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"Clinical profile in Children with Enteric Fever: A study in Dhaka shishu(children) hospital, Dhaka, Bangladesh"

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Abstract: *We conducted a cross-sectional comparative study in the Department of Paediatric Medicine of Dhaka Shishu (children) Hospital during the period from 10th October 2013 to 9th April 2014 with the aim was to document clinical profile in Children with Enteric Fever. Our study subjects were divided into three groups: 1) Children suspected of enteric fever; 2) Febrile children (other than enteric fever) and 3) Non-febrile children. Total sample size for this study was 150. Around half of the participants were in the '≤ 5 years' age group. Mean ± SD was (5.874±2.943) for group-I, (5.598±3.000) for group-II and (5.740 ± 2.741) for group-III. More than half of the participants in all groups were males. Male: Female ratio was about 1.2:1 in group-I, 1.5:1 in group-II and 1.4:1 in group-III. There was no statistical deference in age distribution between the groups (p=0.972) and male-female distribution (p=0.563). There was no significant statistical difference in Parent's educational qualification (p=0.801) and job (p=0.079). For both enteric group and non-enteric group, fever was present in all (100.0%) participants. Blood culture was done in all 150 participants. Among all 123 individual were culture negative and the remaining 27 (18.0 %%) were culture positive. All culture positive participants were in Group-I. The agglutinin levels against TO and TH antigen of the three groups; for group-I children were either widal positive or culture positive and/or both, for group-II widal positive cases were confirmed by negative blood culture findings. TO was found 1:160 or more in 52.0% in enteric fever patients and 12.0% of non-enteric febrile patient. TH showed ≤1:160 count in 48.0% group-I and 16.0% of group-II children. When double widal test result was considered, it was positive in 94.0% of enteric fever cases; the remaining 6.0% of cases and most (89.0%) of the non-enteric children were found to be Widal negative. In the conclusion, we can say laboratory findings can help to detect enteric fever patients more accurately and can treat adequately.*

Key words: *Clinical profile, Socio-economic status, Enteric fever*

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I. Introduction

Enteric fever, caused by Salmonella enterica serotype typhi and paratyphi A, B and C, occurs in all parts of the world where there is substandard water supply and sanitation. It has almost been eliminated from developed countries because of sewage and water treatment facilities but remains a common disease and a major cause of morbidity and mortality worldwide, causing an estimated 16.6 million new infections and 600,000 deaths each year[1]. It is endemic in the Indian subcontinent including Bangladesh, South-east and Far-east Asia, Africa and South Central America. The disease can occur in all age group with highest incidence among children[2]. The annual incidence of enteric fever has been reported as more than 13 million cases in Asia[3]. Exposure of the individual to contaminated food or water closely correlate with the risk for enteric fever[4,5]. Enteric fever is a febrile illness of prolonged duration marked by step-ladder pattern of fever, diffuse abdominal pain, frontal headache, delirium, splenomegaly, hepatomegaly and many other systemic manifestations due to bacteremia and septicemia. However, with indiscriminate use of antibiotics multidrug resistant strains of *Salmonella typhi* are emerging with changing clinical pattern posing problem in diagnosis[6]. Widal a serological diagnosis test for enteric fever was founded in 1896 by Georges Fernand Isidore Widal[7]. It is an agglutination reaction demonstrating the presence of lipopolysaccharide (LPS) somatic (O) and flagella (H) agglutinins to Salmonella typhi in the serum of a patient using suspensions of O and H antigens[8]. Commercial kits are

available for antigens of Salmonella para-typhi A, B and C. The recommended method of performing the widal test is by the tube agglutination technique were serial two-fold dilutions of the subject's serum from 1:20 to 1:1280 are tested[9]. Now a days a rapid slide test is most commonly used technique in local laboratories and hospitals because of its convenience. Widal test is easy, inexpensive and relatively non-invasive The widal test has been used extensively in the serodiagnosis of enteric fever and so remains the only practical test available in most developing countries[10], including Bangladesh.

The definitive diagnosis of enteric fever requires the isolation of *Salmonella typhi* or *paratyphi* from the blood, feces, urine or other body fluids. Blood culture is regarded as the gold standard for diagnosis and carry 70-75% diagnostic yield in the first week of illness[11].In developing countries, facilities for isolation and culture are often not available especially in smaller hospitals and rural areas and diagnosis relies upon the clinical features of the disease and the detection of agglutinating antibodies to *S. typhi* and *S. paratyphi* by the Widal test. Bacteria can be isolated from blood in 73-97% of cases before antibiotic use[12]. But in our country bacteria can be isolated from blood is only 40-60% of the cases. The relative low sensitivity of blood culture in diagnosing enteric fever is understandable in the wake of widespread antibiotic use in Bangladesh and the difficulties of obtaining large enough blood volumes for culture from children[13] and the long waiting time for culture results have been identified as reasons for the preference for the widal test[14]. One of the major drawback of widal test is cross-reactivity due to which some other bacteria of same genus often produces false positive results, so the positive results must correlate clinically before prescribing medicine. However, many studies[15-18], have produced data which have casted serious doubts on the value of the Widal Test. Typhidot is another rapid slide test used to ascertain the diagnosis of enteric fever, but not cost effective as widal[19]. So widal test is the choice for diagnosis of enteric fever especially in rural area. Classically, a fourfold rise of antibody in paired sera is considered diagnostic of enteric fever[20]. In enteric fever, however, such a rise is not always demonstrable, even in blood culture-confirmed cases. This situation may occur because the acute-phase sample was obtained late in the natural history of the disease, because of high levels of background antibodies in a region of endemicity, or because in some individuals the antibody response is blunted by the early administration of an antibiotic[21].So, there is a great need for the people to be aware of difficulties in diagnosis and all the consequences of enteric fever and it is the most important area where the health personnel should take serious measures to create an understanding and awareness among the public regarding diagnosis of enteric fever. Enteric fever is endemic in Bangladesh, where there is a high incidence in children[22]. Enteric fever continues to be a major health problem in Bangladesh. Many children with enteric fever are treated at outpatient department as well as inpatient department of the hospital. The Widal test is one of the most utilized diagnostic tests for typhoid fever in developing countries. The unavailability of microbiologic facilities and the long waiting time for culture results have been identified as reasons for the preference for the Widal test; as it remains the only practical test available. However, many studies have produced data which had cast serious doubts on the value of the Widal Test and thus reappraisal of the role of a Widal test is needed. It was mentioned earlier that, a fourfold rise of antibody in paired sera is considered diagnostic of typhoid fever. However, paired sera are often difficult to obtain and specific chemotherapy has to be instituted on the basis of a single Widal test.[10]In view of the doubts expressed on the value of the Widal test, it is thought to be worthwhile to reassess the utility of a single Widal test in the diagnosis of typhoid fever.

II. Objectives

General objective:

To document clinical profile in children with enteric fever

Specific objectives:

To find out sign and symptoms of enteric fever in children in Bangladesh

To document the characteristics of enteric fever in children with enteric fever in Bangladesh

III. Method and Materials

This was a cross sectional comparative study conducted at the Department of Paediatric Medicine of Dhaka Shishu (children) Hospital, Dhaka, Bangladesh during the period from October 2013 to April 2014. We maintained a purposive sampling technique to select study subjects. Subjects were children with or without fever, coming to the Dhaka Shishu Hospital, Dhaka at the age from 2 years to 15 years. We taken 150 children in total and divided into three groups. In each group 50 participants were included. Group-I: enteric fever suspected; group-II: febrile illness other than enteric fever and group-III: a febrile children. Prior to data collection a questionnaire was designed for this study by reviewing all the available questionnaire of previous studies including all variables. The questionnaire was finalized following pretesting. After selection of a participant according to the inclusion and exclusion criteria and getting written informed consent from their guardian, they were included in respected group and their demographic and clinical information was gathered from the respondent by asking face-to-face questions. Blood specimens were collected from children of all the

groups and sent to the Departments of Microbiology and pathology, Dhaka Shishu(children) Hospital (Bangladesh Institute of Child Health), Dhaka, Bangladesh. Data were presented in the form tables and graphs.

Inclusion criteria:

Group I: Age: 2 to 18 years, both sexes, Febrile Children suspected of enteric fever

Group II: Children suffering from febrile illness other than enteric fever.

Group III: Children with no history of fever in the past 3 months, Hospitalized for treatment of diseases other than fever

Exclusion criteria:

(1) Age < 2 year (2) Enteric encephalopathy (3) Febrile convulsion (4) Encephalitis, meningitis (5) Immuno-compromised children (6) Unwillingness to participate in the study

IV. Results

This study was undertaken with the objective to evaluate the sensitivity and specificity of widal test in children with enteric fever. A total of 150 children, out of whom 50 were suffering from enteric fever (group-I), 50 were non-enteric febrile illness (group-II) and 50 non-febrile children (group-III), were included in this study.

Table-1: Distribution of the children by their age (n=150)

Age	Group-I (n=50)%	Group-II (n=50)%	Group-III (n=50)%
≤ 5 years	50.0	50.0	56.0
5-10 years	40.0	40.0	36.0
> 10 years	10.0	10.0	8.0
Total	100.0	100.0	100.0
Mean ± SD	5.874±2.943	5.598±3.000	5.740±2.741
Range	2y 4m - 15y	2y - 14y	2y - 13y

χ^2 = 0.512, df=4; p-value = 0.972

Table-2: Distribution of the children by their gender(n=150)

Gender	Group-I (n=50)%	Group-II(n=50)%	Group-III (n=50)%
Male	54.0	60.0	58.0
Female	46.0	40.0	42.0
Total	100.0	100.0	100.0

χ^2 = 0.763, df = 2, p-value = 0.763

Table-3: Distribution of the children by their Respondents' information (n=150)

Respondents' information	Group-I (n=50)%	Group-II (n=50)%	Group-III(n=50)
Education			
Illiterate	4.0	8.0	6.0
Primary	20.0	16.0	14.0
Secondary	24.0	26.0	30.0
Higher secondary	28.0	24.0	20.0
Graduate and above	24.0	26.0	30.0
Occupation			
Housewife	78.0	88.0	90.0
Job outside	12.0	4.0	4.0
Others	10.0	8.0	6.0
Area of residence			
Urban	66.0	56.0	50.0
Rural	26.0	30.0	32.0
Slum	8.0	14.0	18.0
Monthly income			
≤ 10,000 taka	34.0	46.0	38.0
10,000-20,000taka	44.0	30.0	34.0
>20,000 taka	22.0	24.0	28.0

Education: $\chi^2 = 6.16$, df = 10, p-value = 0.801, Occupation:$\chi^2 = 8.37$, df = 2, p-value = 0.079, Area of residence: $\chi^2 = 6.72$, df = 4, p-value = 0.152, Monthly income: $\chi^2 = 5.54$, df = 4; p-value = 0.236

Table-6: Distribution of the children by the character of fever (n=150)

Characteristics of fever		Group-I (n=50)%	Group-II (n=50)%	Statistical calculations
Type of fever	Continued	12.0	34.0	RR=0.4565; 95% CI: 0.2754-0.7567 OR=0.2647; 95% CI: 0.1274-0.5501 Fisher Exact Test: p= 0.000174
	Intermittent	12.0	48.0	RR=0.3182; 95% CI: 0.1888-0.5362 OR=0.1477; 95% CI: 0.0719-0.3033 Fisher Exact Test: p= 1.617335
	Step-ladder pattern	76.0	18.0	RR=3.5709; 95% CI: 2.4780-5.1459 OR=14.4259; 95% CI:7.2632-28.6524 Fisher Exact Test: p= 4.144012
Duration	≤ 10 days	48.0	54.0	$\chi^2 = 0.792$, df = 2, p = 0.673
	10-20 days	44.0	38.0	
	> 20 days	8.0	8.0	
	Mean ± SD	12.60± 6.295	12.04 ± 5.918	t-test = 0.503, df = 49, p = 0.617
	Total	100.0	100.0	

Table-7: Distribution of the children by their blood culture findings (n=150)

Blood culture	Group-I	Group-II	Group=III
Positive	27	0	0
Negative	23	50	50
Total	50	50	50

V. Discussion

This study was aimed to document clinical profile in children with enteric fever. A total of 150childrenwere included in this study. In all three groups around half of the participants were in the '≤ 5 years' age group; 50.0% of group-I, 50.0% of group-II and 56.0% of group-III were in the age group. Mean ± SD of age was calculated to be, (5.874±2.943) for group-I, (5.598±3.000) for group-II and for group-III (5.740 ± 2.741). The p-value was 0.972 for chi-square. Similarly, Alam ABMS, Rupam FA, Chaiti F found that, the mean age of 153 patients (86 with definitive typhoid fever, 17 with suspected typhoid fever and 50 with non-typhoidal febrile illness), was 5.2 ± 2.8 years[23]Their age ranged from 2 years to 15 years (group-I: 2y 4m - 15y; group-II: 2y - 14y and group-III: 2y - 13y). [Table 3.1] Another study in Dhaka found participants of younger age as, the youngest and oldest patients were 0.7 and 14 years respectively.[60]More than half of the participants in all groups [27 (54.0%)], [30 (60.0%)] and [29 (58.0%)] were Males. Male: Female ratio was about 1.2:1 in group-I, 1.5:1 in group-II and 1.4:1 in group-III. The difference in male-female distribution between the groups was not statistically significant ($\chi^2 = 0.763$, df = 2, p-value = 0.683). Again, Alam ABMS, Rupam FA, Chaiti F found that, over half (54%) of patients was male with male to female ratio being roughly 1:1[23]In all the group fathers' educational qualification showed similar pattern of distribution. Illiteracy and primary education constituted a smaller proportion; 12.0% in each group. Chi-square calculates: $\chi^2 = 8.29$, df = 10, p-value = 0.601; which explains that there was no significant statistical difference in the groups. Low earning job like day labourer, Rickshaw puller, driver, tailor, etc.constituted small portion in the groups (14.0%, 8.0% and 12.0%) in people with lesser education(12.0% in each group) and with higher educational qualification more fathers had got jobs in different sectors (58.0%, 60.0% and 56.0%). There was no significant statistical difference between the groups ($\chi^2 = 2.13$, df = 4, p-value = 0.0711). Like their fathers Illiteracy of the mothers was 4.0%, 8.0% and 6.0%. Other educational status like madrasa was counted similar to regular level in years of education. Chi-square was calculated as, $\chi^2 = 6.16$, df = 10, p-value = 0.801; that means there was no statistically significant difference between the groups. Low incoming family was more in group-II (46.0%)] than group-III(38.0%) or group-I(34.0%).Mean ± SD of monthly income was (18,240.00 ± 10,98.616) in group-I, (18,000.00 ± 14,532.160) in group-II and (18,000.00 ± 10,688.540)in group-III. There was no statistically significant difference among the groups ($\chi^2 = 5.54$, df = 4; p-value = 0.236. For both enteric group and non-enteric group fever was present in cent percent (100.0%) of participants. For group-I most of the patients (76.0%) had step-ladder pattern of fever; while for group-II intermittent type (48.0%) and continued type of fever (34.0%) prevailed. For both enteric (Mean ± SD = 12.60 ± 6.295) and non-enteric (Mean ± SD = 12.04 ± 5.918) fever group had similar pattern of distribution for duration of fever; both quantitative (t-test = 0.503, df = 49, p = 0.617) and qualitative ($\chi^2 = 0.792$, df = 2, p = 0.673) analysis showed that there was no statistical significant difference in duration of fever. A cross-sectional study at Central Hospital Ltd., Dhaka, showed about 17% of patients had a history of suffering between 1 – 5 days, 24.6% between 11 – 15 days and 58.5% between 6 – 10 days. The mean duration of illness was 8.2 ± 3.3 days and the minimum and maximum durations were 1 and 15

days respectively[23] Blood culture was done in all of the 150 participants; out of them negative culture was obtained in 123 individual and the remaining 27 (54.0%%) were culture positive.

VI. Limitations of the study

This study was conducted in a tertiary care hospital in Dhaka. So the study findings may not reflect the exact scenario of all around the country regarding enteric fever. The current study was conducted among 150children, not a large study to draw a definite conclusion. Not only in Bangladesh but also in the whole world, study of enteric fever in the perspective of the objective of current study is rare. So, difficulty was faced to compare the findings to other research findings.

VII. Conclusion and recommendations

This was a small scale study done at a single centre over a brief period of time. A large scale, multi-centre study over long duration will give a complete picture on enteric fever with various factors. However, clinical profile can give a positive direction to the clinicians for better treatment in children with enteric fever.

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