

## Original Research Article

# A study on clinical profile of typhoid fever in children

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### ABSTRACT

**Background:** Typhoid fever is caused by *Salmonella typhi*. It is a major public health problem in India. Typhoid fever is endemic in many developing countries. Wide variations in the clinical manifestations of typhoid fever make its diagnosis a challenging task. This study was conducted to understand the wide range of clinical manifestations, complications and antibiotic sensitivity patterns of typhoid fever in children.

**Methods:** Prospectively, 113 children admitted in pediatric unit with confirmed Typhoid fever from September 2015 to December 2016 at KIMS hospital, Bangalore were included. In each case, age, sex, presenting complaint, laboratory investigations and antibiotic sensitivity pattern are collected and analysed.

**Results:** Out of 113 cases, 72 cases (63.8.1%) were males, 41 cases (36.2%) were females. The most common age group was 5-10 years. The most common symptom was fever, seen in 100% cases, followed by anorexia (61%), vomiting (44%) and abdominal pain (18%). The most common sign observed was toxic look in 68% of the cases, followed by coated tongue in 49% and hepatomegaly in 44%. Leucocytopenia was found in 34% of cases. Eosinopenia was found in 39% of cases. Anaemia was found in 16% of cases. Thrombocytopenia was found in 15% of cases. Blood culture was positive in 20% of cases. Use of municipal water for drinking was found in 65% of cases. Outside eating was found in 40% of cases. Unhygienic practices were found in 64% of cases. Duration of hospital stay varied from 3-10 days. No mortality reported.

**Conclusions:** Typhoid fever is most commonly observed with unhygienic practices and eating of unhealthy outside food. This major public health issue can be tackled by bringing awareness among people regarding disease transmission and its various preventive measures.

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

### INTRODUCTION

The word typhoid is derived from Greek word 'TYPHOS' meaning smokes or stupor.<sup>1</sup> Typhoid is a multi systemic bacterial illness caused by *Salmonella* species, subspecies enterica and serovar typhi. A milder form of the disease is caused by serovars paratyphi A, B and C. About 26.9 million typhoid cases and more than 2 lakh deaths occur each year, with majority of the cases reported in Asia.<sup>2</sup> The incidence of typhoid varies substantially within Asia, with a very high incidence noted in India and Pakistan.<sup>3</sup> Low standards of living and

poor hygiene practices have contributed to the disease burden and made India endemic to typhoid fever. For developing countries like India, it is a big public health problem as the sanitation and public health standards are poor. Back in the 19<sup>th</sup> century, Typhoid fever was an important cause of hospital admission and death in the overcrowded and unsanitary urban conditions of the Europe and United states.<sup>4</sup> The introduction of clean water and good sewage systems contributed to a dramatic decrease in the incidence of typhoid. Today most of the disease burden is seen in developing countries, where sanitary conditions are poor.

The incubation period ranges from 7-14 days. However, it may vary from 3-30 days depending on infective dose.<sup>2</sup> 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<sup>2</sup>. 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.<sup>5</sup>

The clinical presentation of typhoid varies widely from mild constitutional symptoms to severe complicated disease. Typhoid fever has wide range of manifestations in the pediatric age group, it can present as septicemia in neonates, as diarrhoea in infants, and as lower respiratory tract infections in older children.<sup>6-8</sup> Typically, it manifests as step wise increasing, high grade fever, headache, lethargy, vomiting, abdominal pain, hepatosplenomegaly and rarely stupor. There is also significant difference in age distribution and population at risk. This is mainly a disease of school age children and young adults. The wide range of clinical symptoms especially in children often mimic other endemic infectious diseases, causing delays in diagnosis and treatment, in turn leading to severe complications including death.<sup>9-11</sup> Typhoid can involve multiple organs therefore resulting in diverse symptoms.<sup>12</sup> An atypical presentation of typhoid in older children includes liver abscess, splenic abscess, meningitis, ataxia, cholecystitis, chorea, palatal palsy, osteomyelitis, peritonitis, aphasia and even psychosis.<sup>13-20</sup>

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.<sup>2</sup> Stool and urine culture results become positive after 1<sup>st</sup> 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.<sup>2</sup>

Complications are reduced now because of use of antibiotics prior to initiation of appropriate therapy. However, rarely, clinically significant hepatitis, jaundice and cholecystitis may be seen. Intestinal haemorrhage and perforation are very rare in children. Toxic myocarditis usually manifests as arrhythmias or sinus block. CNS complications are relatively uncommon in children; this includes delirium, psychosis and raised intracranial tension. Other complications include DIC, bone marrow failure, hemolytic uremic syndrome, meningitis, pyelonephritis and nephrotic syndrome.<sup>2</sup>

Chloramphenicol was introduced in 1948. It was the standard antibiotic but within 2 years of its introduction, resistance started. However, Chloramphenicol-resistant typhoid fever became a major issue in 1972 when outbreaks occurred in Asia and Latin America.<sup>21-23</sup> *S*

*typhi* developed multi drug resistance to chloramphenicol, trimethoprim and ampicillin later in 1980 when these drugs were used as 1<sup>st</sup> line drugs. This led to outbreaks in Asia and Africa.<sup>24-27</sup> Fluoroquinolones were very effective in early 1990s, but later resistance to these drugs occurred.<sup>28</sup> Now, resistance to ceftriaxone is seen in certain sporadic cases.<sup>29</sup>

Treatment of typhoid includes proper hydration, correction of electrolyte imbalance, antipyretic therapy and appropriate antibiotics. Soft and easily digestible food should be continued. The prognosis depends on the rapidity of diagnosis and the institution of appropriate antibiotics. Other factors which decide prognosis include patient age, general health status and nutrition. Children with malnutrition and multidrug resistance are at higher risk. Preventive measures include proper hand washing with disinfectants after defecation and before consumption of food. These measures will help in breaking the transmission of typhoid thus reducing the burden of disease. Consumption of outside food items like ice cream and cut fruits, especially in summer, is associated with high risk of acquiring typhoid. Typhoid vaccines play a very important role in reducing the burden of disease. Parents should be encouraged to get their children vaccinated.

## METHODS

This is a prospective observational study, carried out in the Department of pediatrics, KIMS Hospital. Study was conducted for a period of 16 months between September 2015 and December 2016. Children aged 6 months to 18 years who presented to the Pediatric 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. Consent was taken from the parents or guardians after explaining the study. The cases which were discharged against medical advice and cases for which consent was not obtained were excluded from the study. Totally, 113 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 was asked regarding any previous episode of typhoid fever, family member/s suffering from typhoid or any previous treatment for typhoid, and the information was noted and analyzed. 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 4 days of antibiotics,

changes made according to the culture reports. Those cases with culture reports other than salmonella species were excluded from study. 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 7 days duration of fever. 78 cases (69%) had received antibiotics for a minimum period of 4-5 days prior to admission. Out of 113 cases, 72 cases (63.8%) were males and 41 cases (36.2%) were females. This shows male predominance in this study (Figure 1). As shown in Fig-2, most of the cases were aged between 5 and 10 years. 33 cases were below 5 years, representing 29.2%. 26 cases were aged above 10 years, representing 23.0%. 54 cases were aged between 5 and 10 years (47.8%). In all the above age groups male predominance was seen.

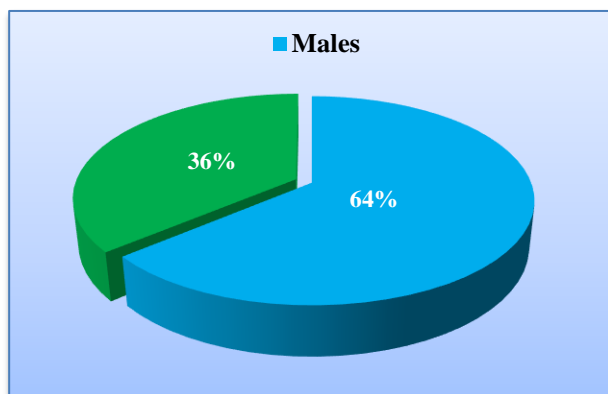


Figure 1: Sex distribution.

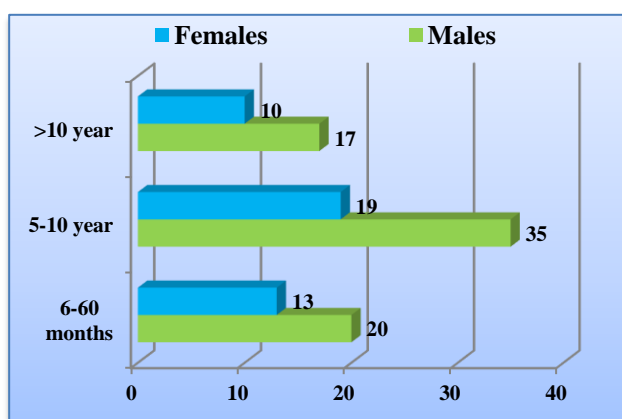


Figure 2: Age wise sex distribution.

Duration of hospital stay varied from 3-10 days. As shown in Table-1, most of the cases (71%) stayed in hospital up to 3rd and 7th day after admission. 23% cases stayed up to 3rd day in hospital and only 14.2% of cases

stayed in hospital for more than 7 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 1: Duration of hospital stay.

Duration of hospital stay	No. Of cases	P-value
Up to 3 <sup>rd</sup> day	26 (23%)	0.12
Between 3 <sup>rd</sup> and 7 <sup>th</sup> day	71 (62.8%)	0.00
More than 7 days	16 (14.2%)	0.23

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 (61%), vomiting (44%), pain abdomen (18%), diarrhea (16%), headache (12%), and cough (10%).

Table 2: Common presenting symptoms.

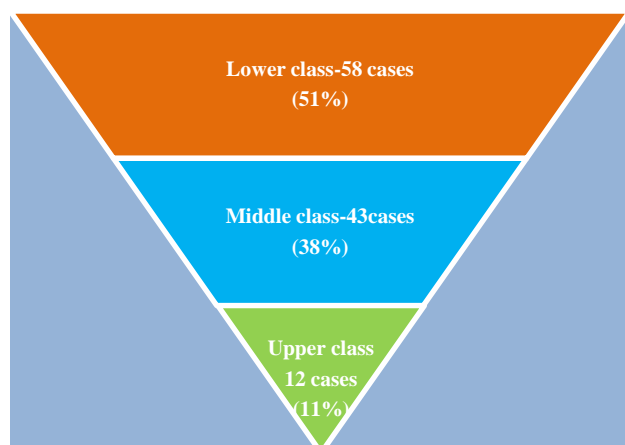
Presenting symptom	No. of Cases	P-value
Fever	113 (100%)	0.001
Anorexia	69 (61%)	0.000
Vomiting	50 (44%)	0.002
Pain abdomen	20 (18%)	0.018
Diarrhea	18 (16%)	0.082
Headache	13 (12%)	0.111
Cough	11 (10%)	0.162

Table 3: Various physical findings.

Signs	No. of Cases	P-value
Toxic look	60 (68%)	0.001
Coated tongue	43 (49%)	0.002
Hepatomegaly	38 (44%)	0.003
Splenomegaly	18 (21%)	0.061
Hepatosplenomegaly	14 (16%)	0.093
Pallor	09 (10%)	0.231

Coming to physical findings, the most common sign we observed was toxic look in 68% of the cases followed by coated tongue in 49%, hepatomegaly 44%, splenomegaly 21%, hepatosplenomegaly in 16% of cases and pallor in 10% of cases. In this study, we also reported the source of drinking water. In most cases (65%), the source of drinking water was through municipal water pipelines; majority of these belonged to the urban area. Only in 35% of cases, the source of drinking water was bore well water; these cases were from rural background.

As shown in Figure 3, the incidence of cases varied according to socio-economic status. Typhoid incidence was found to be more in lower class (51%), followed by in middle class (38%) and least in upper class (11%).



**Figure 3: Distribution of cases according to socio-economic status.**

**Table 4: Laboratory parameters.**

Laboratory parameters	Abnormal values	No. of cases	P-value
Hemoglobin	Anemia (Hb <11g%)	18 (16%)	0.023
Total leukocyte count	Leucocytosis (>11000cells/mm <sup>3</sup> )	17 (15%)	0.036
	Leucopenia (<4000cells/mm <sup>3</sup> )	38 (34%)	0.00
Polymorphs	Neutropenia	46 (40%)	0.00
	Neutrophilia	36 (32%)	0.00
Eosinophils	Eosinophilia	10 (8.8%)	0.22
	Eosinopenia	44 (39%)	0.00
Platelets	Thrombocytopenia	17 (15%)	0.02
SGOT	Elevated SGOT	10 (8.84%)	0.26
SGPT	Elevated SGPT	13 (11.5%)	0.18
Widal titres	TO >1:100	102 (90%)	0.00
	TH >1: 200	92 (81.5%)	0.00
Blood culture positive	Salmonella	23 (20%)	0.02

\*,Significant p<0.01

Among all cases, only 7% (8 cases) had past history of typhoid fever. In all of these cases, the patient had discontinued the treatment without medical advice. Outside food eating practices, especially roadside cooked food was found in 40% (45 cases). Also, unhygienic practices like improper hand washing after defecation or before food intake was found in 64% of cases.

Table 4 depicts the laboratory parameters. Anemia found in 18 (16%) cases, leucopenia and leucocytosis was observed in 38 (34%) cases and 17 (15%) cases respectively. neutropenia found in 46 (40%) cases and neutrophilia was found in 36 (32%) cases. Eosinopenia was seen in 44 (39%) cases, eosinophilia in 10 (8.8%) cases and thrombocytopenia in 17 (15%) cases. SGOT levels was elevated (>200IU/ml) in 10 (8.8%) cases and SGPT (>200IU/ml) in 13 (11.5%) 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 102 (90%) cases and TH titres >1:200 in 92 (81.5%) cases. Blood culture positive for *Salmonella typhi* noted in 23 (20%) cases. Out of 113 cases only 14 cases had been immunized with typhoid vaccine. All of them had taken typhoid polysaccharide vaccine more than 3 years prior to illness.

**Table 5: Antibiotic sensitivity pattern.**

Drug	No. of cases	Sensitivity	P-value
Ceftriaxone	33 (14.66%)	100%	0.000
Cefixime	33 (14.66%)	100%	0.000
Ofloxacin	32 (14.22%)	96%	0.000
Chloramphenicol	28 (12.44%)	84%	0.000
Cefotaxime	27 (12.82%)	82%	0.002
Azithromycin	20 (8.88%)	60%	0.182
Ciprofloxacin	29 (12.88%)	87%	0.002
Amoxicillin	23 (10.22%)	70%	0.082

\*,Significant p<0.01

Table 5 depicts antibiotic sensitivity patterns among culture positive cases. As mentioned in the table, ceftriaxone and cefixime sensitivity was seen in all the cases (100%) followed by ofloxacin (96%), ciprofloxacin (87%), chloramphenicol (84%), cefotaxime (82%), amoxicillin (70%) and azithromycin in 20 cases (60%). *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

Typhoid fever is a major public health problem in India. Present study aimed at understanding the clinical profile, outcome and antibiotic sensitivity pattern in children admitted to KIMS. In present study, male predominance was seen. Similar results were reported in other studies.<sup>30-32</sup> 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.<sup>33</sup> Another study also reported maximum number of cases in the age group above 5 years.<sup>34</sup> Highest incidence of typhoid fever in this age group can probably be attributed to outside food eating practices. 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 between 3<sup>rd</sup> and 7<sup>th</sup> day. Cases were discharged after 2 consecutive days of afebrile period without antipyretics. These results were in accordance with study done by Hyder et al.<sup>35</sup>

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.<sup>36</sup> 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.<sup>33</sup> 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.<sup>37</sup> Kapoor JP et al also reported similar results.<sup>38</sup> Other studies also showed similar clinical picture.<sup>21,39,40</sup> Contradictory to this, a study done by Joshi et al reported headache as the most common symptom next to fever.<sup>41</sup> In our study we reported Toxic look (68%) as the most common sign followed by coated tongue (49%), Hepatomegaly (44%), splenomegaly, Hepatosplenomegaly. Study done by Laishram et al reported coated tongue (80%) as the most common sign followed by Hepatomegaly (76%) and splenomegaly (38%).<sup>42</sup> Other study reported toxic look (93%) and coated tongue (66%) as most common signs.<sup>33</sup> In other study they had reported relative bradycardia and hepatomegaly as the most common sign.<sup>43</sup>

During our study, all cases were positive for Widal. Blood culture was positive in 20% of cases. Other study also reported 16% culture positive cases.<sup>35</sup> A study done by Banu et al also reported 28% culture positive cases.<sup>43</sup> 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.<sup>33</sup> Anemia was seen in 16% of cases. The other studies reported little higher percentage of anemias. A study done by Raj C et al reported anemia in 41.8% of patients and Lefebvre et al reported anemia in 78% of cases.<sup>44,45</sup> in our study Leucocytopenia and Eosinopenia found in 34% and 39% respectively. Similar results reported in Lefebvre et al.<sup>45</sup> Although leucocytosis and eosinophilia are rare in

typhoid, our study reported leucocytosis in 15% of cases and eosinophilia in 8% cases respectively. Thrombocytopenia was found in 15% of cases. Elevated SGOT is seen 9% of cases and SGPT was raised in 12% of the cases. The other study reported elevated liver enzymes in 70% of cases.<sup>46</sup>

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.<sup>41</sup> However sensitivity pattern varies from place to place. Other studies showed return of sensitivity pattern with chloramphenicol, cotrimoxazole, amoxicillin.<sup>39,47</sup> A study done by Mishra et al reported 100% sensitivity to azithromycin.<sup>48</sup> In our study the sensitivity to azithromycin was 60%. A Study done by Hyder et al reported 100% sensitivity to ceftriaxone and ciprofloxacin.<sup>35</sup> All other culture negative cases were treated with ceftriaxone. All cases responded to above antibiotics without any complications and mortality.

## CONCLUSION

Typhoid fever remains a major public health problem in the developing countries predominantly seen in school going children among pediatric age group. Public health interventions like supply of safe drinking water, appropriate sanitation, awareness of the disease and its transmission, and good personal hygiene practices may be employed. Food handlers especially in hotels, hostels and government schools should be educated about proper hand washing techniques. Also typhoid vaccination and rationale use of antibiotics based on the culture sensitivity pattern will help in reducing the burden of the disease.

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