Original Research Article

# Study of Clinico-Demographic and Laboratory Profile of Children Diagnosed With Typhoid Fever

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**Abstract**

**Aims:** Evaluation of Clinical & Laboratory Profile of Typhoid Fever in Children. **Methods:** A prospective observational study was conducted in the Department of Paediatrics at VIMS, Pawapuri, Nalanda, Bihar, India from November 2019 to July 2020. Total 120 Children aged below 18 years with history of fever of more than 5-7 days duration were included in this study. In each case, age, sex, presenting complaint, laboratory investigations and antibiotic sensitivity pattern are collected and analysed. **Results:** Out of 120 cases, 76 cases (63.33%) were males and 44 cases (32%) were females. Most of the cases were aged between 5 and 10 years. 28 cases were below 5 years, representing 23.33%. 36 cases were aged above 10 years, representing 30%. 56 cases were aged between 5 and 10 years (46.67%). Most of the cases (64.17%) stayed in hospital up to 5 to 10 days after admission. 24.17 % cases stayedupto5dayinhospitalandonly11.67%ofcases stayed in hospital for more than 10 days. The most common symptom was fever (100%), followed by anorexia (63.33%), vomiting (45%), pain abdomen (19.17%), diarrhoea (14.17%), headache (10.83%), and cough (6.67%). The most common sign of physical finding was toxic look in 72.5% of the cases followed by coated tongue in 55%, hepatomegaly 38.33%, splenomegaly 20.83%, hepatosplenomegaly in 12.5% of cases and pallor in 8.33% of cases. Anemia was found in 25(20.83%) cases, leucopenia and p leucocytosis were observed in 37(30.83%) cases and 17(14.17%) cases respectively. Neutropenia found in 43(35.83%) cases and neutrophilia was found in 41(34.17%) cases. Eosinopenia was seen in 49(40.83%) cases, eosinophilia in 12(10%) cases and thrombocytopenia in 22(18.33%) cases. **Conclusions:** Typhoid fever should be suspected and investigated in all children with short and long duration fever without localizing signs. Early diagnosis and institution of appropriate antibiotics therapy is of paramount importance in the management of typhoid fever.

**Keywords:** Children, Clinical profile, Coated tongue, Typhoid fever.



## Introduction

Typhoid fever also known as "Enteric fever", is a collective term that refers to both typhoid and paratyphoid fever. It is one of the most common causes of fever in children with variable presentations and significant difference in the signs and symptoms compared to adults.[1]

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Typhoid fever is a life-threatening systemic infection occurring in developing areas of the world and continues to be a major public health problem. Over 21 million people worldwide get infected annually with estimated mortality of 2,00,000 people per year.[2] The presenting signs and symptoms of typhoid fever in children differ significantly from those in adults.[3] The common clinical features of typhoid fever are fever, vomiting, diarrhea, cough, hepatosplenomegaly, anemia and thrombocytopenia.[4,5] Salmonella typhi (*S. typhi*) is the causative agent which is most frequently isolated in the blood during first week of illness. In the wake of emerging multidrug resistant strains of bacteria causing typhoid fever, the disorder is

known to be associated with significant morbidity and mortality. It is also recognized that delay in the diagnosis and institution of appropriate therapy may significantly increase the risk of adverse outcome and mortality. The incubation period ranges from 7-14 days. However, it may vary from 3-30 days depending on infective dose.[6] Disease transmission is mainly by ingestion of the organism. Faeco oral route or ingestion of contaminated food or water is responsible for entry of the organism into the human body.[6] Typhoid carriers shed the organism in stool and urine. The most common mode of transmission of typhoid is through ingestion of food or water contaminated with S. typhi from human stools.[7]

The Widal test continues to be important in the work up of patients with typhoid fever despite its variable sensitivity and specificity in India. Antibodies against O and H antigen of Salmonella typhi are measured by the Widal test. It lacks sensitivity and specificity in endemic areas. Blood culture is the Gold standard for diagnosis.[6] Stool and urine culture results become positive after 1st week. Although the leucocyte count is found to be low in typhoid in relation to toxicity and fever, in younger children leucocytosis is common. Thrombocytopenia is a marker of severity and may accompany DIC.[6] A major epidemic of drug resistant typhoid fever was first reported in 1972 and subsequently resistance to all the first line drugs (chloramphenicol, co-trimoxazole & ampicillin) was reported. These were called as as Multi Drug Resistant typhoid fever (MDRTF).[8] An increasing frequency of resistance has been reported from all parts of the world, but more so from developing countries.[9] Some strains have shown resistance to fluoroquinolones & 3rd generation cephalosporins, which is a matter of great concern.[10] Hence the present study was conducted with the aim to evaluate clinical and laboratory profile of typhoid fever in infants and children in order to improve the understanding of the disease process in the area and enable early and effective management of patients to decrease the morbidity and mortality from typhoid fever.

## Materials and Methods

A prospective observational study was conducted in the Department of Paediatrics VIMS, Pawapuri, Nalanda, Bihar, India, from November 2019 to July 2020.

### Methodology

Total 120 Children aged below 18 years who presented to the Paediatric department with history of fever of more than 7 days duration were included in this study. These cases were included in this study after ruling out other sources of infection like respiratory, nervous system, cardiac and genitourinary; they were either Widal positive (Widal test TO Titer >1:100 or TH titre >1:200) or blood culture positive for Salmonella species. The cases which were discharged against medical advice and cases for which consent was not obtained were excluded from the study. Totally 120 cases met our inclusion criteria In all the cases, age, sex, duration of illness, presenting symptoms and other symptoms pointing towards complications were noted. Further detailed history was taken regarding their food habits, sanitation, unhygienic practices and drinking water source. History regarding previous antibiotic prescription was noted. Further antibiotics were started in each case after blood was drawn for Widal test and blood culture for Salmonella species. Each case was followed up clinically for improvement. For those cases which did not show improvement after 5 days of antibiotics, changes made according to the culture reports. Antibiotic sensitivity pattern was noted for culture positive cases. Cases were followed till discharge. The data collected was analyzed with respect to age, sex and presenting complaints.

## Results

In this study, all the cases presented to OPD with a median of 5-7 days duration of fever. 76 cases (63.33%) had received antibiotics for a minimum period of 3-5 days prior to admission. Out of 120 cases, 76 cases (63.33%) were males and 44 cases (32%) were females. Table 1 shows, most of the cases were aged between 5 and 10 years. 28 cases were below 5 years, representing 23.33%. 36 cases were aged above 10 years, representing 30%. 56 cases were aged between 5 and 10 years (46.67%). In all the above age groups male predominance was seen.

**Table 1: Age wise sex distribution**

| Age (years) | Male | % | Female | % | Total | % |
|---|---|---|---|---|---|---|
| **Below 5** | 17 | 14.17 | 11 | 8.33 | 28 | 23.33 |
| **5-10** | 37 | 30.83 | 19 | 11.67 | 56 | 46.67 |
| **Above 10** | 22 | 18.33 | 14 | 6.67 | 36 | 30 |
| Total | 76 | 63.33 | 44 | 36.67 | 120 | 100 |

Duration of hospital stay varied from up to 15 days. As shown in Table-2, most of the cases (64.17%) stayed in hospital up to 5 to 10 days after admission. 24.17 % cases stayedupto5dayinhospitalandonly11.67%ofcases stayed in hospital for more than 10 days. In these cases, fever persisted beyond 7 days. No mortality was observed during our study period. Although mild elevated liver enzymes were observed in some cases, no complications were seen in any case.

**Table 2: Duration of hospital stay**

| Duration of hosbpital stay | N=120 | P-value |
|---|---|---|
| Below 5 days | 29 (24.17%) | 0.10 |
| 5-10 days | 77 (64.17%) | 0.00 |
| Above 10 days | 14 (11.66%) | 0.20 |

Typhoid fever presents with a wide range of symptoms. Due to the use of antibiotics prior to diagnosis, children may not present with typical symptoms. However, in our study, the most common symptom was fever (100%), followed by anorexia (63.33%), vomiting (45%), pain abdomen (19.17%), diarrhoea (14.17%), headache (10.83%), and cough (6.67%)

**Table 3: Common presenting symptoms**

| Presenting symptom | No. of Cases | P-value |
|---|---|---|
| Fever | 120(100%) | 0.001 |
| Anorexia | 76 (63.33%) | 0.000 |
| Vomiting | 54 (45%) | 0.001 |
| Pain abdomen | 23 (19.17%) | 0.014 |
| Diarrhea | 17 (14.17%) | 0.079 |
| Headache | 13 (10.83%) | 0.99 |
| Cough | 8 (6.67%) | 0.169 |

**Table 4: Various physical findings**

| Signs | No. of Cases | P-value |
|---|---|---|
| Toxic look | 87 (72.5%) | 0.001 |
| Coated tongue | 66(55%) | 0.002 |
| Hepatomegaly | 46 (38.33%) | 0.001 |
| Splenomegaly | 25 (20.83%) | 0.067 |
| Hepatosplenomegaly | 15 (12.5%) | 0.077 |
| Pallor | 10 (8.33%) | 0.182 |

Coming to physical findings, the most common sign we observed was toxic look in 72.5% of the cases followed by coated tongue in 55%, hepatomegaly 38.33%, splenomegaly 20.83%, hepatosplenomegaly in 12.5% of cases and pallor in 8.33% of cases. In this study, we also reported the source of drinking water. In most cases (80%), the source of drinking water was through municipal water pipelines; majority of these belonged to the urban area. Only in 20% of cases, the source of drinking water was bore well water; these cases were from rural background.

**Table 5: Laboratory parameters**

| Laboratory parameters | Abnormal values | No. of cases | P-value |
|---|---|---|---|
| **Hemoglobin** | Anemia (Hb <11g%) | 25 (20.83%) | 0.025 |
| **Total leukocyte count** | Leucocytosis (>11000cells/$mm^3$) | 17 (14.17%) | 0.036 |
| | Leucopenia (<4000cells/$mm^3$) | 37 (30.83%) | 0.00 |
| **Polymorphs** | Neutropenia | 43 (35.83%) | 0.00 |
| | Neutrophilia | 41 (34.17%) | 0.00 |

| | | | |
|---|---|---|---|
| **Eosinophils** | Eosinophilia | 12 (10%) | 0.18 |
| | Eosinopenia | 49 (40.83%) | 0.00 |
| **Platelets** | Thrombocytopenia | 22 (18.33%) | 0.01 |
| **SGOT** | Elevated SGOT | 13 (10.83%) | 0.27 |
| **SGPT** | Elevated SGPT | 16 (13.33%) | 0.23 |
| **Widal titres** | TO >1:100 | 103 (85.83%) | 0.00 |
| | TH >1: 200 | 101 (84.17%) | 0.00 |
| **Blood culture positive** | Salmonella | 22 (18.33%) | 0.01 |

Table 5 depicts the laboratory parameters. Anemia found in 25 (20.83%) cases, leucopenia and leucocytosis was observed in 37(30.83%) cases and 17(14.17%) cases respectively. neutropenia found in 43(35.83%) cases and neutrophilia was found in 41(34.17%) cases. Eosinopenia was seen in 49(40.83%) cases, eosinophilia in 12(10%) cases and thrombocytopenia in 22(18.33%) cases. SGOT levels was elevated (>200IU/ml) in 13 (10.83%) cases and SGPT (>200IU/ml) in 16(13.33%) cases. The elevated levels of liver enzymes lasted only few days. There were no complications observed during our study period. *Salmonella typhi* O titres >1:100 was seen in 103 (85.33%) cases and TH titres >1:200 in 101 (84.17%) cases. Blood culture positive for *Salmonella typhi* noted in 22 (18.33%) cases. Out of 120 cases only 22 cases had been immunized with typhoid vaccine. All of them had taken typhoid polysaccharide vaccine more than 3 years prior to illness.

**Table 6: Antibiotic sensitivity pattern**

| Drug | Sensitivity | P-value |
|---|---|---|
| Ceftriaxone | 97% | 0.000 |
| Cefixime | 97% | 0.000 |
| Ofloxacin | 92% | 0.000 |
| Chloramphenicol | 87% | 0.000 |
| Cefotaxime | 82% | 0.002 |
| Azithromycin | 50% | 0.211 |
| Ciprofloxacin | 80% | 0.001 |
| Amoxicillin | 70% | 0.096 |

**Significant p<0.01**

Table 6 depicts antibiotic sensitivity patterns among culture positive cases. As mentioned in the table, ceftriaxone and cefixime sensitivity was seen in all the cases (97%) followed by ofloxacin (92%), ciprofloxacin (80%), chloramphenicol (87%), cefotaxime (82%),amoxicillin (77%) and azithromycin in (50%). *S. typhi* was more sensitive to ceftriaxone, cefixime followed by ofloxacin. Least sensitivity was seen with azithromycin. During the course of our study, none of the subjects suffered any complications nor were there any fatalities. All the patients regained full health.

## Discussion

Due to the poor water supply and sanitary conditions, it continues to be a major public health problem in developing countries like India, being compounded by emerging resistance to antibiotics that were effective earlier.

The male predominance in our study is thought to be due to fact that, boys are more exposed to external environment, may consume unsafe water or food and hence are more prone to be infected. Moreover, in a male dominated society like india, male child receives more attention than female child. This may be a cause

of more number of male children receiving faster medical attention. Similar results were reported in other studies.[11-13] Common age group reported in our study was 5 to 10 years. A study done by R Modi et al also reported maximum incidence of typhoid in the age group 6 to 10 year.[14] Another study also reported maximum number of cases in the age group above 5 years.[15] These results were in accordance with the concept of typhoid that says typhoid fever is common in school age children. School children are at high risk of consuming contaminated drinking water. They are also exposed to various food items from street vendors. These factors make them more vulnerable to exposure to typhoid bacilli. The duration of hospital stay varies, with maximum number of cases staying in hospital for 5-10 day. Cases were discharged after 3 consecutive days of afebrile period without antipyretics. These results were in accordance with study done by Hyder et al.[16] We observed high incidence of typhoid fever in lower class, lesser in middle class society and least in higher class. This can be explained by differences in drinking water sources and hygienic practices like hand washing and sanitary latrine facilities. Similar results were reported in other study.[17] Typhoid fever was more commonly observed in those who were using municipal water as drinking source compared to bore well water. Similar results reported in the study done by R Modi et al.[14] We also observed higher incidence of disease in cases with history of consumption of outside food. This probably can be attributed to eating food items without hand wash or quality of food handled by road side food vendors.

Typhoid fever manifestations are diverse. The most common symptoms apart from fever were anorexia, vomiting, pain abdomen, diarrhoea followed by headache and cough. A study done by Sinha A et al.[18] Kapoor JP et al also reported similar results.[19] Other studies also showed similar clinical picture.[20-22] Contradictory to this, a study done by Joshi et al reported headache as the most common symptom next to fever.[23] In our study we reported Toxic look (72.5%) as the most common sign followed by coated tongue (55%), Hepatomegaly (38.33%), splenomegaly, Hepatosplenomegaly. Study done by Laishram et al reported coated tongue (80%) as the most common sign followed by Hepatomegaly (76%) and splenomegaly (38%).[24] In other study they had reported relative bradycardia and hepatomegaly as the most common sign.[25]

During our study, all cases were positive for Widal. Blood culture was positive in 18.33% of cases. Other study also reported 16% culture positive cases.[16] A study done by Banu et al also reported 28% culture positive cases.[25] Due to prior use of antibiotics, the culture positive cases are decreasing. Thus, need for relay on other serological tests for diagnosis of typhoid exists. Study done by Modi et al reported 97% Widal positive cases.[14] Anemia was seen in 20.83% of cases. The other studies reported little higher percentage of anemias. A study done by Raj C etal reported anemia in 41.8% of patients and Lefebvre et al reported anemia in 78% of cases.[26,27] In our study Leucocytopenia and Eosinopenia found in 30.83% and 40.83% respectively. Similar results reported in Lefebvre et al.[27] Although leucocytosis and eosinophilia are rarein typhoid, our study reported leucocytosis in 14.17% of cases and eosinophilia in 10% cases respectively. Thrombocytopenia was found in 18.33% of cases. Elevated SGOT is seen 10.83 % of cases and SGPT was raised in 13.33% of the cases. The other study reported elevated liver enzymes in 70% of cases.[28]

Antibiotic sensitivity was similar to other studies. Most of the culture positive cases showed sensitivity to ceftriaxone, cefixime, ofloxacin, ciprofloxacin. Similar sensitivity pattern reported in other study.[23] However sensitivity pattern varies from place to place. Other studies showed return of sensitivity pattern with chloramphenicol, cotrimoxazole, amoxicillin. [21,29,30]. A study done by Mishra et al reported 100% sensitivity to azithromycin.[31] In our study the sensitivity to azithromycin was 50%. A Study done by Hyder et al reported 100% sensitivity to ceftriaxone and ciprofloxacin.[16] All other culture negative cases were treated with ceftriaxone. All cases responded to above antibiotics without any complications and mortality.

## Conclusion

The above study shows that typhoid fever continues to be a major health problem in a developing country like India which has poor water supply and sanitary conditions. To avert the increasing morbidity and mortality from typhoid fever, clinicians and health workers need to work together to raise awareness about thorough hand washing before eating or preparing food and proper sanitary disposal. Typhoid fever should be suspected and investigated in all children with short and long duration fever without localizing signs. Early diagnosis and institution of appropriate antibiotics therapy is of paramount importance in the management of typhoid fever. Antibiotic sensitivity testing may be an added tool in this era of resistant strain emergence.

## References

1. Misra S, Diaz PS, Rowley AH. Characteristics of typhoid fever in children and adolescents in a major

metropolitan area in the United States. Clin Infect Dis. 1997; 24:998-1000.
2. Crump JA, Luby SP, Mintz ED.The global burden of typhoid fever. Bull World Health Organ 2004;82: 346-353.
3. Walia M, Gaind R, Paul P, Mehta R, Aggarwal P, et al.,Age-related clinical and microbiological characteristics of enteric fever in India. Trans R Soc Trop Med Hyg 2006;100: 942-948.
4. Tohme A, Zein E, Nasnas R. Typhoid fever. Clinical and therapeutic study in 70 patients. J Med Liban 2004;52: 71- 77.
5. Yap YF, Puthucheary SD. Typhoid fever in children-a retrospective study of 54 cases from Malaysia. Singapore Med J 1998;39:260-262.
6. Kliegman R, Behrman, Schor, Stanton, Joseph; Nelson textbook of pediatrics. 20th ed. Philadelphia: elsevier; 2015;1:1388-92.
7. Prajapati B, Rai GK, Rai SK, Upreti HC, Thapa M, Singh G, Shrestha RM. Prevalence of Salmonella typhi and para typhi infection in children, a hospital based study. Nepal Med Coll J. 2008;10(4):238-44.
8. Mirza SH, Beeching NJ, Hart CA. Multi-drug resistant typhoid: A global problem. J Med Microbiol 1996;44: 317-9.
9. Rowe B, Ward LR, Threlfall EJ. Multidrug-resistant Salmonella typhi: A worldwide epidemic. Clin Infect Dis 1997;24Suppl 1:S106-9.
10. Mehta G, Randhawa VS, Mohapatra NP. Intermediate susceptibility to ciprofloxacin in Salmonella typhi strains in India. Eur J Clin Microbiol Infect Dis. 2001;20:760–1.
11. Jog S, Soman R, Singhal T, Rodrigues C, Mehta A. Enteric fever in mumbai-clinical profile, sensitivity pattern and response to antimicrobials. JAPI. 2008;56.
12. Ganesh R, Janakiraman L, Vasanthi T, Sathiyasekeran M. Profile of typhoid fever in children from a tertiary care hospital in Chennai-South India. Indian J Pediatr.2010;77(10):1089-92.
13. Sen S.K, Mahakur A.C. Enteric fever-A comparative study of adult and paediatric cases. Indian J Pediat. 1972;39(11):354-60.
14. Gosai MM, Hariyani HB, Purohit PH, et al. A study of clinical profile of multidrug resistant typhoid fever in children. NJIRM. 2011;2(3):87-90.
15. Modi R Clinical profile and treatment outcome of typhoid fever in children at a teaching hospital, Ahmedabad, Gujarat, India. Int J Med Sci Public Health.2016;5:212-6.
16. Arora RK, Gupta A, Joshi NM, Kataria VK, Lall P, Anand AC. Multidrug resistant typhoid fever: study of an outbreak at Calcutta. Indian Pediatr. 1992;29(1):61-6.
17. Hyder R, Yasmeen B, Ahmed S. Clinical profile and Outcome of Enteric Fever in hospitalized children aged 6 months to 2 years. Northern Int Med Coll J. 2013;5(1):301-5.
18. Sood SC, Taneja PN. Typhoid fever, clinical picture and diagnosis. Ind J of Child Health. 1961;10(2):69-76.
19. Sinha A, Sazawal S, Kumar R, Sood S, Singh B, Reddaiah VP et al. Typhoid fever in children aged less than 5 years. Lancet.1999;354:734-7.
20. Parry CM, Hien TT, Dougan G, White NJ. Typhoid fever. N Eng J Med.2002;347:1770-82.
21. Kapoor JP, Mohan M, Talwar V, Daral TS, Bhargava SK. Typhoid fever in young children. Indian Pediatr.1985;22:811-3.
22. Chowta MN, Chowta NK. Study of Clinical Profile and Antibiotic Response in Typhoid Fever. Indian J Med Microbiol. 2005;23:125-7.
23. Kadhiravan T, Wig N, Kapil A, Kabra SK, Renuka K, Misra A. Clinical outcomes in typhoid fever: Adverseimpactofinfectionwithnalidixicacid resistant *Salmonella typhi*. BMC Infec Diseas. 2005;5:37.
24. Joshi BG, Keyal K, Pandey R, Shrestha BM. Clinical profile and sensitivity pattern of salmonella serotypes in children: a hospital based study. J Nepal Paediatr Soc.2011;31(3):180-3.
25. Laishram N, Singh PA. Clinical profile of enteric fever in children. J Evolution Med Dent Sci. 2016;5(2):114-116.
26. Banu A, Rahman MJ, Suza-ud-doula A. Clinical Profile of Typhoid Fever in Children in Northern Areas of Bangladesh. Dinajpur Med Col J. 2016;9(1):53-8.
27. Raj C. Clinical profile and antibiotic sensitivity pattern of typhoid fever in patients admitted to pediatric ward in a rural teaching hospital. Int J Med Res Health Sci.2014;3(2):245-8.
28. Lefebvre N, Gning SB, Nabeth P, Ka S, Ba-Fall K, Rique M et al. Clinical and laboratory features of typhoid fever in Senegal: A 70-case study. Med Trop (Mars). 2005;65(6):543-8.
29. Malik AS, Malik RH. Typhoid fever in malasian children. Med J Malaysia.2001;56(4):478-90.
30. Gautam V, Gupta N, Chaudhary U, Arora DR. Sensitivity pattern of Salmonella serotypes in Northern India. Brazilian J Infect Dis.2002;6:281-7.
31. Mishra SK, Sah JP, Shrestha R, Lakhey M. Emergence of Nalidixic acid resistant Salmonella: a confounding scene in antibiotic armamentarium. J Nepal Med Lab Sci.2008;9(1):61-6.

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