Original Article

Clinical Profile and Laboratory Parameters of Enteric Fever in Children Attending Pediatric OPD in A Tertiary Care Center, Dhaka

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Conflict of Interest: None
Received: 01.11.2020
Accepted: 16.03.2021
www.banglajol.info/index.php/JSSMC

Abstract

Introduction: *Enteric fever, a life threatening systemic bacterial infection commonly occurring in developing countries throughout the world. Children suffer the highest burden of this disease among populations in South Asian countries. The clinical presentations are nonspecific, vary in different age group and are often difficult to distinguish clinically from other febrile illness leading to delay in diagnosis, initiation of treatment and ultimately leads to potentially life threatening complications. The aim of our current study was to observe the different pattern of clinical presentation among different age group and laboratory profiles of children presenting with enteric fever.*

Methodology: *This observational type of cross sectional study was carried out at Pediatric outpatient department (OPD) in a tertiary care center, Dhaka, Bangladesh among 80 children during one-year period from March 2019 to February 2020. 1 to 15 years old children diagnosed as enteric fever on the basis of clinical presentation and confirmed by laboratory investigations were enrolled in this study.*

Results: *Total 80 children presenting with fever for ≥4 days with strong clinical suspicion of enteric fever followed by laboratory confirmation were included in this study. Children with fever that mimic other febrile illness and those who were already on antibiotic treatment were excluded. We categorized the children in 3 age groups to see the variability of symptoms and signs in different age group. Majority (62.5%) of the study population were school aged children with a male to female ratio of 1.5:1. 68.7% children were from lower class family habituated to drink un boiled supply water (60%) and consumed both homemade and outside foods (66.2%). Fever (100%), anorexia (80-90%), vomiting (30-60%) and coated tongue (70-80%) were consistently present in all age groups. Preschool aged children commonly presented with diarrhea (70%), pallor (60%) and hepatomegaly (70%), whereas abdominal pain (84%), constipation (60%), hepatomegaly (70%) and or splenomegaly (20%) was observed among school aged children. Adolescent group had headache (80%), myalgia (70%) and cough (60%) as their prominent symptoms. Laboratory parameters revealed leukocytosis in 45%, positive Widal test among 62.4% and positive blood culture in 37.5% study group.*

Conclusion: *Enteric fever still remains a serious public health concern in pediatric groups in under developed and developing countries mostly due to substandard drinking water supply, defective sewage system and poor sanitation. Early and accurate diagnosis of this disease followed by initiation of appropriate treatment is crucial in lowering case fatality and also identify carriers those may be responsible for acute outbreak of enteric fever.*

Key Words:
Blood culture & sensitivity, Out patienrt department

[J Shaheed Suhrawardy Med Coll 2021; 13(1): 50-57]
DOI: https://doi.org/10.3329/jssmc.v13i1.60932

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Introduction

Typhoid fever, also known as enteric fever, is a potentially fatal multi systemic illness caused primarily by *Salmonella enterica* serotype *typhi* and to a lesser extent, *S enterica* serotypes *paratyphi* A, B and C. The terms typhoid and enteric fever is commonly used to describe both major serotypes.[1] The disease remains a serious health threat in the developing world, especially for children.[2] It predominantly affects children and young adults because they either lack natural immunity or experience high level of exposure to fecal pathogen.[3]

Population-based studies from South Asia indicate that young children under 5 years of age bear a large burden of S. Typhi infection.[4, 5] In the developing world, incidence of typhoid fever ranging from 100-1,000 cases per 100,000 populations. Almost 80% of the cases are in Asia; the rest occur mainly in Africa and Latin America.[6] Typhoid fever occurred in more than 20 million people in the year 2000 and causes approximately 200 000 deaths annually.[7] More than 90% of typhoid fever cases are estimated to occur in Asia. In India and Bangladesh, the highest incidence has been observed among children aged 5–9 years. In Bangladesh, the incidence of typhoid fever was 2.0 episodes/1000 person-years, with a higher incidence in children aged <5 years (10.5/1000 person-years) than in older persons (0.9/1000 person-years) (relative risk=12, 95% confidence interval (CI) 6.3-22.6). The incidence of paratyphoid fever was 0.4/1000 person-years without variation by age group.[8,9,10]

This increased prevalence of typhoid fever in the developing and under developed countries are due to unsafe drinking water supply, poor sanitation, defective sewage system and unhygienic food handling practices.[11] India, Pakistan and Bangladesh are the top 3 countries for travel associated typhoid and paratyphoid fever cases.[12]

There is no major difference in typhoid/paratyphoid fever overall by gender (male to female ratio 1.1:1). The highest notification rate (0.59 cases per 100, 000 populations) was reported in 5 to 14 years old males.[13] In endemic countries, the highest incidence is seen in younger children, whereas incidence is similar in all age groups in low burden settings. A study from 2004 used data from published studies to extrapolate incidence rates by age group and reported the highest incidence in children under the age of 5 in high incidence settings.[14]

The most common mode of transmission of this infectious diseases is through ingestion of food and water contaminated with the organism. The incubation period of enteric fever is 7-14 days but depends on infecting dose and ranges from 3-30 days. The clinical presentation varies from mild to severe illness depending on the factors influencing the severity. The presentation also varies according to age and in different parts of the world. In pediatric age group it can present as sepsis in neonates, diarrhea in infants and as lower respiratory tract infection in older children. The classical presentation of enteric fever in children includes high grade fever, anorexia, vomiting, abdominal pain, diarrhea/constipation, toxicity, coated tongue, hepatosplenomegaly and rashes.[15]

For supporting the diagnosis of the disease laboratory based investigations are essential which includes, complete blood count, blood culture and sensitivity and Widal test during the 1st week of illness, stool culture from 2nd week and onwards, urine culture in 3rd and 4th week. The gold standard of diagnosis is isolation of the organism from blood, bone marrow aspirate, feces and urine. Unfortunately, these facilities are often not available in areas where typhoid fever is endemic.[16]

Untreated enteric fever is a grueling illness that may progress to delirium, obtundation, intestinal hemorrhage, bowel perforation and death.[17] So early and definitive diagnosis and initiation of appropriate antibiotic treatment is crucial in management of enteric fever cases and avoidance of life threatening complications. Our current study was conducted with an aim to see the variable clinical presentation among different pediatric age group and laboratory parameters of children diagnosed with enteric fever. Due to high prevalence we should also think about its possible effective preventive measures and grow public awareness on maintaining personal hygiene.

Materials and Method

Study setting

The current study was conducted at a tertiary care hospital located at the center of capital city Dhaka. The patients included in this study came from surrounding areas like Green Road, Panthopath, Elephant Road, Dhanmondi, Mohammadpur and Azimpur. These are quiet densely populated areas where a combination of lower, middle and upper class people reside. There are also some slum areas in these locations which are inhabited by poor and lower class families where residential, sanitation, drinking water supply and sewage conditions are typical of any congested urban settlement. As a result of which communicable diseases like respiratory tract and gastrointestinal tract infections are very frequent among population residing in these areas particularly affecting pediatric age groups.

Study procedure

This cross sectional observational study was conducted during 1-year period from March 2019 to February 2020 among 80 children attending Pediatric outpatient department (OPD) in a tertiary care hospital. Children aged 1-15 years presenting with history of fever for at least ≥4 days with clinical symptoms strongly suspicious of enteric fever, without history of antibiotic pretreatment and confirmed by Blood Culture and Sensitivity and or positive Widal tests were included in the study. Study population showing strong suspicion of other febrile illness like

Dengue, Malaria, Meningitis, UTI, acute gastroenteritis was excluded from this study. Information regarding sociodemographic data (age, sex, socioeconomic condition), food habit, drinking water source were collected in an interviewer administered questionnaire on 1st day of visit to OPD. Blood tests were sent on the same day followed by initiation of empirical antimicrobial treatment. Investigation reports were collected on availability and treatment was changed if required (nonresponding patients or drug resistant cases).

A small number of children were admitted indoor due to marked toxicity and presence of other indications of hospitalization and were managed accordingly. Case fatality rate was zero. Informed consent was obtained from the accompanying caregiver of the child.

Laboratory investigations

To support the diagnosis of enteric fever the following investigations were sent in all cases on the 1st day of visit to OPD those who fulfilled the inclusion criteria. These included complete blood count (CBC), Blood Culture and Sensitivity (Blood C/S) and Widal test.

Blood C/S was done using Bact/Alert, Computerized bacterial detection system. Culture was incubated aerobically for 24/48/72 hours. Widal test was done among all study group. Though not specific for enteric fever, in typhoid endemic areas like Bangladesh, this test is widely available, easy to perform, cost effective and gives quick result. This test also helps in presumptive diagnosis of enteric fever. Widal test titre of TO > 1:160 for both O and H antibody or at least 4-fold rise in antibody titer was considered to be significant.

Ethical consideration

The proposal of the study was approved by the Ethical Committee of Green Life Medical College. Written informed consent of the parents of all study population and consent of the patients who were older than 7 years were taken. Confidentiality of the data derived from the sample were maintained.

Statistical analysis

The data were entered into statistical package for social science (SPSS) version 22 for windows. Categorical data was presented as frequency and percentage in tables. Comparison of categorical data between different groups was done by Chi square test.

Case definition of Enteric Fever

A suspected case of enteric fever was defined as any child presenting with history of fever of > 100.4°F for ≥3 days plus disturbances in abdominal function like abdominal pain, vomiting, constipation/diarrhea is suggestive of enteric fever in epidemiological area like Bangladesh. A laboratory confirmed case of enteric fever was defined as a patient whose blood culture was positive for *Salmonella* typhi/paratyphi.

Results:

Total 80 children diagnosed as enteric fever on the basis of strong clinical suspicion and confirmed by positive Blood C/S and or positive Widal test were enrolled in the study. Table 1 shows majority of study population were school aged (62.5%), followed by adolescent 25% and 1-5 years old were 12.5%. There was no child below 1-year-old so this age group was excluded. Out of 80 children 48 (60%) were male and 32 (40%) were female, with a male to female ratio of 1.5:1 (table II).

Table I

Distribution of study population by age (n=80)

Age Group (in years)	Frequency	Percentage (%)
1-5 yrs	10	12.5
6-10 yrs	50	62.5
11-15 yrs	20	25
Total	80	100

Table II

Distribution of study sample by gender (n=80)

Gender	Frequency	Percentage (%)
Male	48	60
Female	32	40
Total	80	100

Table III shows socioeconomic status of the parents of study population. It reveals, 68.7% belonged to lower class family followed by middle class 21.2% and upper class 10%. Drinking water source among the study group was mainly supply water of which 60% drunk water without boiling and 40% drunk boiled supply water (table IV). 33.7% children had history of ingestion of solely homemade foods whereas majority children (66.2%) were habituated to consume both homemade and outside foods (table V).

Table III

Distribution of study population by socioeconomic status of parents (n=80)

Socioeconomic status of parents	Frequency	Percentage (%)
Lower	55	68.7
Middle	17	21.2
Upper	08	10
Total	80	100

Table IV

Distribution of study sample according to source of drinking water supply (n=80)

Source of Drinking water	Frequency	Percentage (%)
Supply water Without boiling	48	60
Supply water With boiling	32	40

Table V

Distribution of study population by food habit (n=80)

Food habit	Frequency	Percentage (%)
Accustomed to only Homemade foods	27	33.7
Accustomed to both Homemade & outside foods	53	66.2

Table VII shows common symptoms of the study group. Fever and anorexia was seen among all children (100%) with enteric fever followed by vomiting (60%), diarrhea (57.5%), abdominal pain (50%), constipation (42.5%) and cough in 32.5%. 8 (10%) children from adolescent group complained of headache and 5 (6.2%) had myalgia. Table 8 shows distribution of sample according to frequency of signs. 68 (85%) had coated tongue, 55 (68.7%) had toxic look, abdominal tenderness among 30 (37.5%), hepatomegaly (60%), splenomegaly (18.7%) and pallor was seen among 31.2%.

Table VI

Clinical features of study population at presentation (n=80)

Clinical features	Number of cases	Percentage (%)
Fever	80	100
Anorexia	80	100
Vomiting	48	60
Abdominal pain	40	50
Diarrhea	46	57.5
Constipation	34	42.5
Headache	08	10
Myalgia	05	6.2
Cough	26	32.5

Table VII

Symptoms of enteric fever by age of study population (n=80)

Symptoms	1-5 years			6-10 years			11-15 years		
	N	n	%	N	n	%	N	n	%
Fever	10	10	100	50	50	100	20	20	100
Anorexia	10	08	80	50	45	90	20	16	80
Vomiting	10	04	40	50	30	60	20	06	30
Abdominal pain	10	03	30	50	42	84	20	12	60
Diarrhea	10	07	70	50	20	40	20	12	60
Constipation	10	03	30	50	30	60	20	08	40
Headache	10	02	20	50	20	40	20	16	80
Myalgia	10	0	0	50	10	20	20	14	70
Cough	10	03	30	50	20	40	20	12	60

Table VIII

Signs of enteric fever by age of study population (n=80)

Signs	1-5 years			6-10 years			11-15 years		
	N	n	%	N	n	%	N	n	%
Coated tongue	10	07	70	50	16	80	20	15	75
Toxic look	10	04	40	50	30	60	20	06	30
Abdominal tenderness	10	03	30	50	42	84	20	12	60
Hepatomegaly	10	07	70	50	30	60	20	08	40
Splenomegaly	10	01	10	50	10	20	20	02	10
Pallor	10	06	60	50	20	40	20	02	10
Rash	0	0	0	0	0	0	0	0	0

Complete blood count report of majority of study population showed leukocytosis (45%), leucopenia in 32.5% and normal WBC count among 22.5% (table IX). Positive Blood C/S was seen among 30 (37.5%) children with isolation of either salmonella typhi or paratyphi. Culture positive rate was highest among school aged children (25%) followed by adolescent group (10%) and (2.5%) positivity rate among 1-5 years old (table X). Table 11 shows highest (37.5%) positive Widal test result among school aged children followed by positive Widal test 18.7% among adolescent and 6.2% among 1-5 years group.

Table IX

Distribution of study population by Total Leucocyte Count (n=80)

Total WBC count/mm^3	Number of cases	Percentage (%)
<4000	26	32.5
4000-11,000	18	22.5
>11,000	36	45

Table X

Distribution of study population by Blood C/S positivity (n=80)

Age group	Blood C/S positive Frequency	Blood C/S positive Percentage
1-5 years	02	2.5
6-10 years	20	25
11-15 years	08	10
Total	30	37.5

Table XI

Distribution of study population by Widal test positivity (n=80)

Age group	Widal test positive Frequency	Widal test positive Percentage
1-5 years	5	6.2
6-10 years	30	37.5
11-15 years	15	18.7
Total	50	62.4

Table XII

Relation of food habit of the study population with Blood C/S and Widal test positivity

Food habit	Blood C/S positive	Widal test positive
Accustomed to only homemade food	09 (34.6%)	16 (20%)
Accustomed to both Homemade and Outside foods	21 (70%)	34 (42.5%)

Table XII shows relation of food habitus with blood C/S and Widal test positivity. Positivity rate of both tests were seen higher among children eating both homemade and outside foods. Widal test positive was seen among 34 (42.5%) children eating food from various sources and 16 (20%) among children eating only homemade foods. Blood C/S positive rate was higher 21 (70%) among children habituated to consume both homemade and junk foods, whereas 9 (34.6%) among children eating only homemade foods.

Discussion

Enteric fever, a potentially life threatening systemic illness is one of the leading causes of morbidity and mortality in developing countries, the pediatric age group being more vulnerable. In our present study, 80 children aged 1 to 15 years diagnosed as enteric fever on the basis of clinical suspicion followed by laboratory confirmation were analyzed. Majority children were school aged (62.5%) followed by adolescent (25%) and under 5 years (12.5%) (Table 1). The habit of school going children to consume street foods and drinking unsafe water from school or even eating unhieginically prepared canteen snacks predispose them to develop this illness in this age group. The finding of increased prevalence among this age group child was similar to other studies by Md. Ibrahim Khalil et al (70%), AFM Arshedi Satter et al (79.7%), Narendra Laishram et al (51%) and Ranganatha et al (47.8%). [15,17,18,19] However, study by Siddique SS showed increased prevalence among 2-7 years old children (44.5%) and 10.5/1000 person among children aged under 5 (Aliya Naheed et al).[20,21] Study by Aliya Naheed conducted at urban slum Dhaka revealed that the highest incidence of enteric fever was seen among under 5 children with increased case fatality in this age group.[21]

Male to female ratio in our study was 1.5:1 (Table 2). This finding of male predominance was similar to multiple studies done in Bangladesh and abroad.[21] Majority of our study population (68.7%) were from lower class family followed by middle class (21.2%) and upper class 10% (Table 3). The lower class people of our study group resided in urban slum areas with poor access to safe drinking water, lack of adequate hygiene and improper sewage system. Knowledge of basic hygiene like washing hands before eating or preparing food and after return from toilets, drinking safe water and eating street or cheap restaurant foods were the usual habit of this group leading to increased chance of contamination among them. Study by Md. Ibrahim Khalil et al and Aliya Naheed et al also revealed similar result of increased prevalence of the disease among population residing in urban slum areas.[18,21] 10% of our study population who belonged to upper class family also suffered from the disease which was probably due to habit of consuming restaurant foods regularly where food hygiene and handling is doubtful.

Drinking water source was un boiled supply water in 60% cases and boiled supply water in 40% children (Table 4). Other studies by Chandrashekhar et al, Sameer Sarwat et al, Md. Ibrahim Khalil et al and AKM Matiur Rahman et al showed increased incidence of enteric fever among population using un boiled drinking water in 73.1%, 75.3%, 66.7% and 62.5% respectively.[11,18,22,23]

Majority (66.2%) of our study population were habituated to eat both homemade and outside foods in comparison to children eating only freshly and hygienically prepared homemade foods in 33.7% (Table 5). Increased incidence of enteric fever was seen among this majority group. This finding was consistent with study result by AKM Matiur Rahman et al[11], Ranganatha[15] et al who found drinking unsafe water and eating unhealthy outside foods in 65% and 40% cases respectively.

Widespread antibiotic pretreatment for febrile illness, prevalence of self-medication and poor health care seeking behavior causes musk of typical clinical manifestation and diagnostic era of enteric fever. So children with history of pre antibiotic treatment for their current fever were excluded from this study. Common symptoms of our study population at presentation included fever, anorexia, vomiting, abdominal pain, constipation/diarrhea, headache, myalgia and cough. On examination we found toxic look, coated tongue, abdominal tenderness, hepatomegaly with or without splenomegaly and pallor. In our study these features were categorized according to different age groups. Fever (100%), anorexia (80-90%), vomiting (30-60%), and coated tongue (70-80%) was consistently found in all study group. Diarrhea (70%), pallor (60%) and hepatomegaly (70%) were common among preschool aged children. School going children commonly presented with abdominal pain (84%), constipation (60%), hepatomegaly (70%) and splenomegaly in 20% cases. Adolescent commonly presented with headache (80%), myalgia (70%) and cough (60%) as prominent symptoms (Table 6, 7, 8). This variability of presentation in different age group was found in another study by Asma Azmatullah et al.[24] Study by Chandrashekhar et al showed anorexia and diarrhea were the predominant symptoms among under 5 children, whereas cough was a common symptom of children older than 5 years.[22]

The mean white blood cell count (WBC) was 6120 cells/mm^3 with a range from 2500 to 23, 000 cells/mm^3. Majority (45%) of our study population had leukocytosis (>11,000 cells/mm^3) followed by leucopenia (<4000 cells/mm^3) in 32.5% and normal white blood cell count (4000-11,000 cells/mm^3) in 22.5% (Table 9). The finding of leukocytosis was similar to study by Asma Azmatullah et al and Sameer Sarwat et al who found leucopenia in only 4.1% of their study group.[23,24] However, Farhana Rahat et al in their study found normal WBC count in majority (76%) of their study population.[25] Serologic testing for Salmonella lacks overall sensitivity and specificity and varies with the stage of infection. The WBC count in enteric fever is often low and leukocytosis is common during the 1st 10 days of illness in children.[26]

Diagnosis of enteric fever on the basis of clinical features alone is difficult, as the symptoms are diverse and often similar to other common febrile illness specially during the 1st week of illness. The gold standard of diagnosis of this disease is isolation of the causative agent from blood, stool, urine or bone marrow in 1st, 2nd 3rd and 4th week and onwards. As our study population presented during the 1st week of fever we performed Blood C/S and Widal tests in all study group. Sample for Blood C/S was collected before initiation of antibiotic to avoid lower C/S positivity rates.

Our study showed Blood C/S for salmonella typhi/para typhi positive among 30 children (37.5%) (Table 10). This finding was lower in comparison to other studies by Farhana Rahat et al (43.3%) and by Jeeyani HN et al (49.3%).[25,27] Culture positivity rate was 32.5% in a study by Md. Ibrahim Khalil and 20% by Ranganatha et al.[15,18]

Widal test is performed for presumptive diagnosis of enteric fever. Although the test is no longer performed in United States and other developed countries due to lack of sensitivity and specificity, it is still widely used in enteric endemic areas due to cost effectivity and quick result.[22] A raised TO > 1:160 was considered to be significant in our study. The total Widal test positive cases was 62.4% in our study (Table 11). Widal test positive rate was higher in study conducted by Md. Ibrahim Khalil et al and Sudharsan Raj C et al.[18,29]

In our current study we observed the relation of food habit of the children with Blood C/S and Widal test positivity rate (Table 12). Study group who were habituated to eat both homemade and outside foods had more Blood C/S (70%) and Widal test (42.5%) positive values in comparison to children eating only homemade foods (Blood C/S positive in 34.6% and Widal test positive in 20%). Similar finding was observed in study by Md. Matiur Rahman et al.[11]

Enteric fever is preventable through proper hygiene practice, drinking safe water and maintaining food hygiene. Another preventive approach is vaccination. Center for Disease Control and Prevention (CDC) recommends vaccination for people traveling to places where typhoid fever is common, such as South Asia, especially India, Pakistan, or Bangladesh.[30] As typhoid vaccines are not 100% effective and require booster dose, there is no alternative to safe eating and drinking habits to help prevent infection.

Conclusion

Despite of vast improvement in control of communicable diseases, enteric fever is still endemic in most underdeveloped and developing countries affecting all age groups. By maintaining simple hygiene practices one can prevent the disease. Now it's time for the government, policy makers, community leaders and health care professionals to raise not only awareness about this disease but also provision of safe drinking water, proper sewage system, strict monitoring of food hygiene in food shops, educational institutions and hostels should be ensured.

Limitation of the study

Our current study was conducted among small sample size (80 children) at a single center tertiary care hospital, Dhaka. So the study findings may not represent the clinical presentation and laboratory findings of children suspected of suffering from enteric fever of the whole country, specifically those of the rural areas.

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