Original Article

ANTIMICROBIAL SENSITIVITY PATTERN OF COMMONLY USED ANTIBIOTICS AMONG ADULT ENTERIC FEVER PATIENTS

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ABSTRACT

Background: Enteric fever which is a very common bacterial infection in the Bangladeshi population is most commonly acquired by ingestion of water and food contaminated with feces or urine of carriers. Drug resistance in typhoid fever is considered one of the important factors in the morbidity and mortality of the disease. The emergence of strains of Salmonella Typhi resistant to multiple antibiotics poses a serious problem. The increasing frequency of antibiotic resistance has been reported from all parts of the world, but more so from developing countries. Thus this study aim to assess the antimicrobial sensitivity pattern of commonly used antibiotics among adult enteric fever patients.

Methods: This cross-sectional comparative study was conducted in the Department of Medicine of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from January 2015 to December 2015. In total 150 individuals were included in this study as the study subjects who were divided into two groups. In Group A, a total of 50 confirmed enteric fever cases and in Group B, a total of 100 non-enteric febrile adult patients were included. A non-probability purposive sampling technique was used in sample collection. All data were processed, analyzed and disseminated by using the MS Office program. For this analysis to fulfill the objective of this study, mainly data from 50 confirmed enteric fever cases were considered.

Results: In this study, among the total of our 50 enteric fever cases with isolated salmonellae organisms including S. typhi and S. Paratyphi, during the treatment procedure, as the antibiotics cefepime, cefixime, ceftazidime, ciprofloxacin, imipenem, meropenem and ofloxacin showed 100% sensitivities. Besides ceftriaxone, cotrimoxazole, chloramphenicol and azithromycin showed 98%, 68%, 66% and 54% sensitivities respectively (>50%). On the other hand, more than 50% of resistant cases were found in treatment by nalidixic acid (76%), ampicillin (98%) and amoxicillin (98%).

Conclusion: Till today, considering the lower treatment cost and better patient compliance ciprofloxacin may be considered as the drug of choice in treating adult enteric fever patients. Besides cefepime, cefixime, ceftazidime, ciprofloxacin, imipenem, meropenem or ofloxacin can be used in such cases confidently.

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INTRODUCTION

In many developing countries, enteric fever caused by *salmonella typhi*, is widely recognized as a major public health problem. The disease emerged as an important infectious disease in the early 19th century. It is endemic in the Indian sub-continent including Bangladesh, South-East and Far East-Asia, the Middle East, Africa, and Central and South America [1]. Enteric fever is a systemic infection and is transmitted through the fecal-oral route by the consumption of contaminated water and food, particularly raw or undercooked meat, poultry, eggs and milk. The consumption may occur either directly from person to person or by ingestion of food or water contaminated with feces or urine carrier as well as through flies [2]. The disease, enteric fever may occur in all age groups, with the highest incidence found particularly in children [3]. In Bangladesh, enteric fever is a round-the-year problem that sometimes takes epidemic proportions [4]. Enteric fever, also known as typhoid fever, is a systemic infection by *Salmonella typhi* or by the related but less virulent *Salmonella paratyphi* [5]. Early antibiotic therapy has transformed a previously life-threatening illness of several weeks' duration with an overall mortality rate approaching 20.0% into a short-term febrile illness with negligible mortality. Case fatality rates of 10.0-50.0% have been reported from endemic countries when diagnosis is delayed [5]. However, community-based studies in areas of endemic disease indicate that many patients with enteric, particularly children under five years of age, may have a nonspecific illness that is not recognized clinically as enteric [6,7]. Enteric causes many complications of which gastrointestinal bleeding, intestinal perforation, and enteric encephalopathy are the most important. Gastrointestinal bleeding is the most common, occurring in up to 10.0% of patients [8]. Perforation may be manifested by an acute abdomen or, more covertly, by simple worsening of abdominal pain, rising pulse, and falling blood pressure in an already sick patient. In the management of enteric fever, the emergence of resistance to chloramphenicol and other antimicrobial agents has been a major setback [9]. Recently, continued dependence on Ciprofloxacin for the empirical treatment of typhoid fever in many developing countries including Bangladesh has led to the emergence of resistance of *Salmonella typhi* to this drug. So antibiotic susceptibility test (AST) has an important role in the treatment of typhoid fever. The sensitivity of blood culture is higher in the first week of the illness, is reduced by prior use of antibiotics, and increases with the volume of blood cultured and the ratio of blood to broth [11]. The role of the Widal test is controversial because the sensitivity, specificity, and predictive values of this widely used test vary considerably among geographic areas [5]. However, the most important contributor to a poor outcome is probably a delay in instituting effective antibiotic treatment [12]. The objective of this current study was to assess the antimicrobial sensitivity pattern of commonly used antibiotics among adult enteric fever patients.

METHODS

This cross-sectional comparative study conducted in the Department of Medicine of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh from the period January 2015 to December 2015. In total 150 individuals were included in this study as the study subjects who were divided into two groups. In group A, a total of 50 confirmed enteric fever cases and in group B, a total of 100 non-enteric febrile adult patients were included. A non-probability purposive sampling technique was used in sample collection. The ethical clearance of the study was taken from committee of Bangabandhu Sheikh Mujib Medical University. Before data collection, written consent was taken from all the participants. As per the inclusion criteria of this study, patients of the adult age group of both sexes with a fever of any duration, irrespective of antibiotic treatment having blood or stool culture positive for *Salmonella typhi* and *S. Paratyphi* for group A, were included. On the other hand, according to the exclusion criteria of this study, febrile patients with any obvious focus for viral infection, patients with end-stage organ damage or immunosuppressive conditions, cases with any emergency medical conditions and patients with a history of immunization with typhoid vaccines were excluded. All the demographic and clinical information of the participants was recorded. All data were processed, analyzed and disseminated by using the MS Office program. For this analysis, only data from 50 confirmed enteric fever cases were considered.

RESULTS

In this study among the total of 50 enteric fever cases, 62% were male and 38% were female. In the majority of the cases (*S. enterica* positive febrile patients), 20 (40%) were found in the age group of 10-20 years followed by 13 (26%), 9 (18%) and 8 (16%) in the 21-30, 31-40- and 41-50-years age groups respectively. According to the duration of fever at presentation, we found that in more than half of the patients, fever was present in the 2nd week. [Fig-1]
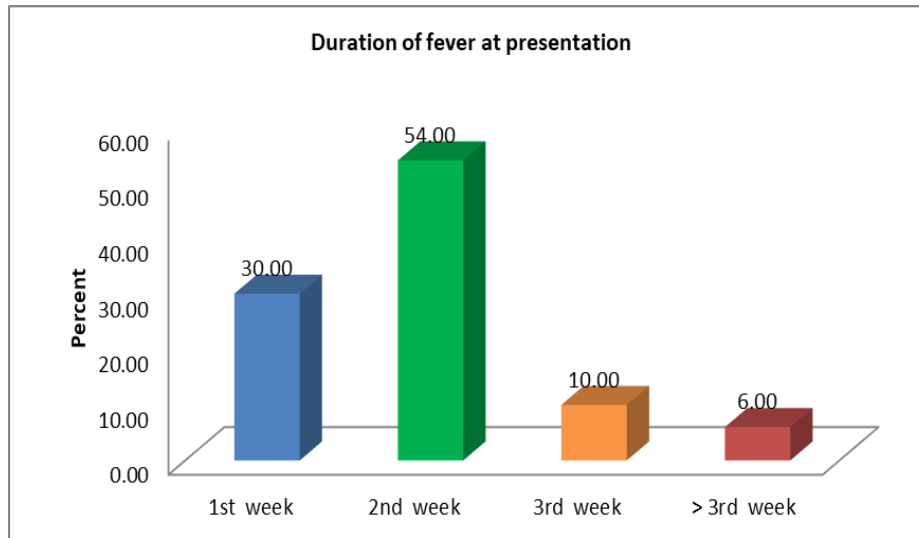

Figure 1: Distribution of participants as per the duration of fever. (n=50)

Table-1 revealed that more than 75% of patients had headache, anorexia. malaise, myalgia, abdominal pain and chills. Besides, in 50%-75% of cases, step ladder fever, diarrhoea, vomiting, arthralgia, rigors and sweating were present.

Table 1: Distribution of participants as per the frequency of symptom. (n=50)

Symptoms	n	%
Headache	45	92.00%
Anorexia	46	92.00%
Malaise	43	86.00%
Myalgia	40	80.00%
Abdominal pain	39	78.00%
Chills	38	76.00%
Step ladder fever	37	74.00%
Diarrhoea	37	74.00%
Vomiting	37	74.00%
Arthralgia	35	70.00%
Rigors	34	68.00%
Sweating	27	54.00%
Cough	23	46.00%
Constipation	11	22.00%
Dysuria	1	2.00%

Table-2 illustrated that among the total 50 enteric fever cases, 3 (6%), 13 (26%), 4 (8%) and 30 (60%) were well looking, anxious, depressed and toxic respectively.

Table 2: Distribution of participants as per appearance. (N=150)

Appearance	Group A		Group B	
	Fever with S. enterica		Fever without S. enterica	
	(n=50)		(n=100)	
	n	%	n	%
Well looking	3	6%	20	20%
Anxious	13	26%	28	28%
Depressed	4	8%	20	20%
Toxic	30	60%	32	32%
Total	50	100%	100	100%

Table-3 shows the signs of culture-positive enteric fever patients, we found that in more than 75% of cases, relative bradycardia, tender RIF, dehydration and splenomegaly were present. Besides, in more than 50% of cases, coated tongue, appearance (Toxic) was present.

Table 3: Distribution of participants as per sign of culture-positive enteric fever. (n=50)

Sign	Fever with S. enterica	
	n	%
Relative bradycardia	46	92%
Tender RIF	45	90%
Dehydration	40	80%
Splenomegaly	38	76%
Coated tongue	36	72%
Appearance (Toxic)	30	60%
Caecal Gurgling	22	44%
Hepatomegaly	14	28%
Anemia	12	24%
Hepatosplenomegaly	9	18%
Jaundice	5	10%
Oedema	4	8%
Clubbing	2	4%
Lymphadenopathy	2	4%
Ascites	2	4%
Bony tenderness	1	2%

Figure-2 shows among the total of our enteric fiver cases, 41 (82%) were infected by *S. typhi* and the rest 9 (18%) were by *S. paratyphi*.
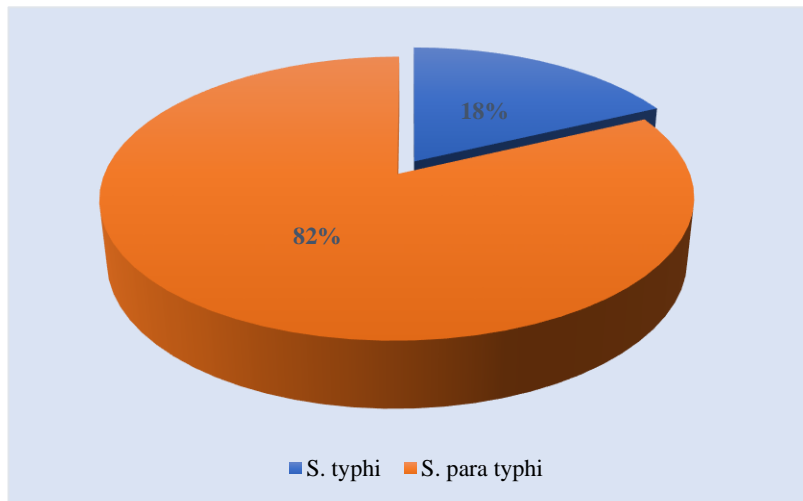

Figure 2: Distribution of cases according to S. typhi & S. paratyphi positivity

Figure-3 illustrated that among the total of our 50 enteric fever cases with isolated salmonellae organisms including *S. typhi* and *S. Paratyphi,* during the treatment procedure, as the antibiotics cefepime, cefixime, ceftazidime, ciprofloxacin, imipenem, meropenem and ofloxacin showed 100% sensitivities. Besides ceftriaxone, cotrimoxazole, chloramphenicol and azithromycin showed 98%, 68%, 66% and 54% sensitivities respectively (>50%). On the other hand, more than 50% of resistant cases were found in treatment by nalidixic acid (76%), ampicillin (98%) and amoxicillin (98%).
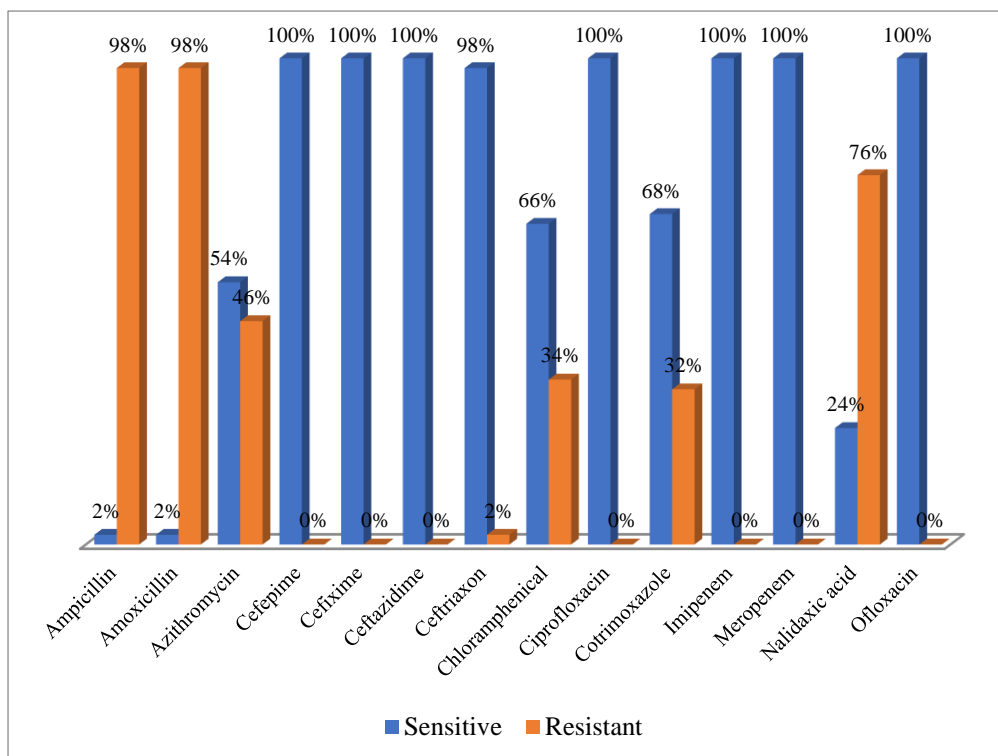

Figure 3: Antibiotic sensitivity profile of isolated salmonellae organism (n=50)

DISCUSSION

This study aimed to assess the antimicrobial sensitivity pattern of commonly used antibiotics among adult enteric fever patients. The majority of the cases (*S. enterica* positive febrile patients) 20 (40%) were found in the age group of 10-20 years and the male-female ratio was 1.6:1. We found that in more than half of the patients, fever present in the 2nd week. We observed that in more than 75% of patients, headache, anorexia. malaise, myalgia, abdominal pain and chills were present. Among the total 50 enteric fever cases, 3 (6%), 13 (26%), 4 (8%) and 30 (60%) were well looking, anxious, depressed and toxic respectively. In this study, analyzing the sign of culture-positive enteric fever patients, we found that in more than 75% of cases, relative bradycardia, tender RIF, dehydration and splenomegaly were present. Besides, in more than 50% of cases, coated tongue, appearance (Toxic) was present. In a comparison of symptoms and signs found in some other studies, they were more or less similar to the present study [10,13]. Among the total of our enteric fiver cases, 41 (82%) were infected by *S. typhi* and the rest 9 (18%) were by *S. paratyphi*. In other studies, 73 of the 119 study patients (61%) were positive for *Salmonella typhi* while the rest had *Salmonella paratyphi* [14]; a total of 136 isolates of Salmonella spp. were isolated from 408 blood cultures and *S. typhi* was the predominant serotype (107, 78.7%) followed by *S. Paratyphi* (29, 21.3%) [15]. All these findings are consistent with that of the present study. Among the total of our 50 enteric fever cases with isolated salmonellae organisms including *S. typhi* and *S. Paratyphi*, during the treatment procedure, as the antibiotics cefepime, cefixime, ceftazidime, ciprofloxacin, imipenem, meropenem and ofloxacin showed 100% sensitivities. Besides ceftriaxone, cotrimoxazole, chloramphenicol and azithromycin showed 98%, 68%, 66% and 54% sensitivities respectively (>50%). On the other hand, more than 50% of resistant cases were found in treatment by nalidixic acid (76%), ampicillin (98%) and amoxicillin (98%). These findings were similar to the findings of another study conducted by Mohamed et al. (2023) [16]. Another study by Bulbul Hasan et al. [10] found an antimicrobial susceptibility pattern of 16 isolates of *S. typhi* showing that no isolate was resistant to Ceftriaxone and Ceftazidime, only 03(18.75%) was resistant to Ciprofloxacin and Azithromycin whereas 10(62.5%) were MDR showing resistance to Ampicillin, Co-trimoxazole and Chloramphenicol which are first-line anti typhoidal drugs. Safe water supply and improvement in sanitation facilities will go a long way in the control of typhoid especially in developing countries [17].

Limitation of the study:

This was a single-centered study with small sample size. Moreover, the study was conducted over a very short period. That's why findings of this study may not reflect the exact scenario of the whole country.

CONCLUSIONS

As per the findings of this current study, we can conclude that, till today, considering the lower treatment cost and better patient compliance ciprofloxacin may be considered as the drug of choice in treating adult enteric fever patients. Besides cefepime, cefixime, ceftazidime, ciprofloxacin, imipenem, meropenem or ofloxacin can be used in such cases confidently. To decrease the relapse rate in treating enteric fever cases some older molecules like ampicillin and amoxicillin should be avoided. For getting more specific results, we would like to recommend conducting similar studies in several places with larger-sized samples.

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