

# Sensitivity Patterns of Isolated Salmonella Typhi in Children with Typhoid Fever

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**Abstract:** *Background and objective:* Enteric fever is a common febrile illness and one of the major health problem in Bangladesh. So the present study was conducted to determine the demographic characteristics, clinical profile, hematological feature and current sensitivity patterns of isolated S typhi in patients suffering from enteric fever in some of the tertiary care hospitals in Dhaka. *Materials & Methods:* This was a cross sectional study conducted in the Department of Pediatrics, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka Medical College Hospital (DMCH) and SSMCH – Sir Salimullah Medical College & Hospital (SSMCH), Dhaka, Bangladesh for a period of one year from July 2015 to June 2016. A total number of 100 children with enteric fever were studied and diagnose were based on clinical features, Wedel test and blood culture. *Results:* Out of 100 diagnosed enteric fever children, 60 (60%) were male and 40 (40%) were female. Fever was present in all patients. Other most common manifestation are loss of appetite, vomiting, diarrhea, headache and constipation. Coated tongue was the predominant examination finding followed by hepatomegaly, splenomegaly and abdominal tenderness. Sensitivity to ceftriaxone was 100% in our study while resistance to nalidixic acid was 90%. MDR S.typhi is still a threat but there was re-emergence of sensitivity to Cotrimoxazole and Chloramphenicol. *Conclusion:* The study concluded that clinical pattern of typhoid fever conforms well to that of known pattern of the disease in children. Blood culture profile shows widespread emergence of nalidixic acid related resistant strains and the sporadic occurrence of cephalosporin resistant strains of S. Typhi. However, the first line antibiotics such as chloramphenicol and cotrimoxazole still have a role to play in the treatment of typhoid due to re-emergence of sensitivity.

**Keywords:** Typhoid Fever, Antimicrobial, Sensitivity, Isolated, Salmonella Typhi, Pediatrics, Cotrimoxazole

## 1. Introduction

Enteric fever, an acute generalized infection may affect nearly all the systems but more commonly the reticuloendothelial system, intestinal lymphoid tissue, and the gallbladder. It includes 'typhoid fever' caused by *Salmonella enterica* serovar Typhi (*Salmonella typhi*) and 'paratyphoid fever' caused by *Salmonella paratyphi* A or *Salmonella paratyphi* B (or rarely, *Salmonella paratyphi* C). [1] Humans

are the natural host and reservoir of these organisms. *Salmonella* can survive for days in groundwater or seawater and for months in contaminated eggs and frozen oysters. [1] The infectious dose varies between  $10^3$ - $10^6$  organisms given orally. [2] Transmission of infection occurs by ingestion of food or water contaminated with faeces. Other established risk factors include recent contact with a typhoid patient or carrier, eating ice cream, flavored iced drinks or food from street vendors, and raw fruit and vegetables grown in fields fertilized

with sewage. [2] Because of the provision of clean water and good sewage system, it is a sporadic disease in developed countries and occurs mainly in travelers returning from endemic regions. Today, most of the burden of the disease is limited to the developing countries where standards of hygiene and sanitation remain poor. [3]. Despite the use of antibiotics and the development of newer antimicrobial agents, enteric fever continues to be a major public health problem causing high morbidity and mortality in developing countries. [4] The first-line drugs ampicillin, chloramphenicol, and cotrimoxazole were used as a standard treatment regimen for enteric fever until the mid-1980s. [5] However, the indiscriminate use of these drugs and acquisition of plasmid-mediated resistance led to the development of typhoid resistant to ampicillin, chloramphenicol, and cotrimoxazole –multi-drug resistant (MDR) typhoid – by end of 80<sup>th</sup>. The knowledge of the prevalence of Salmonella serovars and determination of their antimicrobial resistance pattern are very important for the guidance of clinical management of enteric fever. [6] This overall assessment is conducted over the profile of patients, and it is done to bring in the results how the Typhoid Fever and Antimicrobial Sensitivity patterns of Isolated Salmonella Typhi are related. Thus, this may help in developing appropriate strategies for the management of typhoid fever.

## 2. Objectives

### a) General objective:

To examine the clinical profile of patients with typhoid fever and sensitivity patterns of isolated *S. typhi*.

### b) Specific Objectives:

- 1) Demographic characteristics of the patients with typhoid fever.
- 2) Clinical profile of the patients with typhoid fever.
- 3) The antimicrobial susceptibility pattern of the isolated *S. typhi*.

## 3. Methodology and Materials

This was a Cross-sectional observational study. The study was carried out under the department of Pediatrics of Bangabandhu Sheikh Mujib (BSMMU) Medical University, Dhaka Medical College Hospital (DMCH) and Sir Salimullah Medical College Hospital (SSMCH). From these areas, 75, 10 and 15 cases were selected respectively. In the above centers, a lot of pediatric patients with typhoid fever are admitted every year for evaluation and management. Overall, period of study was July 2015 to June 2016 (One year). Ethical clearance was taken from Institutional Review Board (IRB) of BSMMU and the participants were explained that there will be no physical or social risk. The Children admitted in the Pediatrics wards of the above mentioned hospital during the study period with suspected diagnosis of typhoid fever were the study population. Children with positive blood culture were diagnosed as ‘confirm case’ and cases with a titer of TO  $\geq$  1:160 or rising titer of Wedel test were diagnosed as ‘probable case’. All children with

diagnosis of ‘confirmed’ or ‘probable cases’ admitted in those hospital during the study period were the sample. During the study period febrile patients admitted in above mentioned hospital with the diagnosis of suspected typhoid fever was screened. Suspicion was made on the basis of clinical features like continued fever, toxic look, diarrhea/constipation, splenomegaly, hepatomegaly, diffuse tenderness and caecal gurgling. Clinically suspected cases undergone laboratory investigation that includes CBC, Widal test and blood culture and other tests as per individual case merits. To determine the sample size the following formula 100 children with the diagnosis of typhoid fever and fulfilling the inclusion and exclusion criteria’s during the study period were selected purposively.

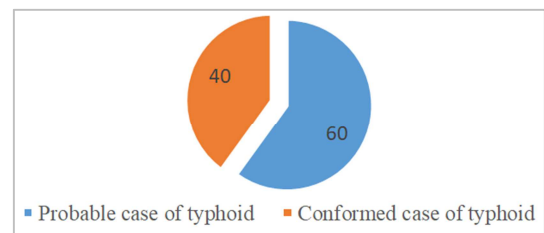
### Inclusion Criteria

- 1) Patient diagnosed as typhoid fever and admitted in mentioned hospitals during the study period.
- 2) Pediatric age group of both sexes

### Exclusion Criteria

- 1) Patient with severe co-morbidities unrelated to typhoid fever.
- 2) Patient with paratyphoid fever.
- 3) Care-giver not willing to give written consent

## 4. Results



**Figure 1.** Distribution of typhoid patient according to case definition (n=100).

A total number of 100 children’s were taken for the study. (Figure 1) showed, out of 100 patient 60% were probable case and 40% were confirmed case of typhoid fever. (Table 1) showed homogenous distribution of cases amongst the three age groups with a male to female. Children from 1-5 years (37%), from 5-10 years (35%) and above 10 years (28%) were studied for this case. (Figure 2) showed, BMI of studied 100 children showed that majority (65%) were in the normal range of nutritional status. (Figure 3) showed, predominant sign was coated tongue (65%) followed by hepatomegaly (63%) and splenomegaly (38%). Abdominal tenderness was found in 25% of children. (Table 2) revealed significant number (20%) isolates were still MDR while maximum number (90%) isolates were NARST. (Figure 4) showed, sensitivity pattern of Salmonella typhi. Highest (100%) in case of sensitivity was seen with Ceftriaxone followed by Cefixime, Ciprofloxacin, Azithromycin, Chloramphenicol, Cotrimoxazole, Amoxicillin and lowest (10%) in Nalidixic acid. (Table 2) showed most (86%) of the children had abatement of fever < 5 days while 58.1% children achieved normal liver span between 3-5 days

of treatment and mortality was 0%.

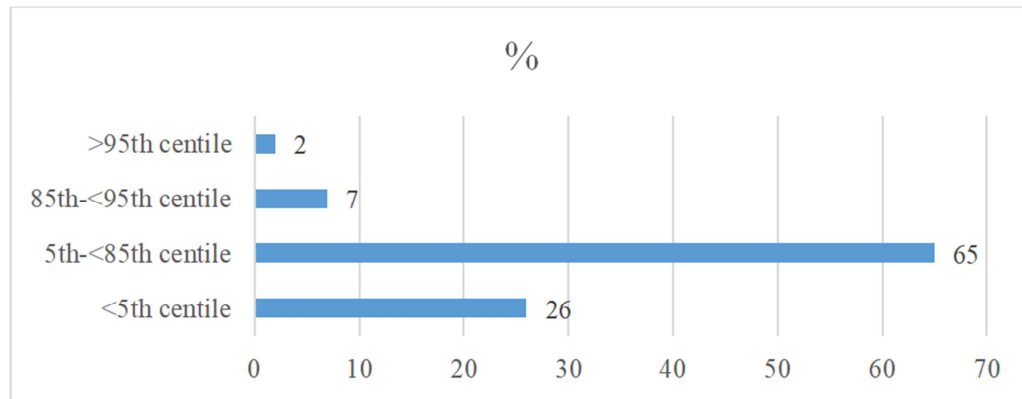
**Table 1.** Age distribution of the studied participants (n=100).

Age	N	%
1-5 years	37	37
5-10 year	35	35
>10 year	28	28

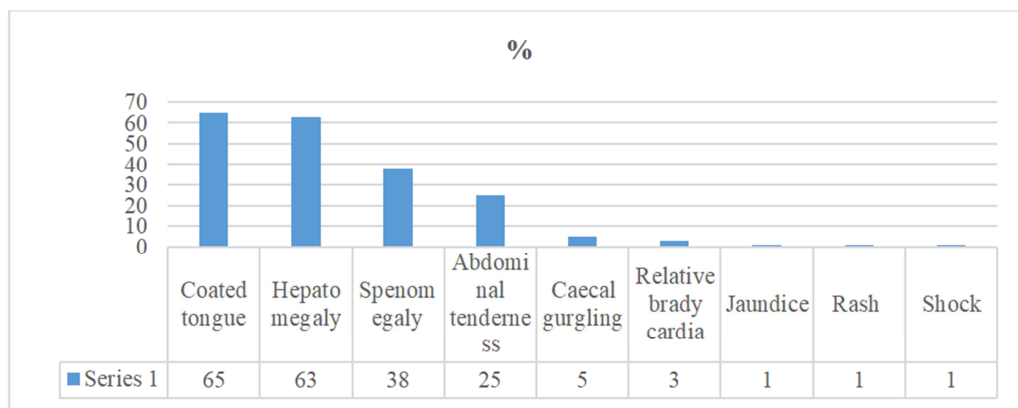
**Table 2.** Percentages of MDR & NARST in isolated *S. typhi* (n=40).

Isolates	Number of children	%
MDR	08 (40)	20
NARST	36 (40)	90

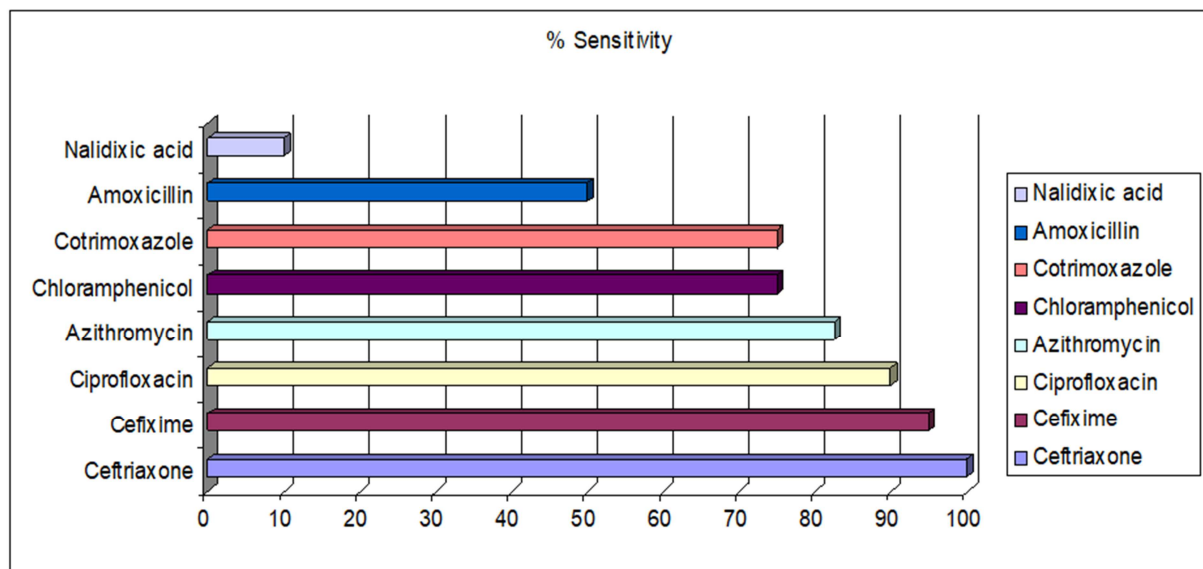
MDR- Multi-drug resistant typhoid, NARST- Nalidixic-Acid Resistant Salmonella Typhi



**Figure 2.** BMI of the studied children with typhoid fever (n=100).



**Figure 3.** Physical findings of children with typhoid fever (n=100).



**Figure 4.** Antimicrobial sensitivity patterns of isolated *S. typhi*. (n=40).

## 5. Discussion

Typhoid fever is endemic in our country and affect all ages beyond infancy as found in this study. Similar findings were reported [2, 7] This may be due to poor sanitary condition and non-availability of safe water. The present study showed male preponderance 1.5:1. This is consistent with the result. [8, 9] However, other report suggests similar prevalence amongst both sexes. [10] Probable explanation might be that in a male dominant society like ours male child has higher access to medical care. It may also be due to the fact that the male children are more independent and has more chance of exposure to street food. Many studies showed higher prevalence amongst poor socioeconomic background. But in the present study the distribution was quite even in all three economic categories. This may suggest that the division was inappropriate or the availability of safe water or exposure to contaminated food was wide and rampant. High percentage of cases in children with normal range of BMI in present study may also support the above. Most (87%) of the children had improved sanitation facility in their home but needs to be cent percent. According to BBS 2014 report the distribution of sanitation in Dhaka division were improved sanitation 70%, unimproved sanitation 29%, others 1%. Though the use of improved sanitation in case of typhoid patient were similar to general population in Dhaka but percentage of hand washing seems to be less. In our study sensitivity pattern of salmonella typhi to first line conventional antimicrobials showed sensitivity to Amoxicillin (50%), Chloramphenicol (75%), Cotrimoxazole (75%). Abdullah Brooks et al. (2005). [9] in their study in Bangladesh S. Typhi was isolated from 27 children and revealed sensitivity to Amoxicillin (55.1%), Chloramphenicol (57.1%) and Cotrimoxazole (57.1%) [11] in their study of 68 isolated S. typhi from children, revealed sensitivity to amoxicillin 28.3%, cotrimoxazole 27.4% and chloraphenicol 22.6%. A study of 175 isolated S. typhi in Bangladesh revealed sensitivity to Amoxicillin (33%), Chloramphenicol (65.7%), Cotrimoxazole (64%) [7, 12] et al. (2015) in their study of 56 isolates from children at ICDDR, revealed sensitivity to Amoxicillin (66%), Chloramphenicol (76.78%) and Cotrimoxazole (76.78%). The reason of re-emergence of sensitivity of Chloramphenicol and Cotrimoxazole that these drugs are less frequently being used in children now a days. In present study out of 40 isolates, 08 (20%) isolates were MDR strains. Among the isolates from Bangladesh, 82% and 40% were resistant to various concentrations of nalidixic acid and ciprofloxacin, respectively. Several resistance mechanisms, including alteration in gyrase A, the presence of QnrS and enhanced efflux pumps, were involved in the reduced susceptibility and resistance to fluoroquinolones<sup>13</sup>. The majority of S. typhi MDR isolates from Bangladesh belong to haplotype H58, a prevalent MDR clone that has spread over all of Asia and Africa. In more than 50% of these MDR isolates from Bangladesh, the genes responsible for resistance reside on the

chromosome [13, 7] in their study of 56 isolates from children at ICDDR, revealed 14.3% were MDR. The present study sensitivity to Azithromycin was 82.5% while in their study of 56 isolates from children had 100% sensitivity to Azithromycin.

## 6. Limitations of the Study

Study depict picture of limited number of tertiary care hospitals. It may not be the picture of the community as a whole.

## 7. Conclusion and Recommendations

Clinical profile of typhoid fever in children admitted in tertiary care hospitals in Dhaka matches to what had been seen in the past and recorded in textbooks. Nalidixic acid associated resistance was found to be high. However, Ceftriaxone was 100% sensitive. Moreover, there was resurgence of sensitivity to first-line drugs. Recommendations: Efforts should be taken to find the sensitivity patterns of typhoid fever before starting treatment. Continuous surveillance of typhoid fever and drug sensitivity pattern may be initiated. Community oriented study may be done to know the disease.

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