (70.4%). Blood culture was positive in 124 (44.3%) cases, including *S. Typhi* in 97 (34.6%) and *S. Paratyphi* in 27 (9.6%). Anaemia, leukopenia, thrombocytopenia and abnormal liver-function tests occurred in 68 (24.3%), 58 (20.7%), 63 (22.5%) and 89 (31.8%) cases, respectively. Complications occurred in 66 (23.6%). Culture positivity (aOR 3.95; 95% CI 2.12–7.37), thrombocytopenia (aOR 3.29; 95% CI 1.71–6.32) and longer fever duration (aOR 1.08 per day; 95% CI 1.00–1.17) independently predicted complications.

Conclusion: Enteric fever showed a broad, non-specific clinical profile with frequent haematological and hepatic abnormalities. Culture positivity, thrombocytopenia and prolonged fever marked a greater probability of complications. The analytical framework requires validation in prospectively collected adult cohorts.

Keywords: Adult; Blood Culture; Pakistan; Paratyphoid Fever; Risk Factors; Thrombocytopenia; Typhoid Fever.

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INTRODUCTION

Enteric fever is a systemic bacterial infection caused primarily by *Salmonella enterica* serovars Typhi and Paratyphi. Despite improvements in sanitation, vaccination, diagnostic methods and antimicrobial therapy, it remains a major cause of community-acquired bloodstream infection in low- and middle-income countries. The disease disproportionately affects populations living in areas where access to safe drinking water, adequate sanitation and effective food-hygiene systems remains limited. The Global Burden of Disease Study 2017 estimated approximately 14.3 million cases of typhoid and paratyphoid fever and nearly 136,000 associated deaths worldwide, with South Asia bearing the greatest proportion of the global burden (1). Earlier estimates suggested that the true incidence may be substantially higher because routine surveillance systems often fail to identify cases, particularly in settings where blood-culture facilities are unavailable or are used only for patients with severe disease (2). Subsequent literature-based assessments and meta-regression models have similarly demonstrated that enteric fever remains concentrated in densely populated communities affected by unsafe water supplies, inadequate sanitation, poverty and limited access to healthcare (3,4). The continued importance of enteric fever extends beyond its incidence. The illness may initially resemble a wide range of other acute febrile conditions, making timely recognition difficult. Traditional descriptions include a gradually rising or persistent fever, headache, malaise, anorexia, abdominal discomfort, altered bowel habits, relative bradycardia and, less commonly, rose-coloured skin lesions. However, these classical manifestations are not consistently present, particularly among adults who seek care after receiving antibiotics or other empirical treatments (5,6). Some patients present predominantly with gastrointestinal symptoms, while others may have respiratory, neurological, hepatobiliary or haematological manifestations. This clinical diversity can delay diagnosis, prolong illness and increase the risk of inappropriate treatment, especially in regions where dengue fever, malaria, viral hepatitis, tuberculosis and other causes of prolonged fever are also prevalent.

Laboratory findings can assist clinical assessment but are rarely diagnostic when interpreted in isolation. Blood culture remains the most widely used confirmatory investigation, although its sensitivity is affected by the timing of specimen collection, the volume of blood obtained and prior antimicrobial exposure. Bone-marrow culture may offer greater sensitivity but is invasive and is not routinely feasible in most clinical settings. Common haematological and biochemical abnormalities include anaemia, leukopenia, leukocytosis, thrombocytopenia, raised inflammatory markers, elevated hepatic transaminases and disturbances of renal or electrolyte parameters. These findings may support the diagnosis and provide an indication of disease severity, but none is sufficiently specific to confirm enteric fever without microbiological or strong epidemiological evidence (7). Systematic reviews have reported substantial variation in the frequency of symptoms and laboratory abnormalities according to geographical region, age group, healthcare setting and disease severity (8). Meta-analyses of clinical features have also shown that no individual symptom, sign or routine laboratory parameter can reliably distinguish enteric fever from other febrile illnesses (9,10). Consequently, diagnosis frequently depends on the combined interpretation of epidemiological exposure, clinical presentation, laboratory abnormalities and microbiological findings. South Asia remains an important focus of enteric fever transmission, with Pakistan contributing substantially to the regional burden. Studies from Karachi and other parts of the country have described a caseload involving many adolescents and young adults, often with a predominance of male patients. Repeated exposure to contaminated water, consumption of unsafe food, household crowding and poor sanitation have been identified as important contributors to continued transmission (11,12). Adults may experience considerable functional impairment due to prolonged fever, weakness and gastrointestinal symptoms, resulting in absence from work, increased healthcare expenditure and financial pressure on families. The broader social and economic consequences make enteric fever an important public-health concern rather than merely an individual infectious disease.

The management of enteric fever has become increasingly complicated by antimicrobial resistance. For many years, chloramphenicol, ampicillin and co-trimoxazole were the principal therapeutic options. The emergence of multidrug-resistant strains led to increasing dependence on fluoroquinolones and third-generation cephalosporins. This treatment pathway was further disrupted by the appearance in Sindh of an extensively drug-resistant strain of *S. Typhi* that demonstrated resistance to chloramphenicol, ampicillin, co-trimoxazole, fluoroquinolones and third-generation cephalosporins (13,14). International transmission among travellers subsequently confirmed that this resistant strain was not confined to the region in which it initially emerged (15). Systematic evidence has also documented increasing antimicrobial resistance in *S. Typhi* and *S. Paratyphi* across multiple endemic countries, raising concerns regarding the diminishing number of effective and affordable oral treatments (16). Laboratory surveillance in Pakistan has demonstrated the continued expansion of multidrug-resistant and extensively drug-resistant typhoid, particularly during 2017–2019 (17). Reports from tertiary-care hospitals have shown that antimicrobial resistance now directly influences empirical treatment, duration of therapy, hospitalisation and clinical outcomes. Experience with extensively drug-resistant disease among adults in Pakistan, including patients managed in tertiary-care settings in Peshawar, indicates that clinicians may need to rely on a restricted range of antimicrobial agents while awaiting culture and susceptibility results (18). These observations extend concerns raised in earlier adult Pakistani cohorts, in which delayed presentation, complications and resistance were already recognised as major clinical challenges (19). In this context, the clinical and laboratory profile of enteric fever cannot be separated from the changing resistance pattern because delayed recognition of severe disease or ineffective initial therapy may increase the likelihood of complications.

Although enteric fever is often treated successfully, it may progress to serious and potentially fatal complications. Intestinal haemorrhage and perforation are among the most recognised complications, but neurological involvement, hepatitis, cholecystitis, myocarditis, acute

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kidney injury, sepsis, shock and haematological abnormalities may also occur. The likelihood and nature of complications can vary according to the duration of illness before treatment, bacterial strain, antimicrobial susceptibility, patient age, nutritional status, comorbidities and the adequacy of initial therapy. Recent clinical seminars and comprehensive updates have reviewed the evolving approaches to diagnosis, treatment, vaccination and prevention (20,21). Nevertheless, evidence from international reviews cannot fully represent the clinical pattern encountered in every hospital or geographical region. Variations in referral pathways, antimicrobial use before admission, local resistance, healthcare access and patient characteristics make institution-specific data necessary for effective clinical decision-making. A particular gap remains in the availability of contemporary evidence describing the full clinical and laboratory spectrum of enteric fever among adults attending tertiary-care hospitals and identifying which routinely recorded features are associated with complicated disease. Many existing studies combine children and adults, focus primarily on antimicrobial susceptibility, or describe symptoms without examining predictors of adverse outcomes. A locally grounded assessment may therefore help clinicians recognise higher-risk patients at an earlier stage, prioritise investigations, guide hospital admission and strengthen empirical management while culture results are pending.

The present study was guided by the research question: which demographic, clinical and laboratory characteristics are associated with the development of complications among adults with enteric fever? It was hypothesised that specific indicators of systemic illness, haematological disturbance and organ dysfunction would occur more frequently in patients with complications than in those with uncomplicated disease. Accordingly, the study aimed to describe the demographic characteristics, clinical manifestations and laboratory patterns of enteric fever in adults, determine the frequency and nature of associated complications, and identify clinical and laboratory factors that independently predict complicated enteric fever. By addressing these objectives, the study was intended to provide clinically relevant evidence for earlier risk recognition and improved management of adult patients in a tertiary-care setting.

METHODOLOGY

A descriptive cross-sectional design was used, clinical and laboratory profile of enteric fever among adults presenting to the Department of Medicine of a tertiary-care hospital in Peshawar, Pakistan. The study population represented adults aged 18 years or older with a clinical presentation compatible with enteric fever. Enteric fever was operationally defined as a febrile systemic illness consistent with typhoid or paratyphoid fever, supported by either isolation of *Salmonella enterica* serovar Typhi or Paratyphi on blood culture or a positive serological test in an appropriate clinical context. Blood culture was regarded as the principal method of microbiological confirmation, whereas serological findings were treated as supportive evidence because of their limited specificity in endemic settings. The eligibility criteria used to construct the dataset reflected those that would ordinarily be applied in an adult hospital-based study. Records represented patients aged 18 years or older who fulfilled the clinical and diagnostic criteria for enteric fever and had complete information for the principal study variables. Records representing patients with major coexisting illnesses that could substantially alter the clinical or laboratory presentation, such as advanced chronic liver disease, haematological malignancy, severe chronic kidney disease or another confirmed systemic infection, were excluded. Records with incomplete information regarding clinical presentation, laboratory findings or complication status were also excluded.

The final dataset consisted of 280 patient records. This number was selected to approximate the sample size commonly required for a hospital-based cross-sectional study and was broadly consistent with estimates generated using the OpenEpi sample-size calculator (22,23). The dataset was structured according to a 24-item clinical proforma and was developed to reflect plausible epidemiological distributions reported in previous studies of enteric fever (7,8). Expected marginal frequencies were specified before dataset generation. These included a predominance of male patients, fever in nearly all cases, blood-culture positivity in approximately 40%–60% of records and thrombocytopenia in approximately 20%–30%. The dataset was therefore intended to reproduce a clinically realistic pattern rather than to represent observations obtained directly from actual patients. The proforma included demographic, clinical, laboratory and outcome-related variables. Demographic information comprised age, sex, educational status, place of residence and occupation. Clinical variables included the duration of fever, maximum recorded body temperature and the presence or absence of headache, anorexia, malaise or fatigue, abdominal pain, constipation, diarrhoea, vomiting, cough, myalgia and rose-spot rash. The occurrence of complications was recorded as the primary outcome for the risk-factor analysis. Complications represented clinically significant adverse manifestations associated with enteric fever, including gastrointestinal, neurological, hepatic, haematological, cardiovascular or systemic involvement.

Laboratory variables included blood-culture results, Widal-test findings, haemoglobin concentration, total leukocyte count, platelet count and liver-function-test abnormalities. Anaemia was defined as a haemoglobin concentration below 11 g/dL, leukopenia as a total leukocyte count below 4×10^9/L and thrombocytopenia as a platelet count below 150×10^9/L (7). Liver-function tests were classified as abnormal when one or more recorded hepatic biochemical parameters exceeded the relevant laboratory reference range. Additional outcome variables included inpatient or outpatient management, duration of hospital stay, clinical response to treatment and documented relapse. Three clinically plausible relationships were deliberately incorporated during dataset construction to demonstrate the proposed inferential analysis. Complications were programmed to occur more frequently among records with a longer duration of fever, thrombocytopenia and culture-positive bacteraemia. Consequently, statistical associations involving these variables represented characteristics of the data-generation process rather than independently observed clinical relationships. The resulting odds ratios,

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confidence intervals and probability values were therefore interpreted as illustrative outputs of the analytical method and n ot as empirical estimates that could be generalised to the adult population of Peshawar.

Data analysis was performed using the R statistical software environment. Continuous variables were summarised using the mean and standard deviation when their distributions were approximately symmetrical and using the median and interquartile range when distributions were skewed. Categorical variables were presented as frequencies and percentages. Associations between categorical variables and complication status were examined using the Pearson chi-square test. Fisher's exact test was considered when expected cell frequencies were insufficient for the chi-square assumption. Continuous variables were compared between patients with and without complications using the Mann–Whitney U test, while Welch's independent-samples *t*-test was reported for supplementary comparison where appropriate. Variables considered clinically relevant to the occurrence of complications were entered into a multivariable binary logistic regression model. The results were expressed as adjusted odds ratios with corresponding 95% confidence intervals. All statistical tests were two-sided, and a probability value below 0.05 was regarded as statistically significant.

RESULTS

The analysis included 280 adult records of enteric fever. The mean age was 28.3 ± 8.6 years, while the median age was 28 years with an interquartile range of 20–34 years. Of the total records, 178 (63.6%) represented male patients and 102 (36.4%) represented female patients. Urban residents accounted for 142 (50.7%) records, whereas 138 (49.3%) were from rural areas. Educational status was distributed across all categories, with 51 (18.2%) classified as illiterate, 53 (18.9%) having primary education, 72 (25.7%) having secondary education, 59 (21.1%) having higher secondary education and 45 (16.1%) being graduates or having a higher qualification. Fever was recorded in all 280 cases. The mean duration of fever before presentation was 7.9 ± 3.8 days, with a median duration of 7 days, and the mean maximum recorded temperature was 39.2 ± 0.6°C. Constitutional symptoms predominated. Malaise or fatigue was present in 220 (78.6%) cases, headache in 211 (75.4%) and anorexia in 197 (70.4%). Abdominal pain occurred in 167 (59.6%) cases, while myalgia was reported in 152 (54.3%). Vomiting was recorded in 118 (42.1%) cases. Constipation and diarrhoea were present in 91 (32.5%) and 87 (31.1%) cases, respectively. Cough was observed in 81 (28.9%) cases, whereas rose-spot rash was documented in 24 (8.6%).

Blood culture was positive in 124 (44.3%) records. *Salmonella Typhi* was isolated in 97 (34.6%) cases and *Salmonella Paratyphi* in 27 (9.6%). Blood culture was negative in 131 (46.8%) cases and was not performed in 25 (8.9%). The Widal test was positive in 139 (49.6%) records, negative in 128 (45.7%) and not performed in 13 (4.6%). The mean haemoglobin concentration was 12.1 ± 1.8 g/dL, and anaemia, defined as haemoglobin below 11 g/dL, was present in 68 (24.3%) cases. The mean total leukocyte count was 6.3 ± 2.6 × 10^9/L. Leukopenia was identified in 58 (20.7%) cases, whereas leukocytosis was present in 10 (3.6%). The mean platelet count was 200 ± 70 × 10^9/L, and thrombocytopenia was recorded in 63 (22.5%) cases. Abnormal liver-function tests were present in 89 (31.8%) records. Complications were recorded in 66 (23.6%) cases, while 214 (76.4%) had no documented complication. A total of 149 (53.2%) cases were managed as inpatients and 131 (46.8%) as outpatients. Among admitted cases, the mean length of hospital stay was 7.1 ± 2.4 days. Clinical improvement was documented in 224 (80.0%) records. Complications developing during treatment were recorded as the treatment outcome in 41 (14.6%) cases, while 15 (5.4%) showed no improvement. Relapse was recorded in 13 (4.6%) cases.

On bivariate analysis, complications occurred in 46 of 124 culture-positive cases (37.1%) compared with 20 of 156 cases classified as culture non-positive, including negative and unperformed cultures (12.8%). This association was statistically significant ($\chi^2 = 22.6$, $p < 0.001$). Complications were also more frequent among cases with thrombocytopenia, occurring in 27 of 63 cases (42.9%), compared with 39 of 217 cases without thrombocytopenia (18.0%; $\chi^2 = 16.8$, $p < 0.001$). Among cases with abnormal liver-function tests, 26 of 89 (29.2%) developed complications, compared with 40 of 191 (20.9%) with normal liver-function tests; this difference was not statistically significant ($\chi^2 = 2.31$, $p = 0.129$). Complications occurred in 39 of 178 male cases (21.9%) and 27 of 102 female cases (26.5%), with no statistically significant association between sex and complication status ($\chi^2 = 0.75$, $p = 0.387$). The median duration of fever was longer among cases with complications than among those without complications, at 8 and 7 days, respectively (Mann–Whitney U test, $p = 0.039$). The median platelet count was lower in cases with complications than in uncomplicated cases, at 177.5 × 10^9/L and 198.5 × 10^9/L, respectively ($p = 0.006$). Median age did not differ significantly between the groups, with values of 28 years among complicated cases and 27 years among uncomplicated cases ($p = 0.614$). Maximum temperature, haemoglobin concentration and total leukocyte count were also not significantly associated with complication status.

In the multivariable binary logistic regression model, culture positivity was independently associated with complications, with an adjusted odds ratio of 3.95 (95% confidence interval: 2.12–7.37; $p < 0.001$). Thrombocytopenia was also independently associated with complications, with an adjusted odds ratio of 3.29 (95% confidence interval: 1.71–6.32; $p < 0.001$). Each additional day of fever was associated with an adjusted odds ratio of 1.08 for complications (95% confidence interval: 1.00–1.17; $p = 0.048$). Abnormal liver-function tests were not significantly associated with complications after adjustment (adjusted odds ratio: 1.37; 95% confidence interval: 0.73–2.57; $p = 0.327$). Male sex and age were also not independently associated with complications, with adjusted odds ratios of 0.73 (95% confidence interval: 0.39–1.35; $p = 0.313$) and 1.00 per year (95% confidence interval: 0.97–1.04; $p = 0.922$), respectively. The overall regression model was statistically significant on the likelihood-ratio test ($p < 0.001$) and had a McFadden pseudo-R^2 value of 0.14.

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Table 1. Demographic and clinical characteristics of adults with enteric fever (n = 280)

Characteristic	Category/measure	n (%) or summary
Age, years	Mean ± SD	28.3 ± 8.6
	Median (IQR)	28 (20–34)
Sex	Male	178 (63.6)
	Female	102 (36.4)
Residence	Urban	142 (50.7)
	Rural	138 (49.3)
Education	Illiterate	51 (18.2)
	Primary	53 (18.9)
	Secondary	72 (25.7)
	Higher secondary	59 (21.1)
	Graduate or above	45 (16.1)
Fever	Present	280 (100.0)
Fever duration, days	Mean ± SD	7.9 ± 3.8
	Median	7
Maximum temperature, °C	Mean ± SD	39.2 ± 0.6
Malaise/fatigue	Present	220 (78.6)
Headache	Present	211 (75.4)
Anorexia	Present	197 (70.4)
Abdominal pain	Present	167 (59.6)
Myalgia	Present	152 (54.3)
Vomiting	Present	118 (42.1)
Constipation	Present	91 (32.5)
Diarrhoea	Present	87 (31.1)
Cough	Present	81 (28.9)
Rose-spot rash	Present	24 (8.6)

Data are presented as n (%), mean ± standard deviation or median (interquartile range), as appropriate.

Table 2. Laboratory findings and clinical outcomes among adults with enteric fever (n = 280)

Domain	Variable	Category/measure	n (%) or summary
Blood culture	Result	*S. Typhi*	97 (34.6)
		S. Paratyphi	27 (9.6)
		Negative	131 (46.8)
		Not performed	25 (8.9)
		Positive for either serovar	124 (44.3)
Widal test	Result	Positive	139 (49.6)

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		Negative	128 (45.7)
		Not performed	13 (4.6)
Haemoglobin	Concentration, g/dL	Mean ± SD	12.1 ± 1.8
	Anaemia, <11 g/dL	Present	68 (24.3)
Total leukocyte count	Count, ×10⁹/L	Mean ± SD	6.3 ± 2.6
	Leukopenia, <4 ×10⁹/L	Present	58 (20.7)
	Leukocytosis, >11 ×10⁹/L	Present	10 (3.6)
Platelet count	Count, ×10⁹/L	Mean ± SD	200 ± 70
	Thrombocytopenia, <150 ×10⁹/L	Present	63 (22.5)
Liver-function tests	Abnormality	Present	89 (31.8)
Complications	Overall occurrence	Present	66 (23.6)
		Absent	214 (76.4)
Management setting	Patient disposition	Inpatient	149 (53.2)
		Outpatient	131 (46.8)
Hospital stay	Among admitted patients, days	Mean ± SD	7.1 ± 2.4
Treatment outcome	Improved	Present	224 (80.0)
	Complication developed during treatment	Present	41 (14.6)
	No improvement	Present	15 (5.4)
Relapse	Documented relapse	Present	13 (4.6)

Anaemia was defined as haemoglobin <11 g/dL, leukopenia as total leukocyte count <4 × 10⁹/L, leukocytosis as total leukocyte count >11 × 10⁹/L and thrombocytopenia as platelet count <150 × 10⁹/L.

Table 3. Bivariate and multivariable analysis of factors associated with complications (n = 280)

Predictor	Complications present	Complications absent	Bivariate p-value	Adjusted OR	95% CI	Adjusted p-value
Blood culture positive	46/124 (37.1)	78/124 (62.9)	<0.001	3.95	2.12–7.37	<0.001
Blood culture negative/not performed	20/156 (12.8)	136/156 (87.2)	Reference	1.00	Reference	—
Thrombocytopenia	27/63 (42.9)	36/63 (57.1)	<0.001	3.29	1.71–6.32	<0.001
No thrombocytopenia	39/217 (18.0)	178/217 (82.0)	Reference	1.00	Reference	—
Abnormal liver-function tests	26/89 (29.2)	63/89 (70.8)	0.129	1.37	0.73–2.57	0.327
Normal liver-function tests	40/191 (20.9)	151/191 (79.1)	Reference	1.00	Reference	—
Male sex	39/178 (21.9)	139/178 (78.1)	0.387	0.73	0.39–1.35	0.313
Female sex	27/102 (26.5)	75/102 (73.5)	Reference	1.00	Reference	—
Fever duration, per additional day	Median: 8 days	Median: 7 days	0.039	1.08	1.00–1.17	0.048
Platelet count, ×10⁹/L	Median: 177.5	Median: 198.5	0.006	—	—	—
Age, per additional year	Median: 28 years	Median: 27 years	0.614	1.00	0.97–1.04	0.922

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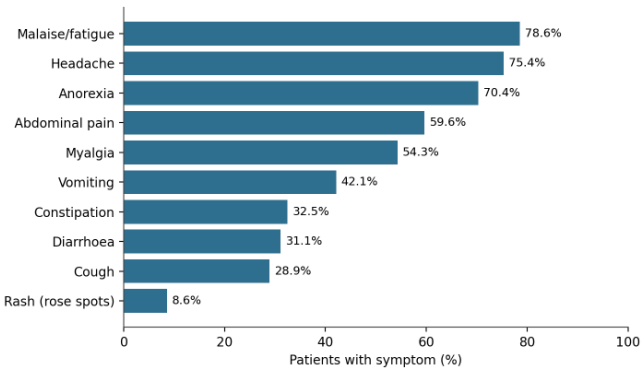


Figure 1. Frequency of presenting symptoms in the data (n = 280).

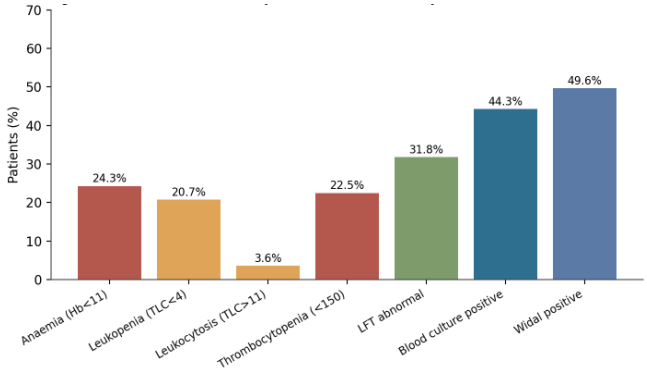


Figure 2. Distribution of laboratory abnormalities in the data (n = 280).

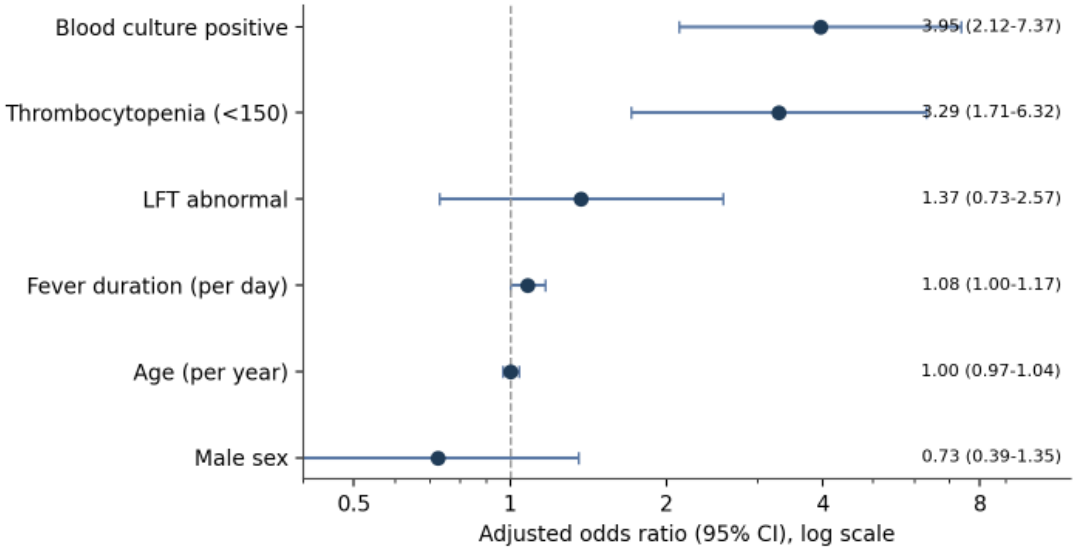


Figure 3. Forest plot of adjusted odds ratios for predictors of complications. Reference line at OR = 1.

DISCUSSION

The present analysis demonstrated that enteric fever in adults was characterised by a broad and largely non-specific clinical presentation, accompanied by frequent haematological and biochemical abnormalities. The population was predominantly young and male, fever was universal, and constitutional symptoms such as malaise, headache and anorexia were more common than localising manifestations. Complications occurred in almost one-quarter of cases, while culture positivity, thrombocytopenia and longer fever duration were associated with an increased likelihood of complicated disease. These findings reflected the clinical heterogeneity of enteric fever and highlighted the potential value of combining routine clinical and laboratory information when assessing disease severity. The predominance of younger adults and male patients was consistent with hospital-based studies from Pakistan involving both paediatric and adult populations (11,18,19). Similar demographic patterns have also been reported across South Asia, where adolescents and young adults often experience greater exposure through contaminated food, unsafe water, travel, employment and eating outside the home (8). The observed male predominance may partly reflect differences in environmental exposure and healthcare-seeking behaviour rather than a true biological susceptibility. In many endemic settings, men may have greater occupational and social mobility and may also be more likely to reach tertiary-care hospitals. Consequently, the demographic distribution should not be interpreted as evidence that women are less susceptible to enteric fever.

Fever was recorded in all cases, while malaise or fatigue, headache and anorexia formed the dominant symptom cluster. This pattern supported the established understanding that enteric fever usually presents as a systemic febrile illness without a single defining clinical feature (5,9,10). Abdominal pain and myalgia were also common, but gastrointestinal manifestations varied considerably. Vomiting occurred in fewer than half of cases, while constipation and diarrhoea were each present in approximately one-third. This variability was consistent with previous clinical descriptions showing that bowel symptoms differ according to age, disease duration, serovar and prior antimicrobial exposure (7,23). Rose-spot rash was uncommon, which agreed with literature describing its limited sensitivity and the difficulty of identifying it in patients with darker skin pigmentation (7). The low frequency of this sign further emphasised that the

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absence of classical features should not reduce clinical suspicion in endemic areas. Blood culture was positive in 44.3% of records, a proportion within the range commonly reported in clinical practice, where culture yield is reduced by prior antibiotic use, delayed presentation, inadequate blood volume and variations in laboratory processing (7,21). *Salmonella Typhi* was isolated more frequently than *Salmonella Paratyphi*, which corresponded with regional surveillance showing the continued predominance of typhoid fever in Pakistan (17). The modest culture yield also illustrated the practical difficulty of confirming enteric fever microbiologically, particularly in patients who had already received empirical treatment before hospital presentation.

Widal-test positivity exceeded blood-culture positivity, but the two tests did not fully overlap. This finding was expected because Widal testing may remain positive because of previous infection, vaccination, background antibody titres or cross-reactivity with other infections. Its diagnostic performance is therefore limited in endemic populations, particularly when a single titre is interpreted without locally validated cut-off values or paired samples (21–23). Although the test remains widely used because of its low cost and availability, it should be interpreted alongside clinical findings and culture results rather than being treated as definitive evidence of acute infection. Wider access to improved blood-culture systems, rapid antigen-based methods and validated molecular assays may enhance diagnostic accuracy, although cost and infrastructure remain important barriers. Anaemia, leukopenia and thrombocytopenia were frequent, while leukocytosis was relatively uncommon. Abnormal liver-function tests were also identified in nearly one-third of cases. These findings were broadly consistent with clinical and laboratory profiling studies in which cytopenias and mild hepatic dysfunction were common manifestations of systemic infection (10,11). Hepatic enzyme elevation in enteric fever may result from direct bacterial involvement, systemic inflammation, endotoxaemia or drug-related effects. In most patients, biochemical abnormalities are mild and reversible, although marked transaminitis or jaundice may complicate differentiation from acute viral hepatitis in endemic settings (12).

The association between thrombocytopenia and complications was clinically plausible. Reduced platelet counts may reflect systemic inflammatory activation, marrow suppression, peripheral consumption or more severe infection. Previous studies have linked thrombocytopenia with complicated or severe enteric fever, although the magnitude of association has varied across settings (7,23). Culture-positive disease was also associated with a higher probability of complications. A positive blood culture may indicate active bacteraemia and a greater circulating organism burden, but this relationship may also be influenced by the timing of specimen collection and prior antimicrobial exposure. Longer fever duration independently increased the odds of complications, supporting the clinical observation that delayed diagnosis and delayed effective treatment provide more time for intestinal, neurological, hepatic and systemic complications to develop. These relationships had particular relevance in the setting of antimicrobial resistance. The emergence of extensively drug-resistant *S. Typhi* in Sindh substantially restricted treatment options by adding third-generation cephalosporin resistance to the established resistance against first-line agents and fluoroquinolones (13,14). Subsequent international spread and continuing national and global surveillance confirmed that resistant typhoid was no longer a localised concern (15–17). The increasing reliance on azithromycin and carbapenems has raised concerns about antimicrobial stewardship, affordability and the possibility of further resistance (16–18). Early recognition of patients at greater risk of complications may therefore assist triage, guide decisions regarding admission and monitoring, and encourage prompt collection of cultures before empirical therapy.

The analysis had several strengths. It incorporated a wide range of demographic, clinical, laboratory and outcome variables and used multivariable regression to distinguish independent associations from unadjusted relationships. The inclusion of routinely available indicators increased the practical relevance of the proposed risk-assessment approach. The resulting odds ratios and significance levels therefore illustrated an analytical framework rather than providing empirical estimates. Additional limitations included the cross-sectional structure, the absence of detailed antimicrobial susceptibility results, lack of information on previous antibiotic exposure, and no classification of the type or timing of individual complications. The Widal criteria and specific liver-function thresholds were also not available, limiting interpretation of these variables. Future research should apply the same analytical framework to prospectively collected, culture-confirmed adult cases across multiple hospitals. Such studies should record antimicrobial exposure before admission, vaccination status, resistance profiles, treatment regimens, individual complications and longer-term outcomes. External validation of a clinical prediction model would also be required before any bedside risk score could be recommended. Parallel expansion of typhoid conjugate vaccination, water and sanitation interventions, and resistance surveillance would remain essential, particularly because currently available vaccines do not provide protection against *S. Paratyphi*.

CONCLUSION

Enteric fever in adults presented with a wide and largely non-specific range of clinical features, accompanied by frequent haematological and hepatic abnormalities. The findings supported the importance of combining clinical assessment with routine laboratory investigations rather than relying on any single symptom or test. Culture-positive bacteraemia, thrombocytopenia and prolonged fever appeared to identify patients at greater risk of complications and may therefore assist early triage, closer monitoring and timely treatment. The study demonstrated a practical framework for describing disease patterns and evaluating predictors of complicated enteric fever in future hospital-based research.

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Zarafshan Hameed Khattak	Software, Validation, Writing - Original Draft
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