Publisher
MEDRESEARCH
www.medresearch.in

Tropical Journal of Pathology and Microbiology
2019 Volume 5 Number 7 July

E-ISSN:2456-1487
P-ISSN:2456-9887
RNI:MPENG/2017/70771

Research Article
Fever

Clinical and microbiological profile of enteric fever in a tertiary care hospital

Balasubramanian K.[1], Madhusudhan NS.[2*], Malini A.[3], Johnson C.[4]

DOI: https://doi.org/10.17511/jopm.2019.i07.03

[1] Kavitha Balasubramanian, Associate Professor, Department of General Medicine, Indira Gandhi Medical College & Research Institute, Pondicherry, India.

[2*] Madhusudhan NS, Assistant Professor, Indira Gandhi Medical College & Research Institute, , Pondicherry, India.

[3] Malini A., Department of Microbiology, Indira Gandhi Medical College & Research Institute, , Pondicherry, India.

[4] Johnson C., Associate Professor, Department of Community Medicine, Indira Gandhi Medical College & Research Institute, , Pondicherry, India.

Background: Enteric fever is largely prevalent in India. This study is done to know the clinical profile of typhoid & paratyphoid fever and to study the pattern of antimicrobial susceptibility among Salmonella species. **Materials and Methods:** This observational hospital based prospective study was conducted from August 2015 to December 2016 in patients admitted in medicine department of a tertiary hospital. The clinically suspected cases were diagnosed by blood culture, stool culture, Widal test and Typhoid test. The antimicrobial susceptibility pattern of Salmonella species was isolated. **Results:** 121 cases of clinically suspected entericfever were found to be either blood culture positive or serology positive for enteric fever. The mean age of the participants was 30.55±12.65 years with 76 (62.81%) males and 45 (37.19%) females. The most common symptom were fever, headache and chills. Other findings were bradycardia 67(55%), abdominal tenderness 25 (21%), splenomegaly 32 (26%) and hepatomegaly 14 (11.5%). Blood culture was done in 80 patients, 6 were growing *S. typhi*; 28 were growing *S. paratyphi*. Out of 107 cases Widal was done, 42 Widal positive for typhoid fever; 37 was paratyphoid positive, 28 Widal negative. Out of 121 cases, 53 were paratyphoid, 58 were typhoid fever, 10 were diagnosed based on clinical criteria of enteric fever. All the isolates were sensitive to ceftriaxone. **Conclusion:** This study points to a higher yield of enteric fever by blood culture, also the no of paratyphoid cases is relatively higher as compared to typhoid cases.

Keywords: Paratyphoid fever, Antimicrobial susceptibility

Corresponding Author

Madhusudhan NS, Assistant Professor, Indira Gandhi Medical College & Research Institute, Pondicherry, India.
Email: drnsmadhu98@gmail.com

How to Cite this Article

Balasubramanian K, Madhusudhan NS, Malini A, Johnson C. Clinical and microbiological profile of enteric fever in a tertiary care hospital. Trop J Pathol Microbiol. 2019;5(7):431-436.
Available From https://pathology.medresearch.in/index.php/jopm/article/view/284

To Browse

Manuscript Received	Review Round 1	Review Round 2	Review Round 3	Accepted
2019-05-19	2019-05-20	2019-05-24		2019-05-28

Conflict of Interest	Funding	Ethical Approval	Plagiarism X-checker	Note
No	Nil	Yes	7%	

Introduction

Enteric fever, caused by *Salmonella enterica serovars typhi* and *paratyphi A* (*S. typhi* and *S. paratyphi A*) is a major public health problem in many developing countries, including India. It is one of the leading causes for morbidity and mortality. Incidence of typhoid fever in India is about 214.2 per 100,000 persons /year [1]. *S. typhi*is the most common etiologic agent and there is an increasing number of cases due to *S. paratyphi A* [2, 3].

This has been attributed to the use of Vi polysaccharide vaccine or monovalent vaccine which provides protection against typhoid fever only [3]. Knowing the proportion of disease due to *S. typhi* and *S. paratyphi A* is significant, as these serovars may have subtle differences in their modes of transmission, clinical course and may necessitate differing control measures.

However, there remains no single test that has proven to be sufficiently sensitive, specific, and practical for use in developing countries. In actual practice, most of the infections by *Salmonella enterica serotype Typhi* are diagnosed clinically without proper laboratory evidence and consequently treated presumptively with antibiotics [4].Though blood cultureisthe gold standardin diagnosis of enteric fever, excessive antibiotic use has reduced the isolation rate to 40-60 percent [3]. Obtaining accurate data on disease burden in developing countries is difficult because the diagnosis of enteric fever is often a clinical one, without blood culture conurbation, and most of the patients are treated as outpatients [4].

The last two decades have seen the emergence of multi-drug resistance against the conventional anti-typhoidal drugs (ampicillin, cotrimoxazole and chloramphenicol) among the Salmonella sp. From 2000, there have been reports of high levels of chloramphenicol susceptibility from many parts of India and the Salmonella strains have regained susceptibility to this drug due to less use [5]. Antibiogram showed 2% of the strains to be sensitive to all the drugs tested and 12% were MDR and showed the presence of plasmids [6-8]. World wide the emergence of multidrug resistant *S. Typhi*and *S. Paratyphi A*strains has been shown to be geographically heterogeneous, stressing the importance of continuing surveillance of antimicrobial resistance among Salmonella isolates [2].

Thus this study was done to know the clinical profile of typhoid & paratyphoid fever and to study the pattern of antimicrobial susceptibility among Salmonella species in our setup.

Materials & Methods

Type of study: Observational hospital based prospective study

Study setting: patients attending the inpatients and outpatient department of a tertiary hospital for a period of one and half year from August 2015 to December 2016

Inclusion criteria

- Patients with age above 12 years
- The patients with Fever ≥ 5 days and those cases fitting into clinical case definition. Clinically suspected case definitions were defined as[9]:

Probable case: Insidious onset of continuous fever, malaise, headache and loss of appetite with GI symptoms of more than one week duration having two or more of the following- toxic look, coated tongue, relative bradycardia, splenomegaly, exposure to confirmed case, presenting with complications like GI haemorrhage and perforation.

Confirmed case: A probable case that is laboratory confirmed either by isolation of *S. typhi/ S. paratyphi A* from blood, body fluids or other specimen or serology demonstration of four-fold rise in anti-salmonella antibodies OR detection of specific IgM antibodies in patient's serum. WIDAL test is considered diagnostic for typhoid fever if titres of more than 1:160 or demonstration of four-fold rise in antibody titre[10].

Exclusion criteria: Fever with other focus of infection like Lower respiratory tract infection, UTI, malaria, leukaemia and lymphoma.

Sampling method: The purposive sampling was done.

Sample collection: The details for every case including their age, gender, occupation and symptoms on presentation, clinical signs and complications if any were collected and recorded as per the proforma. As per the case definition all clinically suspected cases of enteric fever satisfying the inclusion criteria and those who are willing to participate in the study were included in the study.

To confirm the diagnosis blood culture, Widal test and Typhoid test was done as per standard protocols. The treatment administered and its duration was also recorded along with the patient's outcome. The results was recorded and analysed. They were analysed as to those that were diagnosed clinically and those that were confirmed with laboratory support. The clinical profile of typhoid and paratyphoid fever was analysed. The antimicrobial susceptibility pattern of Salmonella species isolated was analysed.

Statistical methods: Enteric fever, common symptoms and sign and blood culture was considered as primary outcome variables. Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables.

Non-normally distributed quantitative variables were summarized by median and interquartile range (IQR). Data wasrepresented using appropriate diagrams like bar diagram, pie diagram and box plots. Proportions and categorical data were analysed byChi-square test and t-test.

Ethical consideration and permission: The ethical clearance was obtained from institutional review board and informed consent was taken from each of the participant.

Results

Our study included a total of 200 clinically suspected cases of enteric fever during the study period. Out of 200 patients included, 121 casesof clinically suspected entericfever were found to beeither blood culture positive or serology positive forenteric fever. Out of 121 cases, 76 (62.81%) participants were males and 45 (37.19%) were females. Male to female ratio was 1.7: 1. The youngest patient was 13 years of age and 65years was the oldest patient's age. 68(56.2%) cases were in the age group of 13y-30years, 44(36.4%) cases were in the age group 31-50years and only 9 (7.4 %) cases were of above 50 years. The mean age was 30.55±12.65 years.

All the 121 cases presented with fever. 63 (52%) had low grade and 58 (48%) had high grade fever. Mean duration of fever was 11.61±7.4 days. 75 patients (62%) had headache; 75 (62%) had chills, 59 (49%) had arthralgias and myalgias; 49 (40%) cases had abdominal pain, 58 (48%) had vomiting, 36 (30%) had diarrhoea; and only 3 had constipation; 38 patients (30%) had loss of appetite. The most common symptom was –fever followed by headache and chills. (Table 1)

Table-1: Descriptive analysis of fever in the study population (N=121).

Grade of fever	Number (%)
Low grade	63 (52.07%)
High grade	58 (47.93%)
Fever duration (Mean ± SD)	11.61±7.4
Clinical symptoms	Number (%)
Headache	75(61.98%)
Chills	75(61.98%)
Myalgia	59(48.76%)
Vomiting	58(47.93%)
Abdominal pain	49(40.50%)
Loss of appetite	38(31.40%)
Diarrhoea	36(29.75%)
Arthralgia	33(27.27%)
Constipation	3(2.48%)

Table-2: Descriptive analysis of clinical signs in the study population.

Clinical signs	Frequency	Percentages
Bradycardia	67	55
Splenomegaly	32	28.32
Abdominal tender ness	25	21.55
Hepatomegaly	14	12.28
Coated tongue	6	5.26
Rash	2	1.77
typhoid pneumonia	1	

Table-3: Descriptive analysis of oral antibiotic in the study population (N=121)

Oral – DRUG (N=23)	
Azithromycin	17 (%)
Cefixime	1
Ciprofloxacin	1
Cotrimoxazole	4

Table-4: Descriptive analysis of organisms grown in blood culture

Organism in blood culture (N=80)		
No Growth	44	55
S. Typhi	6	7.50
S. Paratyphi	28	35
Skin Commensal	2	2.50

Table-5: Descriptive analysis of WIDAL in the study population (N=107).

Widal	Frequency	Percentages
Positive for typhoid	42	39.25

Positive for paratyphoid	37	34.58
Negative	28	26.17

The clinical signs included bradycardia in 67 (55%) individuals, 25 (21%) had abdominal tenderness; 32 (26%) had splenomegaly, 14 (11.5%) hepatomegaly. None had other complications like meningitis or epistaxis, perforation or gastrointestinal haemorrhage.

No deaths were reported (Table 2). Among the study population, 23 patients (19%) patients were treated with oral antibiotic. Most of them were treated with azithromycin (17), 4 patients were treated with cotrimoxazole and 1 each received ciprofloxacin and cefixime.(Table 3)

Blood culture was done in 80 patients, *S.typhi* was isolated in 6 cases, *S. paratyphi A* in 28 cases, 44 had no growth after one week of incubation and 2 samples grew skin commensals. Blood culture not done in 41 cases (Table 4). All the isolates were sensitive to ceftriaxone.

Out of 107 in whom cases Widaltest was done, 42 were positive for typhoid fever; 37 were had a significant titre for paratyphoid fever. In 28 cases, Widal test was negative. Out of 121 cases of enteric fever, after combining the clinical and laboratory criteria, 58 cases were found to have typhoid fever while 53 cases were found to have paratyphoid fever, while 10 were diagnosed purely based on clinical criteria of enteric fever (Table 5).

Discussion

Typhoid fever continues to be a public health problem especially in the tropics. There is a dearth of available epidemiological data to project the actual situation in India [3].

Our study included 121 cases of clinically suspected enteric fever were found to beeither blood culture positive or serology positive forenteric fever. Male to female ratio was 1.7: 1. The mean age was 30.55±12.65 years. In the study by Chowta M N et al[11] observed similar proportion of females and male patients in their study.

Average age of presentation was 23.9 years which was slightly lesser compared to the current study. Gupta, S., et al[12] in a total of 81 culture positive patientsalso had similar proportion of males 62.2% and females as ours. However, averageage of patients was 18.2 (range 2-45) years which was less compared to the current study.

In the current study, the most common symptom was –fever followed by headache and chills, arthralgias and myalgias, abdominal pain, vomiting, diarrhoea; and loss of appetite. The complications included brady cardia, abdominal tenderness, splenomegaly and hepatomegaly. In the study by Chowta M N et al[11] Fever was present in all patients (100%). Vomiting was present in 20.4% patients. Diarrhoea was seen in 20.4% patients. 11.3% patients had pain abdomen. Constipationwas present in 9.09% patients. Hepatomegaly was detected in 18% patients and splenomegaly was present in 34.09% patients. Myocarditis was observed in two patients and bleeding per rectum was seen in one patient. These complications were in according to the current study with different prevalence of the symptoms across various study as the tolerance level of each individual may differ from the other. In the study by Gupta, S., et al[12] all patients presented with fever with a mean duration of 8.8 (range 2 to 30) days. Pain abdomen, vomiting, diarrhoea, headache and cough were other common symptoms.

In the current study, 23 (19%) patients were treated with oral antibiotic. Most of them were treated with azithromycin (17),while Chowta MNetal[11] shows that resistance of *S. typhi* to amoxycillin, chloramphenicol, ampicillin and co-trimoxazole was significantly high. Ciprofloxacin also showed resistance in 18.1% of cases.

Blood culture was done in 80 patients, 6 were growing *S. typhi*; 28 were growing *S. paratyphi A*; 44 were no growth; 2 were growing skin commensals;Blood culture was not done in 41 cases. In the study by Iqbal, N., et al[13] diagnosis of enteric fever was established in allseven cases within a median duration of 6 days ofhospitalization. Blood culture grew *S. Typhi* in four cases (57%) and *S.Paratyphi A* in one case (14%).

In the remaining two (29%) cases, diagnosis was made byculture of S. Typhi from the bone marrow.In the study by Gupta, S., et al[12] All culture isolates were from blood culture. Salmonella enterica subspecies enterica serovar typhi (*S typhi*) was isolated from 65 (80%) patients while Salmonella enterica subspecies enterica serovarparatyphi (*S paratyphi A*) was isolated from the remaining.

Out of 107 cases Widal was done, 42 Widal positive for typhoid fever; 37 was paratyphoid positive, 28 Widal negative.

Out of 121 cases, 53 were paratyphoid, 58 were typhoid fever, 10 were diagnosed based on clinical criteria of enteric fever.

In the study by Gupta, S., et al[12] widal test results (single titres) were positive (defined as *S typhi* O antigens ≥ 160 and *S typhi* H antigen or *S paratyphi* H antigen ≥ 160) in 35/81 (43.2%) of patients.

Widal was positive in 21/54 (38.8%) patients presenting in the first week of fever, while those presenting in second week or after had positive test in 14/27 (51%) cases. Mushtaq S., et al[14]did Widal test for 129 patients, obtained after mean duration of 4 days in hospital. WIDAL test was considered diagnostic for typhoid fever if titres of more than 1:160 or demonstration of four-fold rise in antibody titre[10].

Conclusion

The clinical profile included bradycardia, abdominal tenderness, splenomegaly and hepatomegaly but did not show any serious complications in our study. The results of blood culture and widal test correlated well in the study.

What this study adds to the existing knowledge?

The prevalence, presentation and sensitivity of the typhoid may differ with different geographical area. Variation can be observed at the same site and also variation in place within countries and regions.

This contributes to the rate in a certain geographical area and also determines the susceptibility pattern of different antibiotics in salmonella species.

Acknowledgements

Authors acknowledge the technical support in data entry, analysis and manuscript editing by "Evidencian Research Associates."

Reference

01. Ochiai RL, Acosta CJ, Danovaro-Holliday MC, Baiqing D, Bhattacharya SK, Agtini MD, Bhutta ZA, et al. A study of typhoid fever in five Asian countries- disease burden and implications for controls. Bull World Health Organ. 2008 Apr; 86(4)260-8. *DOI: 10. 2471/blt.06.039818 [Crossref][PubMed][Google Scholar]*

02. Kanungo S, Dutta S, Sur D. Epidemiology of typhoid and paratyphoid fever in India. J Infect Dev Ctries. 2008 Dec1;2(6)454-60. *doi.org/10.3855/jidc.161 [Crossref][PubMed] [Google Scholar]*

03. Banerjee T, Shukla BN, Filgona J, Anupurba S, Sen MR. Trends of typhoid fever seropositivity over ten years in north India. The Indian journal of medical research. 2014 Aug;140(2)310. *[Crossref] [PubMed][Google Scholar]*

04. Connor BA, Schwartz E. Typhoid and paratyphoid fever in travellers. Lancet Infect Dis. 2005 Oct;5(10)623-8. *DOI:10.1016/S1473-3099(05)70239-5 [Crossref][PubMed][Google Scholar]*

05. Sen B, Dutta S, Sur D, Manna B, Deb AK, Bhattacharya SK, et al. Phage typing, biotyping& antimicrobial resistance profile of Salmonella enterica serotype Typhi from Kolkata. Indian J Med Res. 2007 May; 125(5)685-8. *[Crossref][PubMed] [Google Scholar]*

06. Krishnan P, Stalin M, Balasubramanian S. Changing trends in antimicrobial resistance of Salmonella enterica serovar typhi and salmonella enterica serovar paratyphi A in Chennai. Indian J Pathol Microbiol. 2009 Oct-Dec; 52 (4)505-8. *doi: 10.4103/0377-4929.56140 [Crossref][PubMed] [Google Scholar]*

07. Harish BN, Menezes GA. Antimicrobial resistance in typhoidal salmonellae. Indian J Med Microbiol. 2011 Jul-Sep;29(3)223-9. *doi: 10.4103/0255-0857.83904 [Crossref][PubMed][Google Scholar]*

08. Verma S, Thakur S, Kanga A, Singh G, Gupta P. Emerging Salmonella Paratyphi A enteric fever and changing trends in antimicrobial resistance pattern of salmonella in Shimla. Indian J Med Microbiol. 2010 Jan-Mar; 28(1): 51-3. *doi: 10.4103/0255-0857.58730 [Crossref][PubMed][Google Scholar]*

09. Manual for laboratory diagnosis of common epidemic prone diseases for district public health laboratories. IDSP. NCDC, New Delhi. May 2011. *[Crossref][PubMed][Google Scholar]*

10. Manual for Laboratory Diagnosis of Common Epidemic Prone Diseases at District Public Health Laboratories [Internet]. National centre for disease control. 2009 [cited 13 November 2016]. Available from: https://idsp. *nic.in/WriteRead Data/OldSite/Lab_ Manual.pdf [Crossref][PubMed] [Google Scholar]*

11. Chowta MN, Chowta NK. Study of clinical profile and antibiotic response in typhoid fever. Indian J Med Microbiol. 2005 Apr;23(2)125-7. *[Crossref] [PubMed][Google Scholar]*

12. Gupta S, Handa A, Chadha DS, Ganjoo RK, Panda RC. Profile of Culture Positive Enteric Fever from Bangalore. Medical journal, Armed Forces India. 2009;65(4)328-31. *10.1016/S0377-1237(09)80093-2 [Crossref][PubMed][Google Scholar]*

13. Iqbal N, Basheer A, Mookkappan S, Ramdas A, Varghese RG, Padhi S, et al. Clinicopathological profile of salmonella typhi and paratyphi infections presenting as fever of unknown origin in a tropical country. Mediterranean journal of hematology and infectious diseases. 2015;7(1). *Doi: 10.4084/MJHID.2015.021 [Crossref][PubMed][Google Scholar]*

14. Mushtaq S, Bhat AA, Rather GN, Akhter R, Bhat I, Wani T. Clinical profile of enteric fever in tertiary care hospital of Kashmir. International Journal of Contemporary Pediatrics. 2017;4(5)4. *[Crossref] [PubMed][Google Scholar]*