

## Clinical Profile and Antibiotic Sensitivity Pattern of Enteric Fever among Children Admitted in a Tertiary Care Hospital in Dhaka

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### ABSTRACT

**Objective:** In this study our main aims to know the clinical profile of pediatric enteric fever and the sensitivity pattern of the disease to drugs in this region.

**Methodology:** This prospective observational study conducted in a tertiary care hospital at Dhaka from March to December 2016 among suspected case of Enteric fever as per case definition. Among 212 suspected enteric fever 117 children were diagnosed as enteric fever by blood culture and/or Widal test.

**Results:** During the study, Male: female were 1.3: 1. Maximum (70%) children were in age group 5 years or more. Most of the children were from urban slum area (53.6%) of Dhaka city. Cases were admitted throughout the year. Common presentation were fever (100%), anorexia (100%), pain abdomen (74.4%) and loose motions (46.1%). The common signs were hepatomegaly (41.9%), hepatosplenomegaly (5.1%) coated tongue (64.9%), pallor (74.4%). The complications rate was 35.9% and commonest being UTI and pneumonia. The overall positivity of Widal test was 89.7% and the culture positivity was 32.5%. Among isolates, 94.7% were Salmonella typhi and 5.3% Salmonella paratyphi A. Among them 18.1% isolates were multi drug resistant.

**Conclusion:** Enteric fever is most prevalent during summer &

rainy session. WASA supplied water may play a role. Hepatomegaly is common. UTI and pneumonia are the commonest complication. Multidrug resistant cases are not so as high as other countries. Cefixime, Ceftriaxone. Meropenam and Ofloxacin are the drugs of choice. Ciprofloxacin is still could be chosen for the treatment of enteric fever. Higher rate of resistant to Azithromycin is alarming.

**Keywords:** Antibiotic Sensitivity, Enteric Fever, Endemic Disease.

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### Article History:

Received: 22-11-2019, Revised: 15-12-2019, Accepted: 10-01-2020

Access this article online	
Website: <a href="http://www.ijmrp.com">www.ijmrp.com</a>	Quick Response code 
DOI: 10.21276/ijmrp.2020.6.1.021	

### INTRODUCTION

Enteric fever is an endemic disease in many developing countries like Bangladesh. Despite the use of newly developed antibacterial drugs, enteric fevers such as typhoid and paratyphoid are one of major health problems in Bangladesh, especially for the children.<sup>1</sup> Population-based studies from South Asia indicate that young children under 5 years of age bear a large burden of S. Typhi infection.<sup>2,3</sup> In the developing world, incidence of typhoid fever ranging from 100-1,000 cases per 100,000 population. Almost 80% of the cases are in Asia; the rest occur mainly in Africa and Latin America.<sup>4</sup>

Enteric fever is caused by Salmonella enterica var Typhi (S.typhi) and Salmonella enterica Var Paratyphi A (S.Paratyphi A) being the major causative microorganisms are transmitted by the faeco oral route. The disease is mainly associated with low socioeconomic status and poor hygienic practices, with human beings the only natural host and reservoir of infection.<sup>5</sup>

Varied presentations of typhoid fever are known in the paediatric age group, such as septicemia in neonates, as diarrhoea in infants, and as lower respiratory tract infections in older children.<sup>6</sup> Atypical presentations in older children include splenic abscess, liver abscess, cerebellar ataxia, meningitis, cholecystitis, chorea, palatal palsy, osteomyelitis, peritonitis, aphasia and even psychosis.<sup>4,7</sup> Due to these varied and atypical presentations, it is common for typhoid fever in children to be diagnosed late or even remain unrecognized. Also, no vaccine against typhoid fever is available commercially for children under two years of age.<sup>7</sup> Antibiotic therapy is the mainstay of managing enteric fever. In untreated cases a chance of developing a carrier state increases. To complicate matters further, since 1990s, Salmonella typhi has developed resistance simultaneously to all the drugs used in first line treatment (chloramphenicol, cotrimoxazole and ampicillin). Fluoroquinolones were widely regarded as the most effective drug

for the treatment of typhoid fever.<sup>8</sup> But unfortunately, some strains of *S. Typhi* have shown reduced susceptibility to fluoroquinolones.<sup>9</sup> Also there is high rate of clinical failure seen with fluoroquinolones. At present third generation cephalosporins are used in treatment but there are sporadic reports of resistance to these antibiotics.<sup>10</sup> Recently, Azithromycin is being used as an alternative agent in uncomplicated enteric fever. It has been found that it reduces the clinical failure rate and duration of hospital stay in comparison to fluoroquinolones and relapse rate in comparison to ceftriaxone, when used in the treatment of multidrug resistant typhoid fever.<sup>11</sup>

In this study our main aims to know the clinical profile of pediatric enteric fever and the sensitivity pattern of the disease to drugs in this region.

## OBJECTIVES

### General Objective

- To assess the clinical profile of pediatric enteric fever and the sensitivity pattern of the disease to drugs in this region.

### Specific Objectives

- To detect Complications of enteric fever.
- To identify sensitivity patterns of *Salmonella enterica* isolates

## METHODOLOGY

**Type of Study:** Prospective observational study

**Place of Study:** Pediatric inpatient department of Dhaka Medical College Hospital

**Study Period:** March 2016 to December 2016

**Study Population:** A total of 212 children with suspected enteric fever were admitted during this study period. Among them 117 children were diagnosed as enteric fever by blood culture and/or widal test as per case definition.

**Sampling Technique:** Purposive

**Method:** Data were obtained from admitted children upto 14 yrs of age with signs and symptoms suggestive of enteric fever as defined by the case definition (any fever  $\geq 100.4^{\circ}\text{F}$  for  $\geq 3$  days plus disturbance of abdominal function like abdominal pain, vomiting, constipation or diarrhea is suggestive in epidemiological area like Bangladesh). Then investigations were sent from these suspected cases.

Those who fulfilled any of the following criteria were included in the study. (1) Positive culture for *Salmonella enterica* (typhi or paratyphi) (2) Widal titre; TO  $\geq 1:160$ .

Others who were clinically suggestive as enteric fever but had less than significant titre or negative Widal test and negative blood culture were excluded from the study. Thorough and detailed history, clinical examination and laboratory investigations were done in all cases and analyzed

**Data Analysis:** After collection, data were entered into a personal computer and were edited, analyzed, plotted in graphs and tables. Data were analyzed by chi square test, Mann Whitney U tests, using the SPSS version 20.

## RESULTS

In table-1 shows age distribution of the patients where maximum (70%) children were in age group 5 years or more. Only 6.8% children from < 2 years age group, the youngest patient was only 11 months old in this study.

**Table 1: Distribution of the Children by age & Sex**

Age group	Gender of the Children		Total
	Male	Female	
< 2 years	3	5	8
2 - <5 years	16	11	27
5 - < 10 years	33	25	58
10 yrs or more	14	10	24
<b>Total</b>	<b>66</b>	<b>51</b>	<b>117</b>

**Table 2: Sign at presentation**

Sign	N	%
Coated tongue	76	64.9
Hepatomegaly	49	41.9
Splenomegaly	0	0.0
Hepatosplenomegaly	6	5.1
None	62	52.9
Pallor	87	74.4
Tachycardia	110	94.0
Relative Bradycardia	0	0.0
Caecal gurgling	7	5.9
Toxicity	28	23.9
Obtundation	20	17.1

**Table 3: Association between the Investigations with Age group of children & Duration of Fever at Presentation**

Age Group	Investigations			Total
	Only Widal +ve	Only Blood Culture +ve	Both + ve	
< 2 years	2	4	2	8
2 - <5 years	18	5	4	27
5 - < 10 years	42	3	13	58
10 yrs or more	17	0	7	24
<b>Chi-Square=21.6</b>	df=6	P<0.001		
Duration of Fever				
3 - 7 days	10	12	3	25
8 - 14 days	65	0	18	83
>14 days	4	0	5	9
<b>Chi-Square=54.8</b>	df=4	P<0.001		
<b>Total</b>	<b>79</b>	<b>12</b>	<b>26</b>	<b>117</b>

**Table 4: Sensitivity patterns of *Salmonella enterica* isolates**

Name of Antibiotics	S. Typhi N=36 (%)	S. Paratyphi N=2 (%)
Amoxyclav	0 (00)	0 (00)
Amoxicilline	0 (00)	0 (00)
Ampicilline	6 (16.7%)	0 (00)
Chloramphenicol	10 (27.8%)	0 (00)
Cotrimoxazole	14 (38.9%)	0 (00)
Azithromycin	8 (22.2%)	2 (100%)
Cefixime	36 (100%)	2 (100%)
Ceftriaxone	36 (100%)	2 (100%)
Ceftazidime	18 (50%)	1 (50%)
Cefepime	31 (86.1%)	2 (100%)
Meropenam	36 (100%)	2 (100%)
Ciprofloxacin	26 (72.2%)	1 (50%)
Levofloxacin	19 (52.8%)	0 (00)
Ofloxacin	36 (100%)	2 (100%)
Nalidixic acid	0 (00)	0 (00)
Gentamycine	14 (38.9%)	0 (00)

In figure-1 shows distributions of the patients according to percentage of symptom where almost all patients were presented with high grade continued fever along with loss of appetite. No case in this study had stepped ladder type of fever. Abdominal pain experienced in 74.4% children. Diarrhea was more common than constipation.

In table-2 shows distributions of the patients according to frequency of sign where coated tongue was found in 64.9% cases. More than half (52.9%) of the patient had no organomegaly but 41.9% had hepatomegaly only, none of them had splenomegaly. Three-fourth (74.4%) of them was pale. Most (94%) of the patients had tachycardia but relative bradycardia was not found. Caecal gurgling was found only in 5.9% cases.

In table-3 shows association between the Investigations with Age group of children & Duration of Fever at Presentation where about three-fourth of the children (71%) in this study were presented to us during their 8-14 days of illness. During their admission blood was sent for widal test and blood culture irrespective of the duration of illness. Among them 79 cases had

only Significant Widal test, 12 were only Blood culture positive and remaining 26 cases had both blood culture and Widal test positive. In table 4 shows sensitivity patterns of Salmonella enterica isolates where Among 38 Salmonella isolates, 36 were S.Typhi (94.7%) and 2 were S.Paratyphi (5.3%) were found in this study. Among the isolates, 16 antibiotics were tested to see the sensitivity pattern. It was found that Cefixime, Ceftriaxon, Meropenam and quinolone derivatives like Ofloxacin were 100% sensitive among the isolates. The other quinolones Ciprofloxacin was 72.2% sensitive among S Typhi isolates and 50% among S.Paratyphi isolates but the levofloxacin was less sensitive (52.8%) among the isolates. In figure-2 shows complications of enteric fever where all patients recovered, and 35.9% cases developed complications such as UTI (47.6%) and pneumonia (40.4%) but severe complication like Hepatitis (4.8%), cholecystitis (2.4%), peritonitis (2.4%) and encephalopathy (2.4%) were less. In figure-3 shows monthly admission of enteric fever where, enteric fever present almost all the year in this study. But most patient (59%) were prevalent during May to August months.

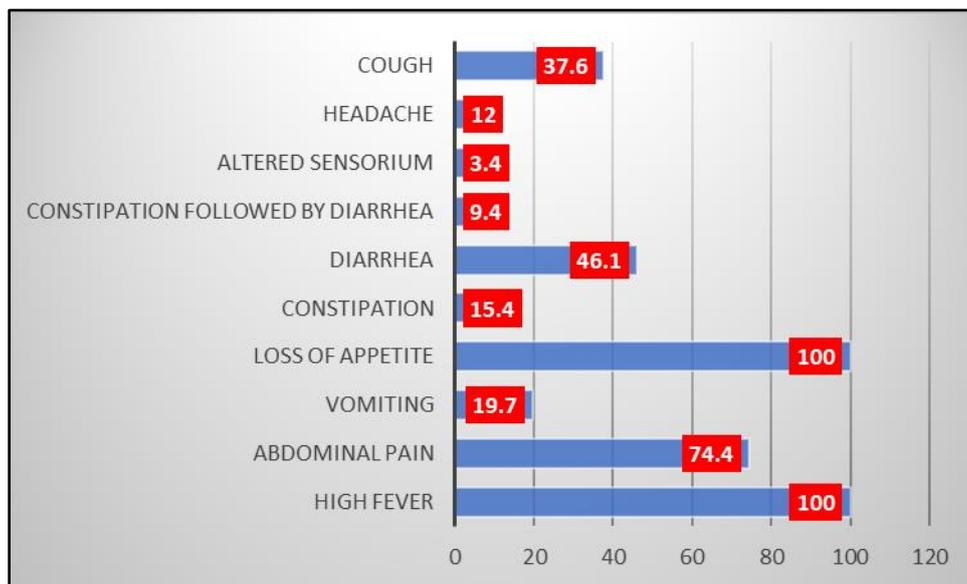


Fig 1: Distributions of the patients according to percentage of symptom.

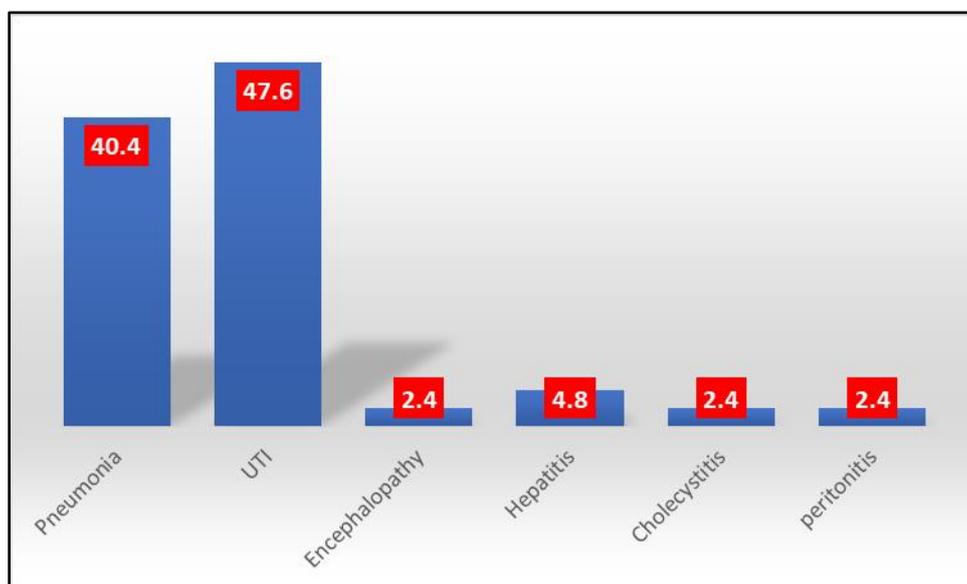


Fig 2: Complications of enteric fever.

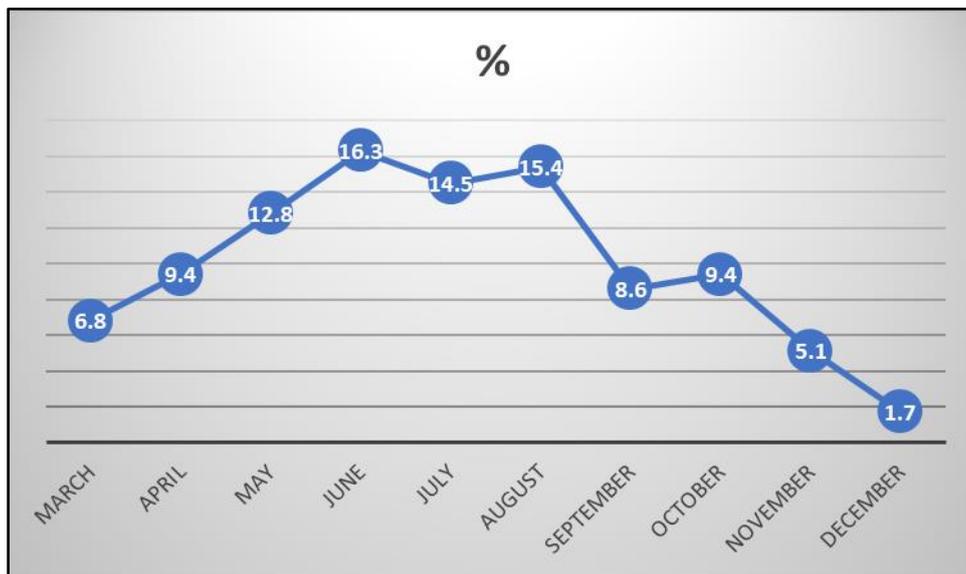


Fig 3: Monthly admission of enteric fever.

## DISCUSSION

In this prospective observational study, a total of 117 children with enteric fever were analyzed. The maximum (70%) children were in age group 5 years or more which is comparable to that in one (73%)<sup>13</sup> study. The male to female ratio in this study was 1.3: 1. Another study reported 1.2:1.<sup>14</sup>

In this study, cases were admitted throughout the year showing the endemicity of the disease. Maximum cases were admitted during May to August months (59%). This period coincides with the onset of monsoon and increase in housefly population, which facilitates faeco-oral transmission. Moreover most of the children in this study were from urban slum area (53.6%) of Dhaka city. Almost all of them drink Dhaka WASA supplied water and maximum of them (66.7%) drink water without boiling. One study<sup>14</sup> reported maximum incidence between May – July, another study<sup>15</sup> reported 45.6% between June-September and another article<sup>16</sup> reported 40.6% cases in the period of September-October.

The most common symptoms in this study were fever (100%), anorexia (100%), pain abdomen (74.4%), loose motions (46.1%), constipation (15.4%), vomiting (19.7%), cough (37.6%) and altered sensorium (3.4%). These symptoms were also seen in studies conducted by many study.<sup>17,15</sup> In the present study maximum cases (71%) had fever for 8-14 days prior to admission which was comparable to that of one<sup>16</sup> study. Almost all cases showed continued high fever. No case in this study had stepped ladder type of fever and this finding is same as reported by one article.<sup>18</sup>

The common signs were hepatomegaly (41.9%), hepatosplenomegaly (5.1%) coated tongue (64.9%), pallor (74.4%) and caecal gurgling (5.9%) cases, which was also reported by two studies<sup>18,15</sup> but they reported isolated splenomegaly > 65% cases. Whereas in this study no cases was found with isolated splenomegaly and more than half (52.9%) of the cases have no organomegaly which was consistent with one study.<sup>19</sup>

The overall positivity of widal test in this study was 89.7% as comparable to one study<sup>15</sup>, they reported 89.8% positivity.

The culture positivity in this study was 32.5%. Which is in concordance with that of one<sup>23</sup> study. Use of antibiotics prior to

admission was probably responsible for low culture positivity rates. Among the 38 culture positive cases, Widal test was positive in 26 cases (68.4%). In 12 cases, Widal test remained negative on repeating after one week. From the total isolates, 5.3% were *Salmonella paratyphi A* whereas the remaining was *Salmonella typhi* (94.7%) in this study. In one study also showed similar result but the reported rate of isolation of *paratyphi A* in literature is 20%.<sup>24</sup>

The present study found 18.1% isolates to be multi drug resistant which was comparable with one<sup>19</sup> (15%) study conducted in Dhaka slum area. No resistance was found to Cefixime, ceftriaxone. Meropenam and Ofloxacin in this study. These results suggest that these drugs resistance are still not high in this part of Bangladesh.

## CONCLUSION

Enteric fever is endemic in Bangladesh but most prevalent during summer & rainy session. WASA supplied water may play a role to develop enteric fever. Fever, anorexia and pain abdomen are the main complaints. Hepatomegaly is common. UTI and pneumonia are the commonest complication. Widal test is still a reliable test for the diagnosis of enteric fever. Multidrug resistant cases are not so as high as other countries. Amoxicilline & Nalidixic acid are almost resistant to all salmonella strain. Higher rate of resistant to Azithromycin is seen in this study. Cefixime, Ceftriaxone. Meropenam and Ofloxacin are the drugs of choice. Ciprofloxacin is still could be chosen for the treatment of enteric fever.

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**Source of Support:** Nil.

**Conflict of Interest:** None Declared.

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**Cite this article as:** Md. Ibrahim Khalil, ATM Shahid, Shahina Akhter Mita, Nasir Hossain. Clinical Profile and Antibiotic Sensitivity Pattern of Enteric Fever among Children Admitted in a Tertiary Care Hospital in Dhaka. *Int J Med Res Prof*. 2020 Jan; 6(1):76-80. DOI:10.21276/ijmrp.2020.6.1.021