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Evaluation of clinico-demographic and laboratory profile of children admitted with enteric fever: A retrospective observational study

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Abstract
Aim: To evaluate the clinical and laboratory findings in children admitted with enteric fever.
Material and Methods: This retrospective observational study was conducted in the Department of Pediatrics of a tertiary care hospital in North India. Medical records of children admitted with a diagnosis of enteric fever (Widal positive or blood culture positive) within a period of one year from July 2018 to June 2019 were retrieved and analyzed. Total 110 children aged below 14 years with enteric fever were included in this study. In each case, the clinical and demographic details and laboratory investigations reports including the blood culture reports and antibiotic sensitivity pattern were collected from the hospital records and analysed.
Results: Out of 110 cases, 75 cases (68.18%) were males and 35 cases (31.82%) were females. Most of the cases were aged between 5 and 10 years (50%). The most common symptom was fever (100%), followed by anorexia (64.55%), vomiting (48.18%), pain abdomen (19.09%), diarrhoea (13.64%), headache (11.82%), and cough (8.18%). The most common sign we observed was coated tongue in 50.90%, hepatomegaly in 44.55%, splenomegaly in 20.90%, hepatosplenomegaly in 12.73% of cases and pallor in 7.27% of cases. Anemia was found in 23 (20.90%) cases, leucopenia and leucocytosis was observed in 39 (35.45%) cases and 16 (14.55%) cases, respectively. Differential leukocyte count was suggestive of neutropenia in 45 (40.90%) cases and neutrophilia in 30 (27.27%) cases. Thrombocytopenia was present in 18 (16.36%) cases. SGOT levels were elevated (>200IU/ml) in 17 (15.45%) cases and SGPT (>200IU/ml) in 15(13.63%) cases. Blood culture was positive for Salmonella Typhi in 7 (6.36%) patients with all isolates sensitive to third gen cephalosporins and fluoroquinolones. 75 (68.89%) cases had a hospital stay of more than 7 days and 33 (30%) required a change of antibiotic to fluoroquinolones.
Conclusion: Typhoid fever is a common paediatric illness with high morbidity and having varied clinical and laboratory presentation. Blood culture though considered standard is rarely positive, mostly due to previous oral antibiotic therapy. This major public health issue can be tackled by bringing awareness among people regarding disease transmission and its various preventive measures.

Keywords: Children, clinical profile, blood culture, typhoid fever, salmonella typhi

Introduction
Enteric fever, representing a systemic infection caused by Salmonella enteric serovar Typhi (S. typhi) and Salmonella enterica serovar Paratyphi (S. paratyphi), is a common cause of morbidity in the developing world, particularly in South and South–East Asia [1, 2]. It is estimated that over 22 million cases and more than 200000 deaths of typhoid fever occurred in the year 2000, with the majority of disease burden being borne by children and adolescents in South and South–East Asia [1]. Highest incidence has been documented in impoverished, overcrowded areas with poor access to sanitation such as the urban slum areas of North Jakarta (Indonesia), Kolkata (India) and Karachi (Pakistan) with annual incidence rates of blood culture–confirmed enteric fever ranging from 180–494/100000 among 5–15 year-olds and 140–573/100000 among those 2–4 years old [3]. Complete blood counts in enteric fever are found to be unremarkable. The hemoglobin is normal in the initial stages but drops with progressing illness. Severe anemia is unusual and should make one suspect intestinal hemorrhage or hemolysis or an alternative diagnosis like malaria. The WBC count is normal in most cases and leucocytosis makes the diagnosis less probable. Leukopenia is perceived to

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be an important feature of typhoid fever and has been reported in only 20-25% cases [4]. The differential count is usually unremarkable except for eosinopenia. Eosinopenia often absolute may be present in 70-80% cases [5]. Presence of absolute eosinopenia offers a clue to diagnosis but does not differentiate enteric fever from other acute bacterial or viral infections. Platelet counts are normal to begin with and fall in some cases by the second week of illness. Overall prevalence of thrombocytopenia is around 10-15% [4]. The emergence of strains of S*almonella typhi* resistant to multiple antibiotics poses a serious problem. Chloramphenicol was considered the antimicrobial gold standard for the treatment of typhoid fever till 1948 [6]. But in the last two decades there has been increase in the resistance of strains of *S. typhi* to chloramphenicol. It was first reported in Britain, in 1950 and in India in 1972 [7, 28]. Gradually, resistance to multiple antibiotics developed [9]. The first major epidemic of multidrug resistant *S. typhi* was reported in 1972 in Mexico [10]. Since then, an increasing frequency of antibiotic resistance has been reported from all parts of the world, but more so from the developing countries [9]. The uses of chloramphenicol, ampicillin and co-trimoxazole have become infrequent and quinolones have become the first line of treatment of typhoid fever. It is one of the common causes of fever in children with varied presentation and significant difference in the signs and symptoms compared to adults. The classic Widal agglutination test is one of the most utilized diagnostic tests for typhoid fever, especially in developing countries. Treatment of typhoid includes proper hydration, correction of electrolyte imbalance, antipyretic therapy and appropriate antibiotics.

Materials and Methods

The present retrospective observational study was conducted in the Department of Pediatrics of a tertiary care hospital in North India. Medical records of children aged below 14 years, admitted with a diagnosis of enteric fever within a period of one year from July 2018 to June 2019 were retrieved and analyzed. These cases were either Widal positive (Widal test TO or TH titre >1:160) or blood culture positive for Salmonella species. The clinical and demographic details were recorded including age, sex, residence and socioeconomic status. The laboratory findings at admission were also noted including haemoglobin, total leukocyte count, differential leukocyte count, platelet count, liver function tests and blood culture and sensitivity pattern. The details of course during hospital stay were also recorded for each patient including total duration of hospital stay, antibiotics given, and whether the patient developed any complication of enteric fever. The data collected was analyzed using appropriate statistical tests.

Results

Table 1 shows that out of 110 cases, 75 cases (68.18%) were males and 35 cases (31.82%) were females. Table 2 shows, most of the cases were aged between 5 and 10 years. 27 cases were below 5 years, representing 24.55%. 28 cases were aged above 10 years, representing

25.45%. 55 cases were aged between 5 and 10 years (50%). In all the above age groups male predominance was seen.

Table 1: Gender distribution of patients

Gender	N = 110	% age
Male	75	68.18
Female	35	31.82

Table 2: Age wise distribution

Age (Years)	N = 110	% age
0-5 years	27	24.55
5-10 years	55	50
10-14 years	28	25.45

As shown in Table-3, most of the cases (68.89%) stayed in hospital for more than 7 days. Duration of hospital stay was less than 7 days in 31.81% of cases. All patients were discharged after an afebrile period of 2-3 days. No life-threatening complication or mortality was observed. Although mild elevated liver enzymes were observed in some cases, no complications were seen in any case.

Table 3: Duration of hospital stay

Duration of hospital stay	N = 110
<7 days	35 (31.11%)
>7 days	75 (68.89%)

Typhoid fever presents with a wide range of symptoms. Due to the use of antibiotics prior to diagnosis, children may not present with typical symptoms. However, in our study, the most common symptom was fever (100%), followed by anorexia (64.55%), vomiting (48.18%), pain abdomen (19.09%), diarrhoea (13.64%), headache (11.82%), and cough (8.18%).

Table 4: Common presenting symptoms

Presenting symptom	N (%)
Fever	110 (100%)
Anorexia	71 (64.55%)
Vomiting	53 (48.18%)
Pain abdomen	21 (19.09%)
Diarrhoea	15 (13.64%)
Headache	13 (11.82%)
Cough	9 (8.18%)

Table 5: Various physical findings

Signs	N (%)
Coated tongue	56 (50.90%)
Hepatomegaly	49 (44.55%)
Splenomegaly	23 (20.90%)
Hepatosplenomegaly	14 (12.73%)
Pallor	8 (7.27%)

Coming to the physical findings, the most common sign we observed was coated tongue in 50.90%, hepatomegaly 44.55%, splenomegaly 20.90%, hepatosplenomegaly in 12.73% of cases and pallor in 7.27% of cases.

Table 6: Laboratory parameters

Laboratory parameters	Abnormal values	N (%)
Hemoglobin	Anemia (Hb <11g%)	23 (20.90%)
Total leukocyte	Leucocytosis (>11000cells/mm^3)	16 (14.55%)
Count	Leucopenia (<4000cells/mm^3)	39 (35.45%)
Polymorphs	Neutropenia (ANC<500/mm^3)	45 (40.90%)
	Neutrophilia (>65%)	30 (27.27%)
Platelets	Thrombocytopenia	18 (16.36%)
SGOT	Elevated SGOT (>200IU/ml)	17 (15.45%)
SGPT	Elevated SGPT (>200IU/ml)	15 (13.63%)
Widal titres	TO >1:160	103 (93.63%)
	TH >1: 160	82 (74.54%)
Blood culture positive	Salmonella Typhi	7 (6.36%)

Table 6 depicts the laboratory parameters. Anemia was found in 23 (20.90%) cases, leucopenia and leucocytosis was observed in 39 (35.45%) cases and 16 (14.55%) cases respectively. Neutropenia found in 45 (40.90%) cases and neutrophilia was found in 30 (27.27%) cases. Thrombocytopenia was seen in 18 (16.36%) cases. SGOT levels was elevated (>200IU/ml) in 17 (15.45%) cases and SGPT (>200IU/ml) in 15 (13.63%) cases. *Salmonella typhi* TO titres >1:160 was seen in 103 (93.63%) cases and TH titres >1:160 in 82 (74.54%) cases. All cases were positive for either TO or TH titres. Blood culture positive for *Salmonella typhi* was noted in 7 (6.36%) cases with all isolates sensitive to third gen cephalosporins and fluoroquinolones. Inj. Ceftriaxone was the most commonly administered first line antibiotic (89% of cases). 33 patients (30%) required change of antibiotic to fluoroquinolones.

Discussion
Although typhoid continues to be seen in large numbers, documented typhoid cases are reducing in recent years. The definitive diagnosis of typhoid fever requires a confirmed diagnosis based on the blood or bone marrow culture. However, blood culture has several limitations including amount of blood required due to low levels of bacteremia and prior antibiotic use [11].

Out of 110 cases, 75 cases (68.18%) were males and 35 cases (31.82%) were females. Similar results were reported in other studies [12]. Most of the cases were aged between 5 and 10 years. 27 cases were below 5 years, representing 24.55%. 28 cases were aged above 10 years, representing 25.45%. 55 cases were aged between 5 and 10 years (50%) In all the above age groups male predominance was seen. A study done by R Modi *et al.* also reported maximum incidence of typhoid in the age group 6 to 10 year [13]. Another study also reported maximum number of cases in the age group above 5 years [14]. The duration of hospital stay varies, with maximum number of cases staying in hospital between 8-10 day. Cases were discharged after 2-3 consecutive days of afebrile period without antipyretics. These results were in accordance with study done by Hyder *et al* [15]. We observed high incidence of typhoid fever in children belonging to low socio-economic status. This can be explained by differences in drinking water sources and hygienic practices like hand washing and sanitary latrine facilities. Similar results were reported in other study [16]. In our study, the most common symptom was fever (100%), followed by anorexia (64.55%), vomiting (48.18%), pain abdomen (19.09%), diarrhea (13.64%), headache (11.82%), and cough (8.18%). A study done by Sinha A *et al* [17]. &

Kapoor JP *et al.* also reported similar results [18]. Other studies also showed similar clinical picture [14-16, 19-21]. Contradictory to this, a study done by Joshi *et al.* reported headache as the most common symptom next to fever [22]. In our study the most common sign we observed was coated tongue in 50.90%, hepatomegaly 44.55%, splenomegaly 20.90%, hepatosplenomegaly in 12.73% of cases and pallor in 7.27% of cases. Study done by Laishram *et al.* also reported coated tongue (80%) as the most common sign followed by hepatomegaly (76%) and splenomegaly (38%) [23]. In other study they had reported relative bradycardia and hepatomegaly as the most common sign [24].

During our study, all cases were positive for Widal test. Blood culture was positive in 6.36% of cases. Other study has reported 16% culture positive cases [15]. A study done by Banu *et al.* also reported 28% culture positive cases [24]. Due to prior use of antibiotics, the culture positive cases are decreasing. Thus, need for other serological tests for diagnosis of typhoid exists. Study done by Modi *et al.* reported 97% Widal positive cases [13]. Anemia was seen in 20.90% of cases. The other studies reported little higher percentage of anemias. A study done by Raj C *et al.* reported anemia in 41.8% of patients and Lefebvre *et al.* reported anemia in 78% of cases [25, 26]. In our study leucocytopenia was found in 35.45% of cases. Similar results have been reported by Lefebvre *et al* [26]. Although leucocytosis is rare in typhoid, our study reported leucocytosis in 14.55% of cases. Thrombocytopenia was found in 16.36% of cases. Elevated SGOT is seen 15.45% of cases and SGPT was raised in 13.63% of the cases. The other study reported elevated liver enzymes in 70% of cases [27].

Conclusion
Typhoid fever is a common pediatric illness with high morbidity and having varied clinical and laboratory presentation. Blood culture though considered standard is rarely positive, mostly due to previous oral antibiotic therapy. It is most commonly observed with unhygienic practices and eating of unhealthy outside food. This major public health issue can be tackled by bringing awareness among people regarding disease transmission and its various preventive measures.

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