Ibrahim Card Med J. 2011; 1(2): 40-44


ORIGINAL ARTICLE

# Clinical Presentation of Typhoid Fever

Md. Shafiqul Islam[1], Md. Hamidur Rahman[2], Bazlul Karim[3], Md. Rakibul Haque Khan[4]


## ABSTRACT

**Background:** Typhoid fever is a severe debilitating and potentially life threatening illness. It is generally one of the most challenging problems in medical therapeutics. Many reports from developing countries show that the clinical presentation of typhoid fever have significantly altered often leading to missed diagnosis, the consequence of which is immense in terms of scarce health resources and patient suffering. The present study was intended to assess the current pattern of presentation of typhoid fever, its pathological and biochemical findings.

**Methods:** Eighty eight consecutive paediatric patients (up to the age of 12 years) of either sex, diagnosed primarily as typhoid fever were included in the study. The diagnostic criteria were either positive blood culture for Salmonella typhi or Salmonella paratyphi or a four-fold rise in antibody titre. Accordingly 42(47.7%) patients were culture positive for Salmonella. Relative bradycardia was considered if children had pulse rate lower than expected average for his age for each degree rise of temperature. The laboratory tests (A complete blood picture, SGPT and serum billirubin) were performed to assess the involvement of liver (if any).

**Results:** Of the 88 patients, 48(54.5%) were male and 40(45.5%) were female with mean age 5.9 years and the lowest and highest ages were 1 and 12 years respectively. Over three-quarter (77.3%) of the patients attended between 1-2 weeks of illness and the rest after 2 weeks. All patients presented with fever with 57% being step-ladder pattern and 43% intermittent. Majority had loss of appetite (98.7%) followed by nausea/vomiting (88.6%), diarrhoea (50%), constipation (26.1%), cough (23.9%) and headache (17%). On examination, 85.2% exhibited coated tongue, 78.4% hepatomegaly and 60.2% splenomegaly. The second most common signs were relative bradycardia (43.2%), abdominal distension (36.4%) and toxic appearance (14.8%). Nearly half (48.9%) of the patients had anaemia (haemoglobin level < 12 gm/dl). About 65% of the patients had WBC count in the range of 6000 - 11000/mm3 (relative leucopenia), 22.7% below 6000/mm3 (absolute leucopenia) and 12.5% > 11000/mm3 (leucocytosis) of blood. Six patients had atypical presentation. Of them 2 had dehydration, 1 had burning micturition, 1 jaundice, 1 altered consciousness and 1 pneumonitis. Of the 64 patients who have had serum ALT tested, nearly three-quarter (73.4%) had raised ALT (> 40 IU/L), while 84.1% had raised serum billirubin (9.1% 1-3 mg/dl and 2.3% > 3 mg/dl).

**Conclusion:** The clinical pattern of typhoid fever conforms well with that of classic pattern of step-ladder fever. Anorexia, coated tongue, diarrhoea, relative bradycardia, relative neutropenia, hepatosplenomegaly are still common manifestations of typhoid fever.


**Key word:** Typhoid fever, clinical presentation, pathological and biochemical manifestations.

## Introduction

Enteric fever is a systemic infection caused by Salmonella enterica, including S. enterica serotype Typhi *(S. typhi)* and serotype Paratyphi *(S. paratyphi).* Enteric fever, being transmissible by faeco-oral route, is primarily a disease of regions where overcrowding, poor sanitation and untreated water are the norm.[1] High fever, toxaemia, constipation during the first week of fever complicated by encephalopathy and perforation during third week of fever are the typical manifestations of the disease.[2] Parry et al[3] reported relative bradycardia at the peak of high fever is an indicator of typhoid fever. Coated tongue, alteration of bowel habits varying from constipation in adults to diarrhoea in children, tender abdomen, hepatomegaly, and splenomegaly are often present. Agarwal et al.[4] in their study found clinical features of typhoid fever to be in conformity with earlier studies.[5, 6]


**Authors' Information:**

1. ***Dr. Md. Shafiqul Islam,*** *MBBS, MCPS (Paed), DCH, MD (Paed), Asst. Professor (Paediatrics), Mymensingh Medical College, Bangladesh.*
2. ***Professor Md. Hamidur Rahman,*** *MBBS, FCPS (Paed), Department of Paediatrics, Ad-Deen Medical College, Dhaka.*
3. ***Professor Bazlul Karim,*** *MBBS, FCPS (Paed), Dept. of Paediatric Gastroenterology and Nutrition, BSMMU, Dhaka.*
4. ***Dr. Md. Rakibul Haque Khan,*** *MBBS, FCPS (Paed), MD (Neonatology) Asst. Professor (Neonatology), Mymensingh Medical College, Bangladesh.*

Correspondance: ***Dr. Md. Shafiqul Islam,*** *Mobile: 01819-277911, E-mail: drshafiquepaed@gmail.com*

However, Durani & Rab[7] reported that classical pattern of step-ladder fever associated with relative bradycardia was not seen in most patients of their series.

Twenty-two percent cases had sudden onset of high grade fever and of them majority were clinically diagnosed as septicaemia. Diagnoses of viral hepatitis, bronchitis, psychosis, meningitis, myocarditis, polyneuropathy and proximal myopathy were also made based on the presenting signs and symptoms. Neuropsychiatric manifestation was less frequent as compared to 45% cases reported from India.[8,9] In a study conducted on 32 culture-positive adult patients of typhoid fever admitted in a tertiary hospital of South India over a period of seven years, nearly half (46.9%) presented with atypical manifestations.[2] Atypical manifestations observed were burning micturation with normal urine examination (15.6%), diarrhooea in first week (6.2%), encephalopathy in first week (3.1%), isolated hepatomegaly (6.2%), pneumonitis (3.1%), and bone-marrow depression (6.2%). Of the 32 patients, 10(31.3%) had multi-drug resistant (MDR) strain. Fifty percent of the patients with MDR strain had atypical presentation. As it results in high morbidity and mortality, reappraisal of presentation, course, complication and treatment is deemed necessary.[10] Typhoid is a severe debilitating and potentially life threatening illness. It is generally one of the most challenging problems in medical therapeutics. Reports from developing countries show that the clinical presentation, diagnosis and treatment of typhoid fever have significantly altered often leading to missed diagnosis. The consequence of missed diagnosis is immense in terms of burden on limited health resources and patients' suffering. Therefore, its clinical spectrum requires constant reappraisal to update our physicians with current knowledge about pattern of typhoid fever.

## Methods

This cross-sectional study was carried out in the Departments of Paediatrics of Bangabandhu Sheikh Mujib Medical University, Sir Salimullah Medical College and Mitford Hospital and Dhaka Shishu Hospital over a period 2 years from January 2006 to December 2007. Eighty eight consecutive paediatric patients up to 12 years of age of either sex, diagnosed primarily as typhoid fever were included in the study. The diagnostic criteria were either positive blood culture for Salmonella typhi or Salmonella paratyphi or a four-fold rise in antibody titre. A complete blood picture was performed to aid in diagnosis. The laboratory tests performed to diagnose involvement of liver were SGPT and serum billirubin. Relative bradycardia was considered if a child had pulse rate lower than expected average for his age for each degree rise of temperature. WBC count 6000 - 11000/$mm^3$ of blood was considered as relative leucopenia, below 6000/$mm^3$ as absolute leucopenia and > 11000/$mm^3$ as leucocytosis. Anaemia was termed when haemoglobin level fell below 12 gm/dl of blood. Jaundice was defined when serum bilirubin level exceeded above 3 mg/dl. Outcome of treatment was judged clinically at the time of discharge and was categorised as cured, partially cured, deteriorated or died.

## Result

Of the 88 patients, 48(54.5%) were male and 40(45.5%) were female with mean age 5.9 ± 3.0 years and the lowest and highest ages were 1 and 12 years respectively. Over three-quarters (77.3%) of the patients at presentation had been suffering from the disease for 1-2 weeks and the rest (22.7%) for > 2 weeks. Fever was invariably present with 57% being step-ladder pattern of fever and 43% intermittent fever. Majority of the patients had loss of appetite (98.7%) followed by nausea/vomiting (88.6%), diarrhoea (50%), constipation (26.1%), cough (23.9%) and headache (17%). On examination, 85.2% exhibited coated tongue, 78.4% hepatomegaly and 60.2% splenomegaly. The second most common signs were relative bradycardia (43.2%), abdominal distension (36.4%). Six patients had atypical presentation. Of them 2 had dehydration, 1 had burning micturition, 1 jaundice, 1 altered consciousness and 1 pneumonitis (Table I).

Nearly half (48.9%) of the patients had mild anaemia (haemoglobin 7-11.9 gm/dl) and 38.6% moderate anaemia (haemoglobin 10 -11.9 gm/dl). About 20% of the patients had raised ESR (> 50 mm at 1st hour) (Table II). Out of 42 patients who demonstrated positive blood culture, 35(83.3%) had

**Table I. Mode of clinical presentation.**

| Clinical presentation | Frequency | Percentage |
|---|---|---|
| **Symptoms** | | |
| Fever | 88 | 100.0 |
| Chills | 19 | 21.6 |
| Headache | 15 | 17.0 |
| Loss of appetite | 86 | 98.7 |
| Nausea/vomiting | 78 | 88.6 |
| Diarrhoea | 44 | 50.0 |
| Constipation | 23 | 26.1 |
| Cough | 21 | 23.9 |
| Pain in the right hypochondrium | 04 | 4.5 |
| Muscle cramp | 03 | 3.4 |
| **Signs** | | |
| Coated Tongue | 75 | 85.2 |
| Hepatomegaly | 69 | 78.4 |
| Splenomegaly | 53 | 60.2 |
| Relative bradycardia | 38 | 43.2 |
| Abdominal distension | 32 | 36.4 |
| Toxic | 13 | 14.8 |

S. typhi and the rest 7(16.7%) had S. paratyphi (Fig. 1). About 65% of the patients had relative leucopenia, 22.7% absolute leucopenia and 12.5% leucocytosis (Fig. 2). Of the 64 patients who have had serum ALT tested, nearly three-quarter (73.4%) had raised ALT (> 40 IU/L), while 84.1% had raised serum billirubin (9.1%) 1 – 3 mg/dl and 2.3% > 3 mg/dl) (Table III).

**Table II. Distribution of patients by investigations (n=88)**

| Investigations | Frequency | Percentage |
|---|---|---|
| **Level of haemoglobin** | | |
| 7 – 9.9 gm/dl (modearte anaemia) | 34 | 38.6 |
| 10 – 11.9 gm/dl (mild anaemia) | 43 | 48.9 |
| > 12 gm/dl (normal) | 11 | 12.5 |
| **ESR (at the 1st hour)** | | |
| < 50 | 71 | 80.7 |
| > 50 | 17 | 19.3 |

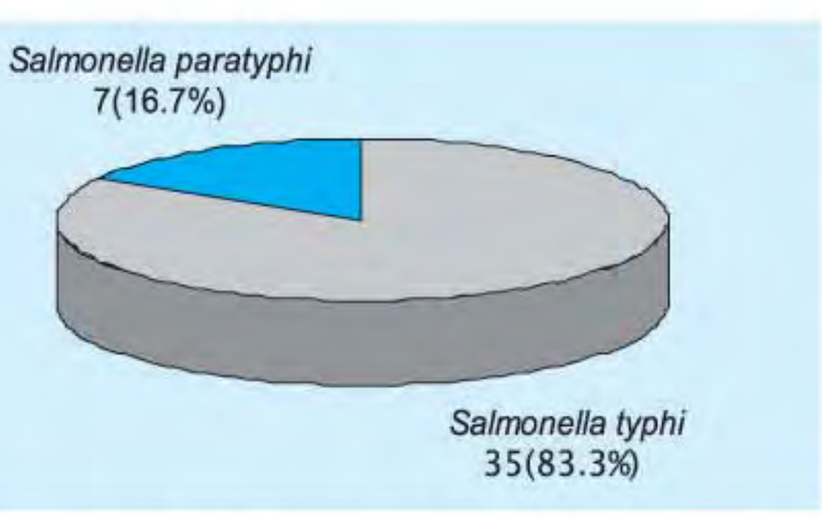


Fig 1: Distribution of patients by type of organism (n=42)

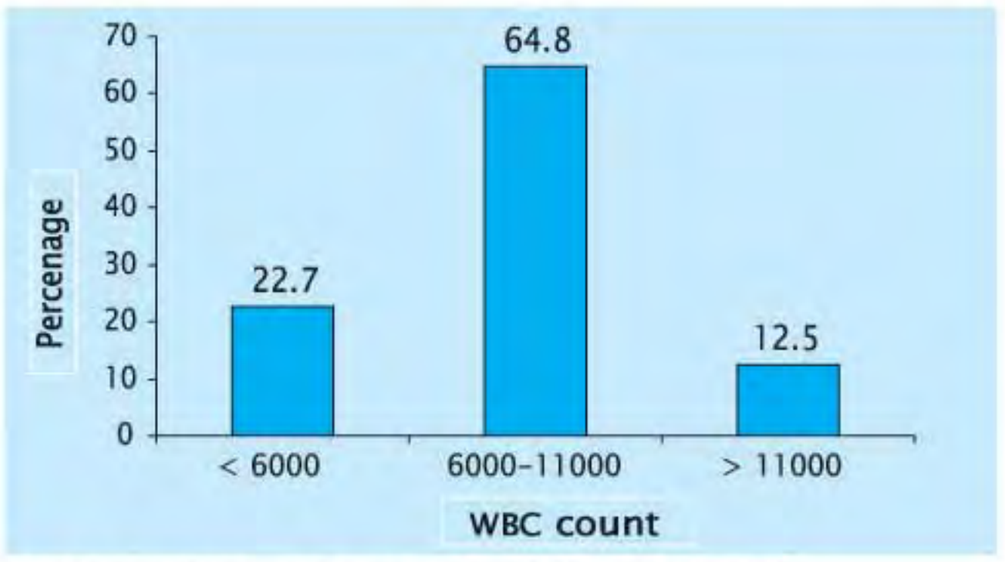


Fig 2: Distribution of patients by WBC count (n=88)

**Table III. Distribution of patients by liver function test**

| Liver Function test | Frequency | Percentage |
|---|---|---|
| **ALT (U/L) (n = 64)** | | |
| < 40 | 17 | 26.6 |
| > 40 | 47 | 73.4 |
| **Serum Billirubin (mg/dl) (n=63)** | | |
| < 1 | 53 | 84.1 |
| 1–3 | 08 | 9.1 |
| > 3 | 02 | 2.3 |

## Discussion

The clinical profiles of typhoid fever are varied and atypical manifestation often makes a serious diagnostic problem, especially in children. The present study was conducted to assess the current pattern of typhoid fever. In our study we found mean age of the patients to be 6 years with youngest and the oldest patients being 1 and 12 years old. No significant association of the disease with sex was evident. The classical typhoid fever is characterized by insidious onset of sustained fever, severe headache, malaise, anorexia, non productive cough (in the early stage of the illness), a relative bradycardia, and hepatosplenomegaly (50%).[4] Common features of typhoid fever found in the study of Haq et al[11] were step-ladder pattern of rise of temperature, loose motion, relative bradycardia and coated tongue. Consistent with the findings of this study, we found step-ladder pattern of fever (57%), loss of appetite (98.7%), coated tongue (85.2%), nausea/vomiting (88.6%), diarrhea (50%), relative bradycardia (43.2%), hepatomegaly (78.4%) and splenomegaly (60.2%). Thus most of the patients in the present series had classic presentation. Dutta et al[2] observed atypical manifestations in nearly half (46.9%) of the total culture positive cases (n = 32) in their study. Atypical manifestations were burning micturition

with normal urine examination (15.6%) diarrhoea (6.2%) and encephalopathy (3.1%) in the first week, isolated hepatomegaly (6.2%), pneumonitis (3.1%) and bone marrow depression (6.2%). They reported that out of 32 Salmonella typhi culture positive patients, 10(31.3%) patients had multidrug resistant (MDR) strain. However, there was no significant difference between patients with MDR strains (50%) and patients having multidrug sensitive strains (45.5%) in terms of atypical manifestations.

The records of 104 patients with culture-proven enteric fever were reviewed and evaluated by Nasrallah and Nassar[12] to study the clinical signs, laboratory findings, pathologic features and complications of the disease. Fever and bradycardia were the leading clinical signs followed by splenomegaly, hepatomegaly and rose spots. The principal complications of enteric fever included anemia, hepatitis and bleeding. Rozkiewicz[13] however, reported a case of typhoid fever in a 5-year old boy presented with respiratory tract infection.

In the present study, the signs of liver involvement were assessed in terms serum ALT and serum billirubin level. The present study showed that nearly three-quarter (73.4%) of the patients had raised ALT (> 40 IU/L), 2.3% had raised serum billirubin (> 3mg/dl) and 9.1% had mildly raised serum bilirubin (1-3 mg/dl). Morgenstern and Hayes[14] studied the course of liver involvement during the first three weeks of typhoid fever on 20 patients and found almost consistent result with present study. In his study, hepatomegaly was found during the 2nd or 3rd week more often than in the 1st wk (36% vs. 11%), whereas jaundice was detectable in 9% of patients after the 1st wk, but never before. SGPT was raised in 91% of cases, during the 2nd and 3rd week but not during the 1st week. This study shows that, although the clinical picture of hepatitis is unusual, liver involvement was invariably present after 1st week, and should not be considered as a complication, but as a feature of the disease.

Of the 42 culture positive cases, 83.3% had S. typhi and 16.7% had Salmonella paratyphi. Verma et al[15] also demonstrated similar finding with 92% of the culture positive cases being S. Typhi and the remaining 8% were S paratyphi. However, a higher incidence of paratyphoid fever (53.8%) compared to typhoid fever (44.9%) has been observed at a tertiary hospital in South India. Relative leucopenia is also a common feature of typhoid fever as majority (64.8%) of the patients had WBC count in the range of 6000 - 11000/mm$^3$, 22.7% below 6000/mm3 of blood, though majority of them had been suffering from the disease for more than 12 days.

## Conclusion

The clinical pattern of typhoid fever conforms with that of classic pattern of step-ladder fever. Anorexia, coated tongue, diarrhoea, relative bradycardia, relative neutropenia, hepatosplenomegaly are still common manifestations of typhoid fever. A few cases had atypical manifestation.

## References


1. Connor BA & Schwartz E. Typhoid and paratyphoid fever in travellars. Lancet InfectDis 2005; 5: 623-8.
2. Dutta TK, Beeresha, Ghotekar LH. Atypical manifestations of typhoid fever J Postgrad Med 2001; 47(4): 248-51.
3. Parry CM Hien TT Dougan G, White NJ, Farrar JJ. Typhoid fever. N Engl J Med 2002; 347: 1770-1782.
4. Agarwal KS, Singh SK & Kumar N. A study of current trend in enteric fever. J Common Dis 1998; 30(3): 171-4.
5. Thisyakorn U, Mansuwan P & Taylor DN. Typhoid and paratyphoid fever in 192 hospitalised children in Thailand. Am J Dis Child 1987; 141: 862-5.
6. Arora RK. Multidrug resistant typhoid fever: a study of an outbreak in Calcutta. Indian Pediatr 1992; 29: 61-6.
7. Durrani AB, Rab SM. Changing spectrum of typhoid. J Pak Med Assoc 1996; 46(3): 50-2.
8. Bhutta ZA. Impact of age and drug resistance on mortality in typhoid fever. Arch Dis Child 1996; 25: 214-7.

9. Sharma A, Gathwal G. Clinical profile and outcome in enteric fever. Indian 1993; 30: 47-50.

10. Gulati PD, Saexena SN, Gupta PS. Changing pattern of typhoid fever. Am J Med 1986; 544: 8.

11. House DJ, Wain VA, Ho TT, Diep NT, Chinh PV, Bay H et al. Serology of typhoid fever in an area of endemicity and its relevance to diagnosis. J Clin Microbiol 2001; 39:1002-1007.

12. Nasrallah SM and Nassar VH. Enteric fever: aclinicopathologic study of 104 cases. Am J Gastroenterol 1978; 69(1): 63-9.

13. Rozkiewicz D, Oldak E, Skorochodzki J, Sulik A and Kurzatkowska B. Typhoid fever with atypical manifestation in 5-year old boy. Wiad Lek 2005; 58: 700-3.

14. Verma M, Parashar Y, Singh A, Kamoji R. Current pattern of enteric fever: a prospective clinical and microbiological study. J Indian Med Assoc 2007; 105(10): 582-6.

15. Morgenstern R, and Hayes PC. The liver in Typhoid fever: always affected, not just a complication. Am J Gastroenterol 1991; 86: 1235-9.

ORIGINAL ARTICLE