

A Study of Clinical Profile of Multidrug Resistant Typhoid Fever In Children.

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Abstracts : Background: Salmonella typhi infection remains a serious problem in developing country. It has been estimated that approximately 12.5 million cases of typhoid fever occurs annually in the developing countries with 7.7 million cases in Asia alone. The disease is predominantly a disease of school age children and young adults and is reported to be a milder in infants and young children. Methods: A total of 150 children with clinical and/or laboratory diagnosis of typhoid fever admitted to the tertiary care level government hospital attached with the Government medical college in Pediatrics ward were reviewed during the months of JUNE to MAY for demographic data such as age, sex, clinical features, result of laboratory tests and antibiotic sensitivity in vivo. Results: There were 88 male and 62 female patients, from the age group ranging from 2 years to 12 years. Predominant symptoms were fever, abdominal pain , vomiting and headache. Hepatomegaly was almost twice as frequent as splenomegaly. Common clinical signs of typhoid fever in adults such as relative bradycardia and rose spots were seldom documented in children. Fever, Toxic look, coated tongue and hepato-splenomegaly were common clinical signs of clinical presentation in children. The positivity rate of WIDAL test and Blood Culture was 71.33% and 5.33% respectively. Hepatitis, Bronchitis and Encephalopathy were commonly observed complications of Multidrug resistant typhoid fever in this study. Antibiotics sensitivity in vivo revealed resistance rates of 78.12% for Ampicillin, 84.2% for Trimethoprim-Sulfamethoxazole (Co-trimoxazole), 19.5% for Ciprofloxacin, 14.28% for Ofloxacin and 20% for Cefotaxime. Conclusions : No resistance was detected against Cefixime and Ceftriaxone. Except the two patients died during the period of observation of this clinical study, all paediatrics patients survive from their illness completely.[Gosai M M et al NJIRM 2011; 2(3) : 87-90]

Key Words: Multidrug resistant typhoid fever (MDRTF), Salmonella Typhi (S.Typhi)

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Introduction: Salmonella typhi infection remains a serious problem in developing country. It has been estimated that approximately 12.5 million cases of typhoid fever occurs annually in the developing countries (Excluding China) with 7.7 million cases in Asia alone.¹ The disease is predominantly a disease of school age children and young adults and is reported to be a milder in infants² and young children.^{3,4} Various organs have been involved in the course of typhoid fever, resulting in a wide array of presentation. Chloramphenicol resistant S.typhi were first reported in 1972.⁵ Since then chloramphenicol or multidrug resistant typhoid fever (MDRTF) has been reported during outbreaks from many parts of the world.^{6,7,8,9,10,11,12} The present study focuses our attention on clinical profile of multidrug resistant typhoid fever in children.

Materials and Methods: We have reviewed the medical records of all patients admitted to the

Ward of Pediatrics in our hospital between the month of June to May. In this study, children were divided into two groups: those who had culture negative and serology positive and had clinical features strongly suggestive of typhoid fever (n = 142) and those who had positive blood culture and clinical features strongly suggestive of typhoid fever¹³ (n = 8). All these children were managed under the supervision of the authors. Patients with a clinical diagnosis of typhoid fever were put on one of the first line antibiotics after collecting blood samples for widal test^{2,14,15,16} and blood culture. X-ray chest was obtained in all the cases.

Other necessary investigations were carried out as and when required. Base on our earlier antibiotics response clinically-Ampicillin, Co-trimoxazole and Amoxycillin were used as first line antibiotics. The decision to use one of these antibiotics was based on clinical condition of the child, drugs used before hospitalization on outpatient bases and availability

of drug(s) in the hospital. Treatment failure was defined as persistence of high grade fever after taking antibiotic(s) orally or parenterally with a proper dose at appropriate intervals for a period of 7 days. Clinical profile of Widal and Blood Culture positive patients was analyzed.

Result : During this period 150 cases were studied with a clinical diagnosis of typhoid fever. Of these, 8 patients were blood culture positive. Peak incidence was seen in the months of **August** and **November** (32.66%).Table 1.

Table 1: Showing Seasonal Variation Of MDR-Typhoid Fever (During study period of 2 years)

Months	No. of patients	% (n=150)
Jun.-Sept.	66	44%
Oct.- Jan	55	36.66%
Feb.-May	29	19.34%

Nearly 68% of children were in the school going age (6-12 years). The youngest patient was around 2 years of age. Male : Female ratio was 1.38: 1 with male preponderance. Age and sex distribution is given in table 2.

Table 2: Age and sex distribution

Age	Sex & No. Of Patients		Percentage (N=150)
	Male	Female	
< 2 years	8 (5.33%)	5 (3.33%)	13 (8.66%)
2-5 years	22 (14.66%)	13 (8.66%)	35 (23.33%)
6-12 years	58 (38.66%)	44 (29.34%)	102 (68%)
TOTAL	88 (58.66%)	62(41.34%)	150

Fever was the main symptoms present in 100% cases. Continuous pattern was seen in 49.34% cases and Intermittent in 50.66% cases. Vomiting (86.66%), Abdominal pain (80.60%) and Anorexia (72%) were three common symptoms at the time of presentation, next to fever. On detail clinical examination : Pallor, Toxic Look, Coated tongue were found in majority of patients in 66.6%, 98%, 92% of cases respectively. Hepatomegaly was found in 53.3 % of cases and splenomegaly was found in 22.6% of cases. Relative bradycardia was not a common feature as seen in adult, among the children and observed only in 2 patients (1.33%). Jaundice was found in 13 patients (8.6%) of cases. Rose spots were not observed in any of our patients. CNS Manifestations (altered sensorium and abnormal behaviour) were found in 4% cases. Anemia (Hb less than 10 gm%) was seen in 107 cases (71.33%). Leucopenia (TLC less than 5000/ Cu.mm) in 28 patients (18.66%) and leucocytosis in 3 patients (2%).Thrombocytopenia (platelet counts less than 1,00,000) was observed in 4 cases (2.66%). Raised SGPT was observed in 16 patients (10.66%).

Serum Widal test were positive in 71.33% and Blood Culture were positive in 5.33 %. Antibiotic sensitivity pattern in vivo shown in Table 3.

Table 3: Showing antibiotic sensitivity PATTERN in vivo

	Antibiotics	No. Of patients in which used	No. of patients responded	No. Of patients resistant	Mean effervescences period
1.	Ampicillin	32	7 (21.8%)	25(78.12%)	7.5 days
2.	Amoxycillin	40	9 (22.5%)	31(77.5%)	8.0days
3.	Cotrimoxazole	19	3 (15.78%)	16(84.2%)	7.2 days
4.	Ciprofloxacin	42	34 (80.5%)	8(19.5%)	5.5 days
5.	Ofloxacin	14	12(85.71%)	2(14.28%)	5.0 days
6.	Amikacin	9	8 (88.8%)	1(11.9%)	5.0 days
7.	Cefixime	6	6 (100%)	-	6.5 days
8.	Cefotaxime	5	4 (80%)	1(20.0%)	6.5 days
9.	Ceftriaxone	38	38 (100%)	-	5.0 days
10.	Chloramphenicol	2	-	2(100%)	-

In the present study majority of patients shows resistance with Ampicillin (78.12%), Amoxycillin (77.5%) and Co-trimoxazole (84.2%). Ciprofloxacin,

Ofloxacin and Amikacin also showed variable resistance in 19.5% , 14.28% and 11.9% cases

respectively. Mean defervescence period was 6.24 days.

Out of 150 patients only 4 patients manifested relapse, that patients were initially treated with Ampicillin and Cotrimoxazole and were again managed successfully. Hepatitis was observed in 16 patients(10.66%), Bronchitis in 9 patients(6%), Cholecystitis in 5 patients(3.33%), Encephalopathy in 6 patients(4%) and Myocarditis in 4 patients(2.66%). 2 patients had fatal outcome. Carrier state was not observed in any of our study group patients during the study period.

Discussion: Salmonella Typhi infection remains a serious problem in developing countries. With an estimation of 12.5–16.6 million cases and 6,00,000 deaths per year.¹⁷ Typhoid fever continues to be a major cause of morbidity and mortality in children. However in more affluent regions of the world, proper sanitation has successfully diminished this infection.

Incidence of typhoid fever has been observed to be highest between 10-19 years of age in past. However, majority of our cases were below 12 years and as many as 31% were below 5 year. Though the school going children were found to be the most vulnerable, incidences of younger children affected with MDRTF are also reported by other study groups.^{18,19} Male preponderance^{18,19,20,21,22} was reported in the present study. Fever of variable pattern, grade and duration was the predominant symptoms along with pain in abdomen, vomiting and anorexia. Its association with chills, cough, chest signs and myalgia in significant number of cases was responsible for its confusion with malaria and respiratory infection resulting in the undue delay in the diagnosis.^{18,19,20,21}

Hepatomegaly (53.5%) and splenomegaly(22.6%) were more frequently detectable clinical signs after pallor, toxic look and coated tongue in the present study of MDRTF in children.^{18,21,23,24} Hepatitis with clinically detectable jaundice was noted with more or less similarly by other workers in 8.6% of cases. Typhoid Encephalopathy was observed in 4% of cases, mainly manifested as an altered sensorium and/or convulsion.^{19,21,25,26,27,28}

Hemogram showed anemia mainly, but leucopenia and thrombocytopenia proved poor diagnostic indicators.^{18,23} The positivity rate of serum Widal test and Blood culture was 71.33% and 5.33% respectively in the present study. The low incidence of blood culture positivity in the present study is due to the fact that majority of patients had taken the treatment from general practitioner before admission and some antibiotics might have been invariably used in all of them.^{20,22,26,28}

Resistance to Ceftriaxone and Cefixime was not observed in the present study in comparison with Ampicillin, Amoxicillin, & Cotrimoxazole. However, resistance to Quinolones was observed - this indicates that the salmonella develops resistance rapidly against quinolones and hence existing quinolones like Sparfloxacin, Levofloxacin, Gatifloxacin and Moxifloxacin should be used very rationally^{18,21,22,29,30} Moreover, there is an urgent need for newer, more effective antimicrobials to combat this menace of multi-drug bacterial resistance.

The mean defervescence period in most of the patients was between 6.24 days. It shows that typhoid fever still has serious morbidity with great impact on school attendance and cost of therapy. These observations also highlight the need of regular immunization, better public health measures, need of more effective and affordable antibiotics with their rational utility and diagnostic tools for an early detection of typhoid fever.

Recognition of varied presentations of multidrug resistant typhoid fever is very important so as not to miss this diagnosis when the disease mimics like malaria (chills and rigors), viral hepatitis (poor appetite and hepatomegaly with or without jaundice), bronchopneumonia or meningitis - as proper therapy instituted early in the course of disease is of immense help.

Conclusion: This study re-emphasize the importance of good drug compliance, judicious selection of antibiotics in adequate doses and optimal duration of therapy to minimize the risk of developing multidrug resistant typhoid fever in children with its variable grave presentations.

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