

## Haematological Profile of Enteric Fever in Children: Study in Dhaka Shishu (children) hospital, Dhaka, Bangladesh.

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### Abstract

**Introduction:** Enteric (Typhoid) fever is considered to be a major public health problem in many developing countries of the world and it has also been gradually testified from the developed countries. It is mainly caused by a bacterium called *Salmonella entericaserovarTyphi* which is related to the bacteria that cause salmonella food poisoning. It is clinically demonstrated by a tenacious fever, headache, constipation, extreme fatigue, joint pain, splenomegaly, inflammation of the intestine with the formation of intestinal ulcers, a characteristic rose-spot eruption on the abdomen. Almost 80% of cases and death occur in Asia. **Aim of the study:** To assess the haematological factors of Enteric fever in children of Bangladesh. **Material & Methods:** This was an observational study which was conducted at the Department of Paediatric Infectious Diseases and Community Paediatrics, Bangladesh Institute of Child Health (BICH), Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh during the period from January 2018 to December 2018. Total 133 cases were selected using random sampling technique. Informed written consent was obtained from each patient before the procedure. A pre-designed questioner had been used to collect all the necessary data from the participants. Program MS-Excel was used in collecting data, SPSS version 21 was used in analyzing data. On the other hand, several tables were used to disseminate data. Following was the inclusion and exclusion criteria of the present study. **Results:** In this study 50(37.6%) cases were culture positive where 44(88%) cases were *S. typhi* and 6(12%) cases were paratyphi; and 83(62.4%) cases were culture negative. Widal test results by the duration of illness in presenting with clinical presentation suspicious of typhoid fever shows that, of the total 121(91%) positive cases duration of illness of  $\leq 7$  days was 50(86.2%), duration of illness of  $>7$  days was 71(94.7%); of the total 12(9%) negative cases duration of illness of  $\leq 7$  days was 8(13.8%), duration of illness of  $>7$  days was 4(5.3%). widal + CS positive shows, 44(33.1%) cases were widalpositive+CS positive, 83(62.4%) cases were widalpositive+CS negative, 6(4.5%) cases were widalpositive+CS negative. Of the total 121 widal test positive, 44 were blood culture positive and 77 were blood culture negative; while out of 12 widal test negative, 6 were blood culture positive and 6 were blood culture negative. **Conclusion:** The present study demonstrated the cases those are widalpositive+CS positive, widalpositive+CS negative, widalpositive+CS negative. Further studies are needed to study the blood indices in patients with typhoid fever.

**Key Words:** Enteric Fever, Typhoid, Haematological Factors, Widal test, Paediatrics.

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### I. Introduction

Enteric (Typhoid) fever is considered to be a major public health problem in many developing countries of the world and it has also been gradually testified from the developed countries. Almost 80% of cases and death occur in Asia.<sup>1</sup> It is mainly caused by a bacterium called *Salmonella entericaserovarTyphi* which is related to the bacteria that cause salmonella food poisoning. Typhoid fever is clinically demonstrated

by a tenacious fever, headache, constipation, extreme fatigue, joint pain, splenomegaly, inflammation of the intestine with the formation of intestinal ulcers, a characteristic rose-spot eruption on the abdomen.<sup>2</sup> After consumption the bacteria, there is an incubation period of about 10 – 14 days.<sup>3</sup> The main cause of typhoid fever is the invasion of *S. typhi* and development within the mononuclear phagocytic cells in the liver, spleen, lymph nodes and Peyer's patches of ileum.<sup>4</sup> By isolation of bacilli from blood, stool, urine and serologically, studies have been performed by Widal test and by the rising titre of antibodies in both ill persons and asymptomatic carriers.<sup>5</sup> Even though culture remains the gold standard for the ultimate diagnosis of salmonella, but for the lack of accessibility of information and longer time in isolating the organism, Widal test has been preferred and still is widely used.<sup>6,7</sup> Increasing titers of "O" and "H" antigens of Widal test are of diagnostic value.<sup>8</sup> Typhoid fever has been associated with some physiological changes in affected persons and these changes form part of the pathophysiology of the disease. The hematological deviations are common in typhoid fever and these include anaemia, leucopenia, eosinophilia, thrombocytopenia, elevated ESR and sub clinical spread intravascular coagulation.<sup>1,4</sup> Usually non-specific parameters are anemia, elevated ESR, thrombocytopenia, reactive lymphocytosis, increased PT, APTT and observed decreased fibrinogen levels. Leukopenia considers as a key feature of Enteric fever, but studies have exposed it to be existing in only 20-25% of cases.<sup>9</sup> Evidence says leukopenia seen in children as a relatively common occurrence of leukocytosis or the presence of a leukocyte count within the normal range.<sup>10,11</sup> In point of fact, leukocytosis is almost 3 times more probable to take place in children than in adults, while children under 5 are >4 times more likely to have an elevated leukocyte count rather than older children. Unusual hematologic complications testified in enteric fever consist of dispersed intravascular coagulation, hemophagocytosis, bone marrow dominance, and bone marrow granulomata, all of which are more frequently labelled in adults than in children.<sup>12</sup>

## II. Methodology And Materials

This was an observational study which was conducted at the Department of Paediatric Infectious Diseases and Community Paediatrics, Bangladesh Institute of Child Health (BICH), Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh during the period from January 2018 to December 2018. The aim of the study was to assess the haematological factors of Enteric fever in children of Bangladesh. Total 133 cases were selected using random sampling technique. Informed written consent was obtained from each patient before the procedure. A pre-designed questionnaire had been used to collect all the necessary data from the participants. Program MS-Excel was used in collecting data, SPSS version 21 was used in analyzing data. On the other hand, several tables were used to disseminate data. Following was the inclusion and exclusion criteria of the present study.

- **Inclusion Criteria**
  - Patients admitted at the Department of Paediatric Infectious Diseases and Community Paediatrics, Bangladesh Institute of Child Health (BICH), Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh
  - Patient aged below 16 years
- **Exclusion Criteria**
  - Patients aged above 16 years

## III. Results

Among the total 133 study subjects, 60.2% were aged <60 months, and the rest 39.8% were aged ≥60 months; Mean age (Mean±SD) in months were 55.26±36.20; age range were between 7-172 months. Male subjects were 71 (53.4%) and female subjects were 62 (46.6%); male to female ratio was 1.1: 1. Of the total study subjects, 116(87.2%) were from urban area, 4 (3%) were from urban slum area and the rest 13 (9.8%) were from rural area. Table II reflects the distribution of the study subjects by H/O typhoid vaccination. Of the total study subjects, only 11.3% had H/O typhoid vaccine and the rest 88.7% had never taken the vaccination. Distribution of the study subjects by clinical parameters (Table III) shows, 129 had fever and Mean±SD was 10.23±5.71. It was observed 92(69.2%) had continuous fever and 41(30.8%) had intermittent. Symptoms were, 53(39.8%) abdominal pain, 48(36.1%) diarrhea, 25(18.8%) constipation, 52(39.1%) vomiting and 14(10.5%) others. Signs were, toxic 85(63.9%), median temperature in (25<sup>th</sup>, 75<sup>th</sup> centile) 102.0 (101.0, 103.0), median pulse in (25<sup>th</sup>, 75<sup>th</sup> centile) 100 (96.0, 110.0), coated tongue 99(74.4%), rose spots 19(14.3%), pallor 69(51.9%), jaundice 6(4.5%), abdominal distension 20(15%), abdominal tenderness 18(13.5%), hepatomegaly 22(16.5%), splenomegaly 5(3.8%) and others 4(3%). Laboratory investigations and Widal test is shown in Table IV and Table V respectively. In Table VII, culture positive is shown which demonstrates that, 50(37.6%) cases are positive where 44(88%) cases were *S. typhi* and 6(12%) cases were paratyphi; 83(62.4%) cases were negative. Widal test results by the duration of illness in presenting with clinical presentation suspicious of typhoid fever (Table VIII) shows that, of the total 121(91%) positive cases duration of illness of ≤ 7 days was 50(86.2%), duration of illness of >7 days was 71(94.7%); of the total 12(9%) negative cases duration of illness of ≤ 7 days was 8(13.8%), duration of illness of >7 days was 4(5.3%). Widal + CS positive (Table IX)

shows, 44(33.1%) cases were widalpositive+CS positive, 83(62.4%) cases were widalpositive+CS negative, 6(4.5%) cases were widalpositive+CS negative. Diagnostic test evaluation is shown in Table X. Of the total 121 widal test positive, 44 were blood culture positive and 77 were blood culture negative; while out of 12 widal test negative, 6 were blood culture positive and 6 were blood culture negative.

**Table I:** Demographic characteristics of the study subjects (n=133)

Demographic characteristics	Frequency	Percentage (%)
<b>Age (in months)</b>		
< 60	80	60.2
≥ 60	53	39.8
Total	133	100.0
Mean±SD	55.26±36.20	
Range	(7 – 172) months	
<b>Sex</b>		
Male	71	53.4
Female	62	46.6
Male : Female ratio	1.1 : 1	
<b>Residence</b>		
Urban	116	87.2
Urban slum	4	3.0
Rural	13	9.8

**Table II:** Distribution of the study subjects by H/O typhoid vaccination (n=133)

H/O of vaccination	Frequency	Percentage (%)
Yes	15	11.3
No	118	88.7
Total	133	100.0

**Table III:** Distribution of the study subjects by clinical parameters (n=133)

Clinical parameters	Frequency	Percentage (%)
Fever	129	97.0
Duration of fever (mean±SD) days	10.23±5.71	
<b>Type of fever</b>		
Continuous	92	69.2
Intermittent	41	30.8
<b>Symptoms</b>		
Abdominal pain	53	39.8
Diarrhoea	48	36.1
Constipation	25	18.8
Vomiting	52	39.1
Others	14	10.5
<b>Signs</b>		
Toxic	85	63.9
Median temperature in (25 <sup>th</sup> , 75 <sup>th</sup> centile)	102.0 (101.0, 103.0)	
Median pulse in (25 <sup>th</sup> , 75 <sup>th</sup> centile)	100 (96.0, 110.0)	
Coated tongue	99	74.4
Rose spots	19	14.3
Pallor	69	51.9
Jaundice	6	4.5
Abdominal distension	20	15.0
Abdominal tenderness	18	13.5
Hepatomegaly	22	16.5
Splenomegaly	5	3.8
<b>Others</b>	<b>4</b>	<b>3.0</b>

**Table IV:** Laboratory investigations (n=133)

Variables	Median	Mean±SD	Range
Hb (gm%)	10.30	10.12±1.59	5.40 – 14.10
TC (mm <sup>3</sup> )	8000.0	8409.5±3366.3	2000-19000
Poly (%)	56.0	56.6±11.47	34 – 80
Lympho (%)	37.0	38.21±11.61	10.0 – 61.0
Platelet count	200000	225376±119245	14600-663000

**Table V: Widal test (n=133)**

Widal test titre(dilution)	TO	TH	AH	BH
1:80	34(25.6%)	58(43.6%)	121(91.0%)	128(96.2%)
1:160	39(29.3%)	33(24.8%)	3(2.3%)	2(1.5%)
1:240	1(0.80%)	0(0.0%)	0(0.0%)	0(0.0%)
1:320	38(28.6%)	24(18.0%)	4(3.0%)	1(0.80%)
1:>320	21(15.8%)	18(13.5%)	5(3.8%)	2(1.5%)

**Table VI: Culture positive (n=50)**

Culture test	Frequency	Percentage (%)
Positive	50	37.6
• S. typhi	44	88.0
• Paratyphi	6	12.0
Negative	83	62.4

**Table VII: Widal test (n=133)**

Widal test titre (dilution)	Blood culture			
	TO	TH	AH	BH
1:80	11(8.3%)	20(15.0%)	46(34.6%)	48(36.1%)
1:160	19(14.3%)	17(12.8%)	1(0.8%)	1(0.8%)
1:240	1(0.80%)	0(0.0%)	0(0.0%)	0(0.0%)
1:320	10(7.5%)	7(5.3%)	0(0.0%)	0(0.0%)
1:>320	2(1.5%)	6(4.5%)	3(2.3%)	1(0.8%)

**Table VIII: Widal test results by the duration of illness in presenting with clinical presentation suspicious of typhoid fever**

Widal test result	Duration of illness		Total	p-value
	≤ 7 days (n=58) No. (%)	> 7 days (n=75) No. (%)		
Positive	50(86.2%)	71(94.7%)	121(91.0%)	0.091
Negative	8(13.8%)	4(5.3%)	12(9.0%)	
Total	58(100.0%)	75(100.0%)	133(100.0%)	

**Table IX: Widal + CS positive**

Variables	Frequency	Percentage (%)
WidalPositive+CS Positive	44	33.1
Widalpositive+CS negative	83	62.4
Widal negative + CS positive	6	4.5
Total	133	100.0

**Table X: Diagnostic test evaluation**

Variables		Blood culture		Total
		Positive	Negative	
Widal Test	Positive	44	77	121
	Negative	6	6	12
Total		50	83	133

#### IV. Discussion

Enteric fever, caused by *Salmonella enterica* subspecies *enterica* serovars Typhi, Paratyphi A, Paratyphi B, and Paratyphi C is a major source of morbidity for human populations in exaggerated counties of the world. Presently, it is assessed that there are more than 26 million patients with a blood culture positive for enteric fever every year with 1% mortality rate.<sup>13</sup> The main stream of remaining epidemiological indication derives from researches in adult populations. There are contradictory estimations about the proportion of syndrome in young children, specifically infants<sup>14-19</sup>, despite the fact a considerable burden of disease is agonized by young children in widespread regions.<sup>14,15</sup> In the present study, of the total 133 study subjects, 60.2% were aged <60 months, and the rest 39.8% were aged ≥60 months. Chandrasekhar, et al.<sup>20</sup> in their study showed that 60% of typhoid patients were above 5 years of age which is almost similar to our study. Another study from a Tertiary care hospital in Chennai, South India showed that 169 (53.48%) out of 316 cases of typhoid fever were > 5 years of age.<sup>21</sup> Also, there were a total of the 14 studies that included to analyze the children under-5 age group, where 3 studies<sup>22-24</sup> estimated that <15% of disease was in this age group, whereas 3

studies<sup>25-27</sup> estimated that more than half the disease occurrence was in this age group. In our study male subjects were 71 (53.4%) and female subjects were 62 (46.6%); male to female ratio was 1.1: 1. Two different studies by Oboegbulam et al.<sup>28</sup> and Agbakwuru et al.<sup>29</sup> showed that typhoid fever is more prevalent in males than females. Meanwhile, Zailani et al.<sup>30</sup> found no influence of age, sex and social class on the distribution pattern of *Salmonella entericaserovar*Typhi and *Salmonella entericaserovar*Paratyphi in Ile-Ife, south western Nigeria. In our study, 129 had fever and Mean±SD duration of the fever was 10.23±5.71. Symptoms in patients were, abdominal pain, diarrhea, constipation and vomiting. There were also signs such as coated tongue, rose spots, pallor, jaundice, abdominal distension, abdominal tenderness, hepatomegaly, splenomegaly and some other symptoms. Typhoid fever normally attacks due to lack of personal hygiene. It mostly occurs to the people live in places with poor sanitation, but particularly where the water supply is responsible to be polluted by human excreta.<sup>31</sup> Studies showed the characteristics presenting features include fever, relative bradycardia, diarrhea or constipation and abdominal pain.<sup>32</sup> In our study, widal test results by the duration of illness in presenting with clinical presentation suspicious of typhoid fever showed that, of the total 121(91%) positive cases duration of illness of ≤ 7 days was 50(86.2%), duration of illness of >7 days was 71(94.7%); of the total 12(9%) negative cases duration of illness of ≤ 7 days was 8(13.8%), duration of illness of >7 days was 4(5.3%). Also, widal + CS positive showed, 44(33.1%) cases were widalpositive+CS positive, 83(62.4%) cases were widalpositive+CS negative, 6(4.5%) cases were widalpositive+CS negative. One of the common features in typhoid fever is the hematological changes including anemia, leucopenia, eosinophilia, thrombocytopenia and sub clinical disseminated intravascular coagulation. hemophagocytosis and bone marrow suppression are considered to be a significant mechanism in producing hematological changes.<sup>33</sup> Toxic marrow suppression during initial septicemia phase of infection is assumed to be a cause of thrombocytopenia.<sup>34,35</sup> The existence of anemia, leucopenia & thrombocytopenia is attributed to invasion of hematopoietic organs by *S. typhi* causing depression of haematopoiesis.<sup>36</sup>

#### LIMITATIONS OF THE STUDY

This was an observational study conducted in a single centered unit. The sample size was comparatively small. So, it might not reflect the scenario of the whole country.

#### V. Conclusion And Recommendations

Enteric fever has noteworthy result on some haematological parameters which can be relief in diagnosis. Hence complete blood count should be well-organized initially by the clinicians for appropriate diagnosis and treatment. The present study demonstrated the cases those are widalpositive+CS positive, widalpositive+CS negative, widalpositive+CS negative. Further studies are needed to study the blood indices in patients with typhoid fever.

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