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Laboratory Findings of Enteric Fever in Children - A Study in a Tertiary Care Hospital, Dhaka, Bangladesh

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Abstract **Original Research Article**

Enteric fever caused by Salmonella enterica serotype Typhi and Paratyphi A and B, is endemic in the Indian sub-continent including Bangladesh, South-east and Far-east Asia, Africa and South Central America. We conducted a cross-sectional descriptive study in the Department of Paediatric Medicine of Dhaka Shishu Hospita during the period from 10th October 2013 to 9th April 2014. Our aim was to document laboratory findings of Enteric Fever in Children. 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.

Keywords: Laboratory findings, Enteric fever, Widal test.

INTRODUCTION

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 [1]. Widal a serological diagnosis test for enteric fever was founded in 1896 by Georges Fernand Isidore Widal [2]. 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 [3]. 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[4]. Now 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[5], 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 [6]. 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 [7]. 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 [8] and the long waiting time for culture results have been identified as reasons for the preference for the widal test [9]. 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 [10-13], have produced data which have casted serious doubts on the value of the Widal Test. Typhoid is another rapid slide test used to ascertain the diagnosis of enteric fever, but not cost effective as widal [14]. 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 [15]. 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 [16]. So, there is a great need for the people to be aware of 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 typhoid fever and its risk factors. Enteric fever continues to be a major health problem in Bangladesh. In the topical areas however, it is endemic in many places, due to the low standard of living, unprotected water supply and unhygienic methods in the preparation and handling of food. Many children with Typhoid fever are admitted in the hospital with various complications. Very few studies have been performed worldwide about laboratory findings of Enteric fever. Such kind of study can help to increase the awareness about Enteric fever and its laboratory findings for enjoying a good quality of life.

Objectives

General objective

- To Document laboratory findings of Enteric Fever in Children in Bangladesh

Specific objectives

- To Assess prevalence of culture positives children with Enteric fever in Bangladesh
- To measure antigen detection among study participants

MATERIALS AND METHODS

We conducted this study at the Department of Paediatric Medicine of Dhaka Shishu Hospital, Dhaka, Bangladesh during the period from 10th October 2013 to 9th April 2014. We adopted a purposive sampling technique to select study subjects. Subjects were children with or without fever, coming to the Dhaka Shishu Hospital, Dhaka. We take 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 Hospital (Bangladesh Institute of Child Health), Dhaka, Bangladesh. Widal test was performed using stained bacterial suspension (Micropath, Omega, UK) containing TO and TH antigen, by slide titration. S. typhi were isolated from blood by the lysis-direct plating centrifugation method described previously by saha et al. All the data were collected and recorded systematically in a questionnaire and were analyzed using computer software SPSS (Statistical Package for Social Sciences). 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

RESULTS

Table-1: Background characteristics of the study participants (n=150)

Respondents	Group-I (%)	Group-II (%)	Group-III (%)	$\chi 2$	P-value
Gender				0.763	0.563
Male	54.000	60.00	58.00		
Female	46.00	40	42.00		
Age groups of the children				0.512	0.972
≤ 5	50.00	50.00	56.00		
5-10	40.00	40.00	66.00		
10>	10.00	10.00	8.00		
Religion				1.709	0.425
Muslim	95.0	90.9	92.00		
Hindu	5.00	8.30	8.00		
Others	00	00	00		
Educational status of the respondents				6.16	0.801
Illiterate	4.20	0.80	2.80		
Primary	30.80	7.50	4.50		
Secondary	21.70	28.30	32.30		
Higher secondary	15.00	51.70	49.70		
Graduate	20.00	11.70	11.70		
University	8.30	0.00	1.20		
Occupation of the respondents				8.37	0.079
Job	57.5	65.8	49.90		
Business	28.3	32.5	38.20		
Others	14.2	1.7	12.40		

Table-2: 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

Table shows that, blood culture was done in all of the 150 participants. Among them negative culture was obtained in 123 individual and the remaining 27 (18.0%) were culture positive. In group-I, positive participants were 27 representing 54% in the group.

Table-3: Distribution of the children with enteric fever by their first widal test findings (n=150)

Titre	Group-I		Group-II		Group-III	
	TO	TH	TO	TH	TO	TH
1:80	48	62	78	74	100	100
1:160	22	16	14	16	0	0
1:320	22	14	8	10	0	0
1:640	6	2	0	0	0	0
1:1280	2	6	0	0	0	0
Total	100	100	100	100	100	100

Table-4: Distribution of the children with Enteric fever by initial Widal test findings (n=150)

Widal test	Enteric fever	
	Present (Group-I)	Absent (Group-II+ Group=III)
Positive	31	11
Negative	19	89
Total	50	100

Table-5: Distribution of the children with Enteric fever by their both first and second Widal test (after 7 days) findings (n=150)

Widal test	Enteric fever	
	Present (Group-I)	Absent (Group-II+ Group=III)
Positive	47	11
Negative	3	89
Total	50	100

When double widal test result was considered it was positive in 94.0% of enteric fever cases; the remaining 6.0% of cases and 89.0% of the non-enteric children were found to be Widal negative.

DISCUSSION

The aim of this study was to document laboratory findings of enteric fever in children in Bangladesh. A total of 150 children were 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). 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 ($\chi2$ = 0.763, df = 2, p-value = 0.683). Alam ABMS, Rupam FA, Chaiti F found that, over half (54%) of patients was male with male to female ratio being roughly 1:1.60 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: $\chi2$ = 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 ($\chi2$ = 2.13, df = 4, p-value = 0.0711). 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.

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. Culture yeild that all were S. typhi in group-I and in group-II 9 (18%) children was found with Escherichia coli (5), Klebsiella spp (2), Pseudomonas aeruginosa (1) and Staphylococcus aureus (1). In Africa, Keddy KH, Sooka A, Letsoalo ME, Hoyland G, Chaignat CL, Morrisseye AB and Crump JA found that, thirty-six (39%) blood cultures grew a pathogen; 28 (78%) of these cultures grew Salmonella Typhi. Other pathogens isolated included Salmonella Typhimurium, Streptococcus pneumoniae, Staphylococcus aureus and Mycobacterium tuberculosis (one culture each) and Cryptococcus neoformans (four cultures). 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 22.0% of non-enteric febrile patient. TH showed ≥1:160 count in 38.0% group-I and 26.0% of group-II children. A total of 11 children in group-II were found to be widal positive; among them 2 children were diagnosed as Dengue fever (diagnosed by IgM and IgG), in the other 9 children blood culture showed other micro-organisms. When double widal test result was considered it was positive in 94.0% of enteric fever cases; the remaining 6.0% of cases and 89.0% of the non-enteric children were found to be Widal negative. Similarly, in another study in Bangladesh, It is seen that more than 97% of the definitive typhoid fever and 82.3% of the suspected typhoid fever cases had an 'O' agglutinin titer of 1:160 or > 1:160 as compared to only 2% cases of non-typhoid febrile illness (p <0.001). Similarly, 20.9% of culture-positive and 29.3% of suspected typhoid fever cases had an 'H' agglutinin titer of equal to or more than 1:160 as opposed to only 4% of the non-typhoid febrile illness cases (p = 0.003). However, Noorbakhsh S, Rimaz S, Rahbarimanesh AA and Mamishi S found that, among the bacteriologically proven cases of typhoid fever, there were 26 (44.8%) with TO≤1:40 and TH>1:40. In 4 cases (6.8%) there were TO>1:40 and TH<1:40. There were 14 (25%) cases in which TH and TO antibody was less than 1:40. TO titer >1:320 not detected in this group but TH >1/320 were seen in 12 cases (20.6%). From 58 cases with bacteriologically documented typhoid fever 23 (39.6%) aged 5-10, in which 21 cases had positive titers; but in 17 cases which aged less than 5 years all of them had positive titers. Therefore a false negative result was high in this group.

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 the whole country. The current study was conducted among 150 children, not a large study to draw a definite conclusion.

CONCLUSION AND RECOMMENDATIONS

Laboratory findings can help to physicians to treat the patients more accurately. 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, widal test is easy, inexpensive and can be done in remote settings. It is sometimes difficult to double obtain sample. So, in a country like Bangladesh one has to rely on single widal test for laboratory findings.

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