

Study on clinical profile and antibiotic sensitivity pattern of enteric fever patients in a tertiary care hospital of East India



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ABSTRACT

Background: Enteric fever is a global health problem which is endemic in the Indian subcontinent. With the changing pattern of clinical presentation and antibiotic sensitivity, physicians are facing a challenge to treat the disease in day-to-day practice. **Aims and Objectives:** The purpose of this study is to know the clinical profile of enteric fever and to study the pattern of antimicrobial susceptibility among *Salmonella* species. **Material and Methods:** This is an observational cross-sectional study including 50 cases of enteric fever admitted under General Medicine Department of a tertiary medical institute of Kolkata from January 2019 to December 2019, diagnosed on the basis of positive results found on blood culture, Widal test, and Typhi dot immunoglobulin M. Proper history taking, detailed clinical examinations, and relevant blood investigations were done. **Results:** The mean age of patients was 21.16 ± 5.72 years with 32 males and 18 females. Fever was the most common symptom, followed by anorexia, abdominal pain, and headache. The predominant sign was coated tongue seen in 20 (40%) patients with hepatomegaly in 4 (8%) and splenomegaly in 9 (18%) patients. *Salmonella* Typhi and *Salmonella* Paratyphi A were isolated in 32 (64%) cases and 5 (10%) cases, respectively, with 100% sensitivity to 3rd generation cephalosporins, azithromycin, and meropenem. Fluoroquinolone resistance was approximately 90%. **Conclusion:** Widely varying clinical presentation makes early diagnosis and proper selection of antibiotics essential for the treatment and prevention of complications of enteric fever. Quinolone resistance still remains an area of concern.

Key words: Antibiotic sensitivity; Clinical profile; Enteric fever

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INTRODUCTION

Enteric fever is a multisystemic infective illness caused by *Salmonella enterica* serotype typhi and serotypes paratyphi A, B, or C. Indian subcontinent is the hotspot of the typhoid activity. Incidence of typhoid fever in India is about 214.2/100,000 persons per year.¹ A recently conducted epidemiological survey involving five Asian countries (China, Vietnam, Indonesia, Pakistan, and India) showed the highest prevalence in India (493.5 cases per 1 Lakh population per year in urban slums).² The classic presentation is fever, malaise, diffuse abdominal pain, and diarrhea or constipation. Physical findings often include

rose spots, coated tongue, hepatomegaly, epistaxis, and relative bradycardia.³ Severe disease develops in 10–15% of patients in the form of life-threatening complications such as gastrointestinal (GI) bleeding (10–20%) and intestinal perforation (1–3%) most commonly in the 3rd and 4th week. Various other complications include disseminated intravascular coagulation, macrophage activation syndrome, pneumonia, arthritis, myocarditis, multiorgan failure, and neurologic manifestations such as meningitis, Guillain–Barre syndrome, neuritis, and neuropsychiatric symptoms. The definitive diagnosis of enteric fever requires the isolation of *Salmonella* Typhi or *Salmonella* Paratyphi from blood, bone marrow, other

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sterile sites, rose spots, stool, or intestinal secretions. The classic Widal test and rapid tests to detect antibodies have lower positive predictive values. Newer tests, such as IDL Tubex and Typhi dot assays, have been developed to detect immunoglobulin (Ig)M antibodies directly and rapidly. Emergence of multidrug-resistant (MDR) strains (resistant to chloramphenicol, ampicillin, and trimethoprim) in the late 1980s in Southeast Asia, Africa, South America, parts of China, and Indian subcontinent was followed by quinolone resistance in the 1990s. Even cephalosporin-resistant *Salmonella* Typhi has been identified in India, Pakistan, Bangladesh, the Philippines, Iraq, and Guatemala.⁴ In 2017, a large outbreak of enteric fever was reported in Sindh, Pakistan, caused by extensively drug-resistant^{5,6} strains (resistant to fluoroquinolones and third-generation cephalosporins in addition to MDR). With this background in mind, this study was initiated with the specific objectives to analyze the varying clinical profile of enteric fever patients and assess the extent of drug resistance before treatment is administered.

Aims and objectives

This study is aimed to know the varying clinical profile of enteric fever in adult patients and to detect the antibiotic sensitivity pattern of *S.typhi* and paratyphi.

MATERIALS AND METHODS

This observational cross-sectional study included 50 cases of enteric fever admitted in the Department of General Medicine of Vivekananda Institute of Medical Sciences, Ramakrishna Mission Seva Pratishthan, Kolkata, from January 2019 to December 2019. The study was conducted after obtaining the permission from the Institutional Ethics Committee. Patients who were above 12 years of age, had fever for at least 5 days, fever associated with GI symptoms, and tested positive in blood culture, Widal test, or Typhi dot IgM were included while cases with other established causes of fever such as malaria, dengue, or proven localized infections were excluded from the study. After taking informed consent, data collection was done by proper history taking (interview questionnaire) and relevant blood tests including blood culture and antibiotic sensitivity testing. The ethical clearance was obtained from the Institutional Review Board.

The blood samples were collected from the patients on admission before starting antibiotics. A total of 5 ml blood sample was collected aseptically using 70% alcohol and 2% tincture of iodine from a peripheral vein in each patient. All blood samples were cultured by BACTEC method aerobically at 37°C for 7 days and bottles which showed

sign of growth were further subcultured on MacConkey agar for 24 h. Antibiotic susceptibility test was performed by broth dilution method.

The drug sensitivity test was performed for ciprofloxacin, ofloxacin, ceftriaxone, cefotaxime, cefixime, azithromycin, and meropenem. Chloramphenicol, ampicillin, and trimethoprim-sulfamethoxazole were not applied on patients as MDR strains are very much prevalent these days.

Statistical analysis

Descriptive statistical analysis was carried out in the present study. Results on continuous measurements are presented on mean±standard deviation or median (interquartile range) for data on continuous scale depending on the distribution of data. The results on categorical measurements were presented in number (%). Significance is assessed at 5%. Inferential statistical analysis: Chi-square/Fisher's exact test was used to find the significance of study parameters on categorical scale, namely, clinical profile for equality of proportion and association inference between the study variables. For biochemical parameters on continuous scale, Student's independent sample t-test was used to find the significance of study parameters between two groups of patients depending on the distribution of data.

RESULTS

The common signs and symptoms of enteric fever, Typhi dot, Widal test, blood culture, and sensitivity of commonly used antibiotics were considered as primary outcome variables. Categorical variables are expressed as number of patients and percentage of patients. Continuous variables are expressed as minimum, maximum, mean, and standard deviation. Data were represented using appropriate diagrams. The statistical software SPSS version 20 has been used for the analysis. An alpha level of 5% has been taken, that is, if any $P < 0.05$, it has been considered as significant.

In our study, we found that maximum (24) patients including 10 females and 14 males were within the age group of 13–20 years with 17 patients (six females and 11 males) and nine patients (two females and seven males) within the age group of 20–27 years and 27–35 years, respectively (Table 1). As a whole, the mean age of patients was 21.16 ± 5.72 years with 32 (64%) male participants and 18 (36%) females. The male-to-female ratio was 1.78:1.

We found that the most common symptom was – fever, present in all 50 patients (100%). Other predominant symptoms were – anorexia, seen in 25 (50%) cases,

abdominal pain in 17 (34%) cases, and headache in 16 (32%) cases. Classical GI symptoms such as diarrhea, nausea-vomiting, and constipation were less frequent (Table 2).

Regarding the clinical signs present in our study population, coated tongue was the most common sign seen in 20 (40%) patients followed by splenomegaly (9, 18%) and hepatomegaly (4, 8%) (Table 3).

Out of 50 cases in our study, Typhi dot IgM was found to be positive in 21 (42%) cases and Widal test was positive for only 8 (16%) cases (Table 4). *Salmonella* Typhi

Table 1: Age and sex distribution of the study population (n=50)

Sex	Age range (years)			Total
	13–20	20–27	27–35	
Female	10	6	2	18
Male	14	11	7	32
Total	24	17	9	50

Table 2: Descriptive analysis of clinical symptoms in the study population

Clinical symptoms	Frequency	Percentage
Fever	50	100.0
Abdominal pain	17	34.0
Diarrhea	11	22.0
Constipation	6	12.0
Anorexia	25	50.0
Nausea/vomiting	9	18.0
Abdominal distension	0	0.0
Arthralgia	0	0.0
Myalgia	3	6.0
Headache	16	32.0
Hematemesis/melena	0	0.0
Neurological symptoms	0	0.0

Table 3: Descriptive analysis of clinical signs in the study population

Clinical signs	Frequency	Percentage
Rash	2	4.0
Coated tongue	20	40.0
Bradycardia	2	4.0
Hypotension	3	6.0
Splenomegaly	9	18.0
Hepatomegaly	4	8.0
Abdominal tenderness	3	6.0

Table 4: Descriptive analysis of Typhi dot and Widal test in the study population

Test	Positive	Negative	Total
Typhi dot IgM	21	29	50
Widal	8	42	50

IgM: Immunoglobulin M

was isolated in 32 (64%) cases, *Salmonella* Paratyphi A in 5 (10%) cases, while 13 (26%) had no growth in blood culture after 1 week of incubation (Figure 1). In our study, the culture sensitivity test showed that all the 37 isolates were sensitive to the 3rd generation cephalosporins (ceftriaxone, cefotaxime, and cefixime), azithromycin, and meropenem. Fluoroquinolone resistance was very common (Figure 2).

DISCUSSION

A similar study by Kavitha et al.,⁷ showed that the mean age of the participants was 30.55±12.65 years and most (56.2%) of the cases were in the age group of 13–30 years with a male-to-female ratio of 1.7:1. In another study by Kakaria et al.,⁸ the mean age of patients was 24±5 years with maximum cases between 15 and 30 years age group and the male-to-female ratio was 1.2:1.

In the study by Kavitha et al.,⁷ all the cases presented with fever and a substantial proportion of patients had headache (62%), abdominal pain (40%), vomiting (48%), and diarrhea (30%). Another study by Iqbal et al.,⁹ had a greater proportion of patients with symptoms such as abdominal pain (71%), diarrhea (43%), and vomiting (29%) with GI bleed in 29% and neck pain in 14% of cases. The cross-sectional study by Habte et al.,¹⁰ had 85% of patients with fever followed by anorexia in 64.8%.

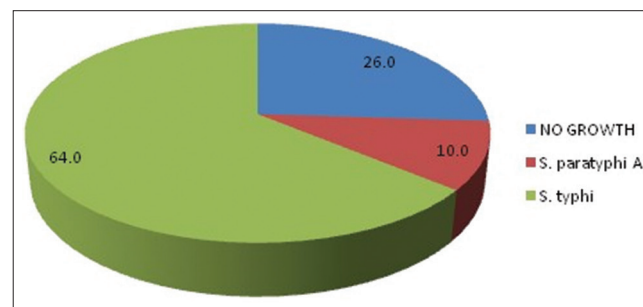


Figure 1: Descriptive analysis of organisms grown in blood culture

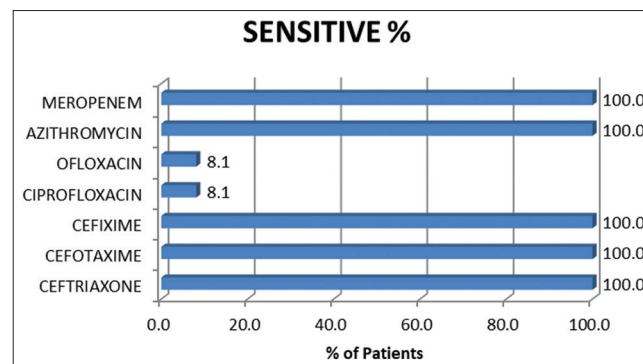


Figure 2: Comparative analysis of sensitivity pattern of antibiotics

In the study by Kavitha et al.,⁷ clinical findings were – rashes in 1.77% of patients, coated tongue in 5.26%, bradycardia in 55%, abdominal tenderness in 21.55%, splenomegaly in 26%, and hepatomegaly in 11.5%. Signs such as jaundice, signs of meningeal irritation, hepatomegaly, splenomegaly, and relative bradycardia each were seen in 1 (14%) patient out of the seven cases included in the study by Iqbal et al.⁹ The study by Kakaria et al.,⁸ had 43%, 42%, and 36% of patients with bradycardia, hepatomegaly, and splenomegaly, respectively.

In the study by Kavitha et al.,⁷ *Salmonella* Typhi was isolated in 7.5% of cases, *Salmonella* Paratyphi A in 35% of cases, and 55% had no growth. Dash et al.,¹¹ conducted a retrospective analysis of blood culture-positive cases of enteric fever in which *Salmonella* Typhi were 70.5% while *Salmonella* Paratyphi A were 29.5% of the total isolated salmonellae.

In a study by Bhetwal et al.,¹² 39.0% and 46.9% of *Salmonella* Typhi and Paratyphi serovars were susceptible to ciprofloxacin, while 55.0% and 65.0% of them were susceptible to ofloxacin. Other than fluoroquinolones, the overall susceptibility of *Salmonella* isolates to chloramphenicol, ampicillin, cotrimoxazole, and azithromycin was found to be excellent, that is, 97.5%, 97.9%, 94.6%, and 96.7% each. The study by Patil et al.,¹³ also showed 100% sensitivity to cefixime, ceftriaxone, and azithromycin; 94.4% to chloramphenicol; and 3.6% to ofloxacin. In another study by Shrestha et al.,¹⁴ all 18 isolates were sensitive to amoxicillin, azithromycin, ceftriaxone and chloramphenicol, ciprofloxacin, and ofloxacin.

Hence, it is evident from the above discussion that fever is the most common symptom present in all patients while classical GI symptoms may vary as may the clinical signs. The 3rd generation cephalosporins, meropenem, and azithromycin showed 100% sensitivity while quinolone resistance was very much predominant (approx. 90%). Changing clinical picture may be attributed to the genetic and the environmental factors. Early diagnosis and proper selection of antibiotics may have led to the absence of complicated cases. The variations of antibiotic sensitivity are mostly attributed to the genetic and the environmental factors and prior antibiotic exposure. Fluoroquinolone resistance still remains an area of concern, but 100% sensitivity to easily available drugs such as cephalosporins and azithromycin provides good treatment options.

Limitations of the study

The small sample size is one of the limitations of the study. However, further large scale studies are recommended to

describe and compare the clinicopathological profile and antibiotic sensitivity pattern of enteric fever patients in different geographical areas.

CONCLUSION

- Enteric fever is more common in the younger age group and among the male population.
- Fever is the commonest symptom.
- Coated tongue was the most common sign followed by splenomegaly and hepatomegaly.
- Blood culture had a yield of 74% with *S. typhi* isolated in 64% cases and *S. paratyphi* in 10%.
- Third generation cephalosporins, meropenem and azithromycin showed 100% sensitivity while quinolone resistance was very much predominant (approx. 90%).

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PC – Concept and design of the study, preparation of the first draft of the manuscript; **SM** – Concept and design of the study, interpretation of the results, and preparation of the manuscript; **SM** – Coordination, statistical analysis, review of the literature, and preparation of the manuscript; and **SC** – Statistical analysis and interpretation, preparation, and revision of the manuscript.

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