



International Journal of Medical Research & Health Sciences

www.ijmrhs.com

Volume 3 Issue 2 (April - Jun)

Coden: IJMRHS

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ISSN: 2319-5886

Received: 5th Dec 2013

Revised: 5th Jan 2014

Accepted: 11th Jan 2014

Research article

CLINICAL PROFILE AND ANTIBIOTIC SENSITIVITY PATTERN OF TYPHOID FEVER IN PATIENTS ADMITTED TO PEDIATRIC WARD IN A RURAL TEACHING HOSPITAL

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ABSTRACT

Introduction: Typhoid is a major endemic health problem among children in India. The last two decades have witnessed the emergence and spread of multidrug resistance against conventional anti typhoid drugs (Ampicillin, chloramphenicol and trimethoprim – sulfamethoxazole) especially in the South and South-East Asia. **Materials and Methods:** Children under twelve years of age with signs and symptoms suggestive of enteric fever were included in this study. Blood cultures were carried by collecting aseptically 5ml of blood and inoculating into bile broth and subcultured onto blood agar and Mac Conkey agar. Antimicrobial sensitivity performed according to CLSI guidelines. Widal test was performed. Other investigations like haemoglobin, total count and differential count of WBC, ESR were carried out. **Results:** The incidence of enteric fever in this study was 3%. The maximum children were in age group more than 5 years. Maximum cases were admitted during June-September. The most common symptoms were fever, anorexia, vomiting, and pain abdomen. The culture positivity of *Salmonella typhi* (*S.typhi*) was 35.4%. The overall positivity of Widal test was 89.8%. Multidrug resistant isolates in this study was 53.6%. **Conclusion:** Majority of the children were greater than 8 years old. Fever (intermittent type), anorexia, vomiting were the three major symptoms. Among the signs splenomegaly, hepatomegaly, coated tongue and toxemia were common. Relative bradycardia was not seen. Widal test was found positive in the majority of cases. Blood cultures were positive mainly in the first week of illness. The sensitivity pattern of *S.typhi* revealed significant proportion of multidrug resistant strains and simultaneous presence of chloramphenicol sensitive and resistant strains in the study.

Keywords: Typhoid, *Salmonella typhi*, multidrug resistant.

INTRODUCTION

Typhoid fever, also known as enteric fever is caused by the Gram negative bacterium *Salmonella enterica* serovar Typhi. The disease is mainly associated with low socioeconomic status and poor hygiene, with human beings the only natural host and reservoir of infection. ¹ Estimates for the year 2000 suggest that there are approximately 21.5 million infections and 2,00,000 deaths from typhoid fever globally each year. ²⁻⁴

Typhoid is a major endemic health problem among children in India. The last two decades have witnessed the emergence and spread of multidrug resistance against conventional antityphoid drugs (Ampicillin, Chloramphenicol and Trimethoprim–Sulfamethoxazole) among typhoid *Salmonellae*, especially in South and Southeast Asia. ^{5,6} Typhoid fever caused by such multidrug-resistant (MDR) strains of *Salmonella enterica* serotype Typhi presents a serious problem in many developing

countries.^{7,6} It has left fluoroquinolones as the antimicrobial agents of choice for the treatment of typhoid fever.⁸ Fluoroquinolones, especially ciprofloxacin, have been in use for more than 18 years and have remained an important weapon against typhoid infections. Effective antimicrobial therapy is required to control morbidity and prevent death from typhoid.

This study aims to know the clinical profile of pediatric enteric fever and the sensitivity of the disease to drugs in this region.

MATERIALS AND METHODS

The prospective study was carried out in a rural teaching hospital over a period of one year.

Data regarding admitted children below 12yrs of age with signs and symptoms suggestive of enteric fever and fulfilling any of the following criteria were included in the study.

Inclusion criteria:

1. Positive culture for *Salmonella typhi*
2. Widal titre; TO and TH \geq 1:160
3. Fourfold or greater rise in Widal titres.

Thorough and detailed history, clinical examination and laboratory investigations were done in all cases.

The following investigations were done:

Routine investigations: Haemoglobin estimation, Total and differential count for white blood cells, Erythrocyte sedimentation ratio, Urine and stool examination, Other investigations such as a chest X ray, liver function test, abdominal sonography were done where ever required

Bacterial cultures: Blood cultures were carried out by collecting aseptically 5ml of blood and added to 50ml of bile broth, incubated at 37°C for 24hrs. Initial subculture was made after 24hrs and if found negative, further subcultures were made after 48hrs, 4days and 7 days. Positive growths were subjected to standard biochemical tests.⁹ Species confirmation was done by agglutination with high titre sera.

Stool specimens were plated directly onto MacConkey and *Salmonella*, *Shigella* agar (SS), and inoculated into Selenite F broth for enrichment. The identity of isolates was confirmed by standard biochemical tests⁹ and slide agglutination with specific antisera.

Widal test: The Widal tube agglutination test was performed according to the manufacturer's instruction, using Tidal (Span diagnostics) containing

O and H antigens of *S. typhi* and *S. paratyphi* A and *S. paratyphi* B. Positive and negative serum controls were included, a titre of 1/160 to either antigen in a single serum specimen (in addition to the seroconversion) was taken to be indicative of typhoid fever. The results were correlated with blood culture results and interpreted in conjunction with the patient's history and recent clinical presentation on admission.

Antimicrobial susceptibility testing: Susceptibility to antimicrobial agents was performed using the Kirby Bauers disc diffusion method as described by the Clinical and Laboratory Standards Institute.¹⁰ Antimicrobial agents (discs) tested and reported were obtained from Hi media and included: ampicillin (10 μ g), trimethoprim – sulfamethoxazole (25/23.75 μ g), chloramphenicol (30 μ g), ceftriaxone (30 μ g), ciprofloxacin (5 μ g), cefixime(30 μ g) and cephalexin(30 μ g). MDR isolates of *S. typhi* were those resistant to all three first line antityphoid drugs (ampicillin, chloramphenicol and trimethoprim–sulfamethoxazole).

RESULTS

In this study a total number of 79 cases of enteric fever in children 12 years or less, admitted to the pediatric ward were studied. Total number of admissions in the pediatric ward during this period was 2601 so the incidence was 3%.

The maximum children were in the age group of more than 5 years (50, 63.3%). The youngest child in this study was 13 months old.

Among the children affected 42 were males and 37 females. The male to female ratio was 1.1:1. Cases were admitted throughout the year showing the endemicity of the disease. Maximum cases were admitted during June-September 36 (45.6%) (Table1).

The most common presenting symptom was fever 79 (100%) followed by anorexia 43 (54.4%) and vomiting 38 (48.1%), pain abdomen 21 (26.6%), loose motions 10 (12.6%), altered sensorium 10 (12.6%). In this study maximum cases 35 (49.3%) had fever for 8-14 days prior to admission. Almost half the cases 39 (49.4%) showed intermittent type of fever. The signs of enteric fever in this study were (table2).

Complications seen in this study were bronchitis 9 (11.3%), encephalopathy 7 (8.9%), cholecystitis 5 (6.3%), enteric hepatitis 3 (3.8%), shock 2 (2.53%) and paralytic ileus 1 (1.26%).

Routine investigations: In this study haemoglobin < 10gm/dl was found in 41.8% of cases. Majority of the children had WBC count in the range 5000-10000/cu mm (70.9%).

Table 1: Month wise distribution of cases

Month	No. of cases	Percentage
January	05	6.3%
February	04	5.1%
March	04	5.1%
April	05	6.3%
May	07	8.8%
June	08	10.2%
July	08	10.2%
August	12	15.2%
September	08	10.2%
October	05	6.3%
November	06	7.6%
December	07	8.8%
Total	79	100%

Table 2: Signs of enteric fever

Signs	Number of cases	Percentage
Tachycardia	64	81%
Splenomegaly	54	68.4%
Hepatomegaly	44	55.7%
Coated tongue	41	51.9%
Pallor	41	51.9%

Table 3: Antibiotic resistance pattern of salmonella typhi

Antibiotic	Number n = 28	Percentage
Multi drug resistant	15	53.6%
Chloramphenicol	18	64.2%
Ampicillin	25	89.3%
Co-trimoxazole	27	96.4%
Ciprofloxacin	28	00%
Ceftriaxone	28	00%
Cefixime	28	00%
Cephalexin	13	46.4%

In this study S.typhi was isolated in 28 out of 79 cases (35.4%), 17 (53.1%) cases were Widal positive in 1st week showed TO & TH >1:160. The positivity

increased in 2nd and subsequent weeks (91.4% & 100%) respectively. Among 15 cases which were widal negative in first week 9 cases (60%) showed rise in titres. The overall positivity of Widal test was 89.8%. The sensitivity of the Widal test was 71.4%. Antibiotic resistance pattern in this study was (table 3)

DISCUSSION

The incidence of enteric fever in this study was 3%, which was in accordance with the studies conducted by Pohawalla et al who also reported an incidence of 3%¹¹ but Bavdekar et al reported 23%¹² and Taneja 19%.¹³ The maximum children were in the age group of more than 5 years (63%) which is comparable to that in Pandey K.K et al 86.5%¹⁴ and Subindra 73%.¹⁵ The male to female ratio in this study was 1.1:1. Pandey et al reported 1.2:1.¹⁴

In this study cases were admitted throughout the year showing the endemicity of the disease. Maximum cases were admitted during June-September (45.6%). This period coincides with the onset of monsoon and increase in housefly population, which facilitates faeco-oral transmission. Pandey K.K et al reported maximum incidence between May-July¹⁴ and Arora et al reported 40.6% cases in the period of September-October.¹⁶

The most common symptoms were fever (100%), anorexia (54.4%), vomiting (48.1%), pain abdomen (26.6%), constipation (25.3%), loose motions (12.6%) and altered sensorium (12.6%). These symptoms were also seen in studies conducted by Taneja Sood et al¹³ and Pandey KK et al.¹⁴

In the present study maximum cases (44.3%) had fever for 8-14 days prior to admission which was comparable to that of Kapoor JP et al (51.6%).¹⁶ Almost half the cases (49.4%) showed intermittent type of fever. No case in this study had stepped ladder type of fever and this finding is same as reported by Pandey KK et al¹⁴, Kapoor JP, et al.¹⁷ The use of antipyretics and antibiotics were probably responsible for this pattern.

The common signs seen were splenomegaly (68.4%), hepatomegaly (55.7%), coated tongue (51.9%), pallor (51.9%) which was also reported by Kapoor JP et al¹⁷. The other signs tachycardias, toxic look, dehydration seen in this study were not reported by others.

In this study haemoglobin < 10 gm/dl was found in 41.8% of cases. This finding was seen in 64.5% by Kapoor et al.¹⁶ and 62% by Arora et al.¹⁶ Majority of the children (70.9%) had a WBC count in the range of 5000-10000/cumm which was comparable to 67.9% and 85.6% as reported by Pandey et al.¹⁴ and Mishra et al.¹⁸

The overall positivity of Widal test in this study was 89.8% as comparable to 90% reported by Manchanda et al.¹⁸ The culture positivity in this study was 35.4% which is in concordance with that of Manchanda et al.¹⁹ Among the 28 culture positive cases; Widal test was positive in 20 cases (71.4%). In eight cases Widal test remained negative on repeating after one week. The sensitivity of the Widal test in the present study was 71.4%. Use of antibiotics prior to admission was probably responsible for low culture positivity rates.

The present study found 53.6% isolates to be multi drug resistant. Garg et al.²⁰ and Arora et al.¹⁶ reported 67% and 82.5% respectively. 64.2%, 89.3%, 96.4% of the isolates were resistant to chloramphenicol, ampicillin and co-trimoxazole. No resistance was found to ciprofloxacin, Cefixime and ceftriaxone. Lower percentage of chloramphenicol (64.2%) resistance may be due to re-emerging sensitivity as reported by Urmila Jhamb.²¹ Widespread use of co-trimoxazole, ampicillin, cephalexin might be responsible for resistance to these drugs.

In this study 37 cases (46.8%) were put on ceftriaxone and 42 cases (53.2%) were given ciprofloxacin. Among the ceftriaxone treated cases the range for time to defervescence (TTD) was 2-6 days, the mean being 3.64±1.06 days. Urmila Jhamb reported a TTD with ceftriaxone of 4 days.²¹ Among the ciprofloxacin treated cases; the TTD ranged from 2-12 days. The mean being 3.56±0.99 days.

CONCLUSION

The disease is endemic and account for a significant proportion of hospital admissions. Boys and girls of all ages > 1 year were seen to be affected, majority being > 8 years old. Fever (intermittent type), anorexia, vomiting were the three major symptoms. Among the signs splenomegaly, hepatomegaly, coated tongue and toxemia were common. Relative bradycardia was not seen. Bronchitis, encephalopathy, hepatitis, and cholecystitis were common complications. Widal test was found

positive in majority of cases. Blood cultures were positive mainly in the first week of illness. The sensitivity pattern of S.typhi revealed significant proportion of multidrug resistant strains and simultaneous presence of chloramphenicol sensitive and resistant strains in the study. Both ciprofloxacin and ceftriaxone were effective in the treatment with no major adverse effects.

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