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"Sensitivity Pattern of commonly used Antibiotics in Children with Enteric Fever: A study in Dhaka Shishu(children) Hospital, Dhaka, Bangladesh."

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Abstract: *This cross sectionalstudy was carried out in the Dept. of Paediatrics, in Dhaka Shishu (Children) Hospital during the period from January 2013 to December 2013. The aim of our study was to identify the culture sensitivity pattern of commonly used antibiotics among Children with enteric fever in a tertiary care hospital. We selected 98 culture positive cases of enteric fever aged between 2 years and 12 years admitted in the above mentioned hospital were enrolled in this study. Majority (62.2%) of the patients belonged to 5-9 years of age. Males were dominating the study 61.22%. Around half (48.9%) of the patients came from Middle class background. Blood C/S for salmonella typhi and paratyphi were 70(71.44%) and 28(28.57%) respectively. Antibiotic sensitivity of S. typhi among patients showed that Ceftriaxone were 100% sensitive followed by Cefixime 80.2%, Chloramphenicol 78.57%, , Ciprofloxacin65.20%,Azithromycin 60%,Ofloxacin 55%, Amoxicillin 54.6%, , Cotrimoxazole 40.3%, Nalidixic acid 20.4% . Antibiotic sensitivity of S. Paratyphiamong patients showed that Ceftriaxone were also 100% sensitivity followed by Cefixime 98%, Chloramphenicol 88%, Amoxicillin &Ofloxacin 80%, Cotrimoxazole 76%, Ciprofloxacin 72%, Azithromycin 66%, Nalidixic acid 17%.. Almost half (51.3%) of the patients received antibiotic during pre-admission period whereas 41.2% of the culture positive patients received pre admission antibiotics. we can conclude that knowledge of antibiotic sensitivity may have fruitful effect in successful treatment of typhoid fever in children. Irrational uses of antibiotic can hinder such sensitivity pattern.*

Key words: *Antibiotic, resistance, sensitivity, enteric fever.*

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I. Introduction

Typhoid fever is an acute systemic infection caused by Salmonella enterica serotype Typhi or Paratyphi. It is an important public health problem in many countries. The worldwide incidence of typhoid fever is estimated to be approximately 16 million cases annually, of which 7 million cases occur in Southeast Asia. More than 600,000 people die due to this disease each year (Ivanoff, 1995)[1]. Typhoid fever is generally considered a disease of school going children and young adults, although there is evidence of a substantial disease burden in preschool children in some countries where disease is endemic (Sinha et al. 1999 and Brooks et al. 2005)[2]. *S. Typhi*is the dominant cause of typhoid fever in most areas, although the proportion of infections attributed to *S. Paratyphi.* A has been increasing in the north of the Indian subcontinent and China (Ochiai et al. 2005 and Dong et al. 2010)[3]. ICDDRB in 2001 conducted a study at Kamalapur in Dhaka and concluded approximate incidence of typhoid fever in our population documented by positive blood culture is 3.9 episodes per year per 1000 populations. The isolation of *S. Typhi* or *S. Para-typhi*-A from blood, bone marrow, rose spots or other sterile sites provides the most conclusive confirmation of typhoid fever. Therefore, culture should be considered as the gold standard and used for evaluating all diagnostic tests, irrespective of their level of sophistication (WHO 2003). Bacterial isolation confirms the clinical diagnosis and allows antimicrobial-susceptibility testing which can detect appropriate therapy yet it is only positive in approximately 40–60% of presumptive cases (Gilman et al. 1975)[4]. In order to effective treatment of typhoid fever, culture and antibiotic sensitivity tests must be donefirst. Once culture & sensitivity test results confirm the type of bacterial infection treatment may be modified (Saana et al 2014)[5].The case fatality rate of Salmonella infections are increasing

globally, especially in South Asian countries (Ochiai et al 2005)[3]. In Bangladesh, physicians are facing difficulties in treating typhoid fever due to its changing pattern of drug sensitivity as well as the development of multidrug resistance. Typhoid fever is not only a problem for patient but also for physician because patient may present to medical care after taking one or more antibiotics by themselves or advised by pharmacist or unqualified physician resulting in no growth of s. typhe or s. paratyphi in blood culture. Indiscriminate and injudicious use of antibiotics in undiagnosed febrile illness is responsible for diagnostic difficulties. There are many reports of changing clinical features and changing sensitivity ultimately developed drug resistant to S. Typhi or Paratyphi leading to difficulty in diagnosis and treatment.[6, 7].

II. Objectives of the study

Specific objective:

1. To detect the current susceptibility pattern of *salmonella Typhi* &*Paratyphi* in children with enteric fever

General objectives:

1. To find out the scenario of enteric fever in Bangladesh

III. Materials and Methods

This cross sectional study was carried out in the Dept. of Paediatrics, Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh during the period from January 2013 to December 2013. The aim was to identify the pattern of commonly used antibiotic's sensitivity among Children with enteric fever in a tertiary care hospital. We selected 98 suspected cases of enteric fever aged between 2 years to 12 years admitted in the above mentioned hospital and enrolled in this study. This study was done in one year and 98 blood culture positive children were included in the study.All confirmed cases of enteric fever were selected, detailed history was taken and clinical examination was done.

Inclusion Criteria: Patients with following characteristics were included in the study.Patients aged 2 to 12 years of age**,** Patients of either sex**,** Fever ≥ 38°C for ≥ 4 days**,** Culture positive for enteric fever.

Exclusion criteria: Patients with following characteristics were excluded from the study: Culture-negative, Evidence of severe disease (complicated enteric fever) and Prior use of antibiotics within one week of hospital admission.

IV. Results

A total of 98 patients, who had a growth of *S. typhi or paratyphi* from blood culture samples were collected and included for analysis. Mean age of the study population was 2-12 years (9.4 ± 6.76). Male were 60 (61.22%) and female were 38 (38.77%). Total 98 culture positive cases were enrolled among them *S. typhi* were 70(71.42%) and *S. paratyphi* were 28(28.57%). Both were 100% susceptible to Ceftiaxone. Antibiotic sensitivity for *S.typhi* was Amoxicillin (54.6%), Azithromycin (60%), Cefixime (80.2%), Ceftriaxone (100%), Chloramphenicol (78.35%), Ciprofloxacin (65.52%), Cotrimoxazole (40.3%), Nalidixic Acid (20.4%) and Ofloxacin (55%). Antibiotic sensitivity for *S.paratyphi* was Amoxicillin (80%), Azithromycin (66%), Cefixime (98%), Ceftriaxone(100%), Chloramphenicol (88%), Ciprofloxacin(72%), Cotrimoxazole (76%), Nalidixic Acid (17.2%) and Ofloxacin (80%) respectively. Antibiotic resistance for S.typhi was Amoxicillin (45.4%), Azithromycin (40%), Cefixime (19.8%), Ceftriaxone (0%), Chloramphenicol (21.65%), Ciprofloxacin (34.48%), Cotrimoxazole (59.7%), Nalidixic Acid (79.6%) and Ofloxacin (45%). Antibiotic resistance for S.paratyphi was Amoxicillin (20%), Azithromycin(34%), Cefixime (02%), Ceftriaxone (0%), Chloramphenicol(12%), Ciprofloxacin (28%), Cotrimoxazole(24%), Nalidixic Acid (82.8%) and Ofloxacin (20%) respectively.

In our study, most susceptible antibiotic was Ceftriaxone then Cefixime and then Chloramphenicol and least susceptible antibiotic was Amphicillin then Nalidixic acid and then Cotrimoxazole.

Table I. Distribution of patients by age, sex and Socio-economic class (n = 98)

Age	Frequency	Percentage
2-5 years	22	22.44
5 – 9 years	60	61.22
>9 years	16	16.32
Mean Age		(9.4 ± 6.76)
Range		(2 – 12) years
Sex		
Male	60	61.22
Female	38	38.77
Socio-economic status		

Poor	26	26.53
Middle Class	48	48.97
Upper Class	24	24.48

Table-2: Antibiotic sensitivity and resistance pattern of *S. typhi* (n=70)

	S. typhi	
Antibiotic	**Sensitive%**	**Resistant%**
Amoxicillin	54.6	45.4
Azithromycin	60.0	40.0
Cefixime	80.2	19.8
Ceftriaxone	100	0 (0)
Chloramphenicol	78.35	21.65
Ciprofloxacin	65.52	34.48
Cotrimoxazole	40.3	59.7
Nalidixic acid	20.4	79`6
Ofloxacin	55	45

*Not all samples were tested against all antibiotic listed

Figue-1: Antibiotic sensitivity of *S. typhi* (n=70)

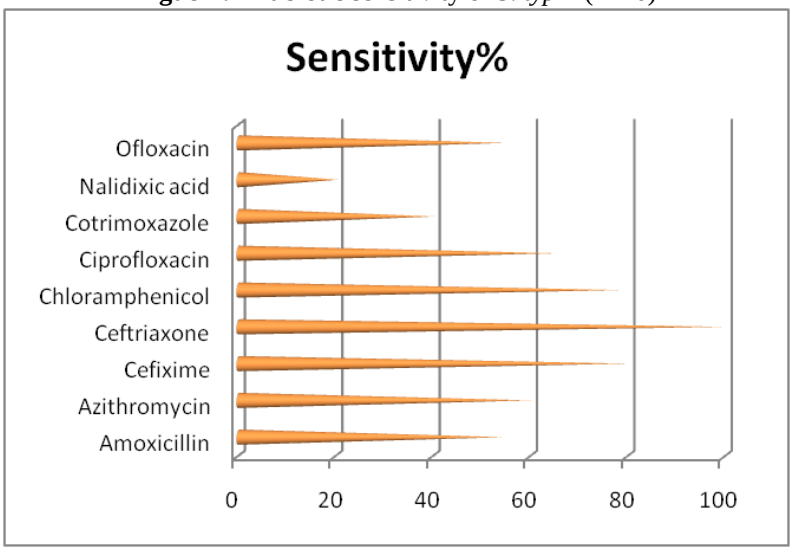
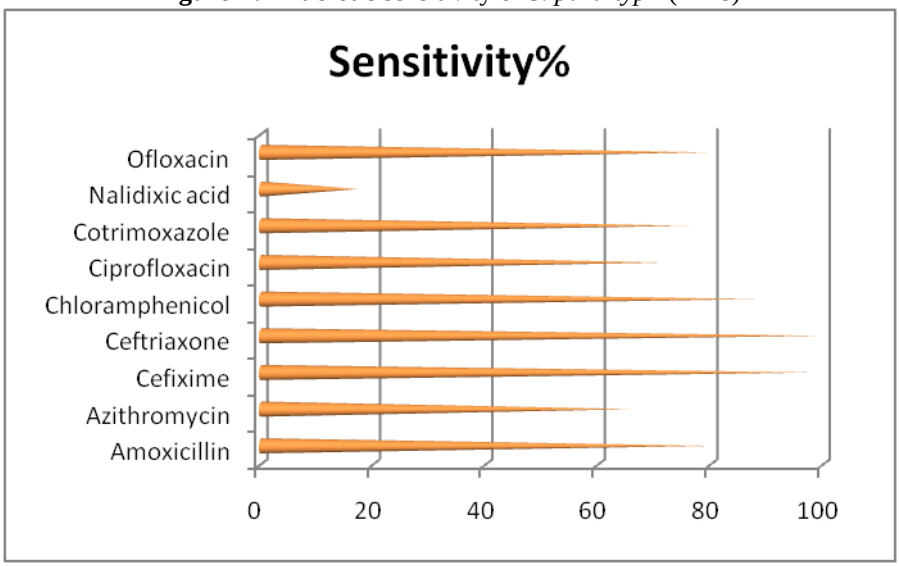


Table-3: Antibiotic sensitivity and resistance pattern of *S. para-typhi*(n=28)

	S. Para-typhi	
Antibiotic	**Sensitive%**	**Resistant%**
Amoxicillin	80.0	20.0
Azithromycin	66.0	34.0
Cefixime	98.0	2.00
Ceftriaxone	100	0 (0)
Chloramphenicol	88.0	12.0
Ciprofloxacin	72.0	28.0
Cotrimoxazole	76.0	24.0
Nalidixic acid	17.2	82.8
Ofloxacin	80.0	20.0

*Not all samples were tested against all antibiotic listed

Figure-2: Antibiotic sensitivity of *S. para-typhi*(n=28)



V. Discussion

The introduction of chloramphenicol for the treatment of typhoid fever in 1948 transformed a severe, debilitating and often fatal disease into a readily treatable condition[8].In spite of reported resistance within 2 years of its introduction, chloramphenicol resistance was not a major problem until 1972[9].After that, large number of antibiotics lost sensitivity to Salmonella species mostly because of their irrational use [10].In our study we found that significant number of cases were multi-drug resistant, which is much lower than previous studies.[11,12,13]. One explanation might be that as 1st line drugs are not used in enteric fever because of high resistance rate, so they are regaining their sensitivity. Not a single patient was resistant to ceftriaxone in our study although ceftriaxone resistance has been reported from Bangladesh[13,14]. Significant numbers of patients were resistant to azithromycin as seen in other studies[14]. Its dosing convenience, easy availability and non-judicious use in non-specific febrile illness might be the contributory factor behind it.Ceftriaxone was sensitive in 100% cases in this study as seen in another study[13] .Cefixime, ciprofloxacin and ofloxacin were sensitive in significant number of cases, but much lower than previous studies[15].Nalidixic acid resistance is increasing. It is recommended that ciprofloxacin, in contrary to previous statements, should no longer be used if the organism is resistant to Nalidixic acid and the clinician should advices to switch over to another antibiotics[11, 13]

VI. Limitations of the study

This study was conducted in a single centre with small sample size that can't be generalized in the whole country. In addition, all samples were not tested against all 1st line antibiotics.

VII. Conclusion and Recommendations

In our study, first line antibiotic like Ampicillin, Cotrimoxazole, Nalidixic acid in most of the cases, they are going to develop resistance. Some previously highly sensitive drugs like ciprofoxacine, cefixime, ofloxacine etc. are showing resistance in some cases. In conclusion, we can say that Ceftriaxone is the most sensitive antibiotic for Salmonella species till now. So, we can recommend that blood cultures need to be sent before prescribing antibiotics in suspected enteric fever to prevent further resistance.

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