

Original Article

Study of Clinical Profile and Antibiotic Response in Typhoid Fever at Faridpur Medical College Hospital.

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Abstract:

The objectives of this present study is to evaluate the clinical profile and pattern of various drugs used in the treatment of typhoid fever. A retrospective analysis of Paediatric patients suffering from typhoid fever was done at Department of Paediatrics, Faridpur Medical College Hospital, Faridpur during the year 2015-2016. Diagnosis of patients was based on clinical features, Widal test and blood culture. The sensitivity pattern of isolates from blood culture was recorded. The mode of presentation, clinical course, treatment history, laboratory investigations reports, antibiotic administered, response to therapy and the complications were recorded. Total number of 50 cases of typhoid fever were studied. Out of these 23 (46%) were males and 27 (54%) were females. Average age of presentation was 8.2 years. Average duration of hospital stay was 10.8 days. Fever was present in all patients. Resistance of *S. typhi* to amoxicillin, chloramphenicol, ampicillin and co-trimoxazole were significantly high. Ciprofloxacin also showed resistance in 21.4% of cases. Sensitivity to cephalosporin was 100% in our study. Ciprofloxacin was the most commonly used antibiotic in our study (26 patients). Chloramphenicol alone was used in 2 patients and in 3 patients it was given after 6 days of ciprofloxacin treatment. Third generation cephalosporin (ceftriaxone) alone were used in 10 patients. Indiscriminate use of drugs in typhoid fever should be discouraged. Appropriate antibiotic as indicated by sensitivity tests should be employed to prevent the development of resistant strains of *S. typhi*.

Key words: Typhoid Fever, Antibiotics, Clinical Profile.

Introduction:

Typhoid fever occurs in all parts of the world where there is substandard water supply and sanitation. In endemic country including Bangladesh with morbidity ranging from 102 to 2219 per 100,000 population¹. Today due to its changing modes of presentation, as well as the development of multidrug resistance, typhoid fever is becoming increasingly difficult to diagnose and treat. Improved standards of public health

have resulted in a marked decline in the incidence of typhoid fever in developed countries². The emergence of strains of *Salmonella typhi* resistant to multiple antibiotics poses a serious problem. Chloramphenicol was considered the antimicrobial gold standard for the treatment of typhoid fever till 1948³. But in the last two decades there has been increase in the resistance of strains of *S. typhi* to chloramphenicol. It was first reported in Britain, in 1950⁴ and in this subcontinent in 1972⁵. Gradually, resistance to multiple antibiotics developed⁶. The first major epidemic of multidrug resistant *S. typhi* was reported in 1972⁷ in Mexico. Since then, an increasing frequency of antibiotic resistance has been reported from all parts of the world, but more so from the developing countries⁶. The uses of chloramphenicol, ampicillin and co-trimoxazole have become infrequent and quinolones have become the first line of treatment of typhoid fever. However, over the last few years there has been increase in the defervescence period in patients treated with quinolones. Hence, this study was undertaken to evaluate the clinical profile and antibiotic response in typhoid fever.

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Materials and Methods:

A retrospective analysis of paediatric patients suffering from typhoid fever was done at Department

of Paediatrics, Faridpur Medical College Hospital, Faridpur during the year 2015-2016. Both males and females were included in the study. Diagnosis of patients was based on clinical features, Widal test and blood culture. The sensitivity pattern of blood culture was recorded. The mode of presentation, clinical course, treatment history, laboratory investigations reports, antibiotic administered, response to therapy and the complications were recorded. Defervescence was defined as the number of days required for abatement of fever after starting the antibiotics.

Results :

A total number of 50 cases of typhoid fever were studied. Out of these 23 (46%) were males and 27 (54%) were females. Average age of presentation was 08.2 years. Average duration of hospital stay was 10.8 days. Fever was present in all patients (100%). Vomiting was present in 18% patient. Diarrhoea was seen in 18% patient. 10% patient had pain abdomen. Constipation was present in 8% patient. Hepatomegaly was detected in 18% and splenomegaly was present in 36% patient (Table-1).

Table - I: Presenting symptoms of patients (N=50)

Symptom	Subjects	%
Fever	50	100
Vomiting	9	18
Diarrhoea	9	18
Headache	8	16
Pain abdomen	5	10
Body ache	1	2
Dry cough	3	6
Breathlessness	1	2
Weight loss	1	2
Constipation	4	8
Hepatomegaly	9	18
Splenomegaly	18	36

Bradycardia was observed in 12 (24%) patients. Bleeding per rectum was seen in one patient. One patient died due to disseminated intravascular coagulation (Table - II).

Table - II: Complications observed during hospitalization. (N=50)

Complications	Number of subjects	%
Bradycardia	12	24
Bleeding per rectum	1	2
Jaundice	1	2
Disseminated intravascular		
Coagulation followed by death	1	2

A single estimation of Widal test was suggestive of enteric fever in significant titre in 88.6% cases (O titre of 1:160 or more). Blood culture was positive in 25% of cases. Malarial smear was positive in one of the patients and dengue antibody was positive in another patient. There was no leucopenia or thrombocytopenia in any patient.

Antibiotic sensitivity pattern in culture proven cases [Table - III] shows that resistance of *S. typhi* to amoxicillin, chloramphenicol, ampicillin and co-trimoxazole was significantly high. Ciprofloxacin also showed resistance in 21.4% of cases. Sensitivity to cephalosporin (ceftriaxone) was 100% in our study. In one of the patients, even though there was in vitro sensitivity to ciprofloxacin, patient did not respond to it, suggesting in vivo resistance.

Table - III: Antibiotic sensitivity in culture proven cases (N=50)

Drugs	Sensitive n (%)	Resistant n (%)
Amoxicillin	3 (27.3)	8 (72.7)
Chloramphenicol	4 (36.4)	7 (63.6)
Ampicillin	5 (45.5)	6 (54.5)
Co-trimoxazole	4 (36.4)	7 (63.6)
Ciprofloxacin	11 (78.6)	3 (21.4)
Third generation		
Cephalosporin	14 (100)	0

Table - IV: Clinical responses to antibiotics in all patients. (N=50)

Antibiotics	No. of patients treated	% of total cases	Clinical response n(%)
Ciprofloxacin	26	52	12 (46.2)
Chloramphenicol	2	4.7	2 (100)
Chloramphenicol+			
Ciprofloxacin	3	6.8	3 (100)
3 rd generation			
Cephalosporin	10	20	10 (100)
Ciprofloxacin +			
3 rd generation			
Cephalosporin	9	20.4	9 (100)

Table IV shows pattern of drug response. Ciprofloxacin was the most commonly used antibiotic in our study (26 patients). Chloramphenicol alone was used in two patients and in three patients it was given after six days of ciprofloxacin treatment.

Third generation cephalosporin (ceftriaxone) alone were used in 10 patients. In nine patients it was given after six days of ciprofloxacin treatment as there was no clinical response. Average duration of treatment was 12 days with ciprofloxacin, 14 days with chloramphenicol and 10 days with third generation cephalosporin. Defervescence period was eight days with ciprofloxacin, 10 days with chloramphenicol and six days with third generation cephalosporin.

Discussion:

Drug resistance in typhoid fever is considered as one of the important factors in the morbidity and mortality of the disease. Since the introduction of chloramphenicol in 1948, it has been the drug of choice in the treatment of typhoid fever in most parts of the world. But the indiscriminate use of the drug and acquisition of plasmid mediated R factor has led to the development of resistance to *S. typhi* against this drug⁸. Tropical countries like Bangladesh have shown widespread distribution of chloramphenicol resistant strains of *S. typhi*, the incidence varying from 38.6% to 83%⁹⁻¹¹. The emergence of chloramphenicol resistance posed a big problem regarding the treatment of patients with typhoid fever. Alternative drugs suggested included co-trimoxazole, ampicillin and amoxicillin. During 1990, drug resistant *S. typhi* not responding to chloramphenicol, ampicillin and co-trimoxazole appeared in various parts of the country, the incidence varying from 50 to 52.9%¹⁰. In our study, incidence of chloramphenicol resistance was found to be 63.6%. Resistance to amoxicillin, ampicillin and co-trimoxazole was also present in significant number of patients. The quinolone group of drugs emerged as useful drugs for the treatment of multiple drug resistant cases of *S. typhi*. But unfortunately, the same factors of indiscriminate antibiotic use and cross resistance within the antibiotic group which led to the emergence of chloramphenicol resistant organisms are still operative. The resistance to quinolone is not plasmid coded but due to an altered DNA gyrase subunit. Resistance to ciprofloxacin is now being reported both from the Indian subcontinent and West¹²⁻¹⁴. In the present study *S. typhi* has shown resistance to ciprofloxacin in 18.1% of cases.

The defervescence period for ciprofloxacin is about 3-5 days^{15,16} according to the literature and for cephalosporin is about three days. But in the present study we have observed that the defervescence period was comparatively longer; about eight days for ciprofloxacin and about six days for cephalosporin. In one patient, although there was in vitro sensitivity to ciprofloxacin patient did not respond to the drug. These findings suggest that sensitivity of *S. typhi* to ciprofloxacin is gradually decreasing. Indiscriminate use of drugs is one of the important factors leading to

drug resistance and in case of ciprofloxacin, moderate cost, advantage of oral route, tolerability, convenient dosage schedule have contributed towards its indiscriminate use. In our study, sensitivity to third generation cephalosporin was 100%, although study done by Ranjuet al¹⁷ has shown significant decrease in the in vitro sensitivity to cephalosporin. High cost of cephalosporin may not permit its indiscriminate use for minor infection.

Conclusion:

The indiscriminate use of drugs in typhoid fever should be discouraged. Appropriate antibiotic indicated by sensitivity tests should be employed to prevent the development of resistant strains of *S. typhi*.

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