



## Enteric fever - Clinical presentation, lab parameters, Complications and Sensitivity pattern in a tertiary care centre in Rural Maharashtra

Authors

**Dr Mahesh H Ahirrao<sup>1</sup>, Dr Bhagyashri Ahirrao<sup>2</sup>, Dr Jagdish Pakhare<sup>3</sup>,  
Dr Nandkumar V Dravid<sup>4</sup>, Dr Karuna Shejwal<sup>5</sup>, Dr Ashish Patil<sup>6</sup>**

<sup>1</sup>Associate Professor, <sup>3</sup>Professor, <sup>5</sup>Resident, Department of Pediatrics ACPM Medical College Dhule.

<sup>2</sup>Assistant Professor, <sup>4</sup>Professor and HOD, Department of Pathology ACPM Medical College Dhule.

<sup>6</sup>Assistant Professor Department of Microbiology ACPM Medical College Dhule

Corresponding Author:

**Dr Bhagyashri Ahirrao**

Assistant Professor, Department of Pathology ACPM Medical College Dhule, India

### Abstract

**Introduction:** Enteric Fever is endemic in South East Asia and poses a significant health problem in developing countries including India. Though treatable, enteric fever is known to cause potentially life threatening complications such as encephalopathy and enteric perforations. Diagnosis and management of enteric fever in pediatric age group pose several problems because of non-specific symptomatology. We conducted this prospective study to analyze clinical presentation, lab parameters, Sensitivity pattern and Complications in pediatric patients admitted with the diagnosis of enteric fever.

**Materials and Methods:** This was a prospective cohort study in which pediatric patients having enteric fever were included on the basis of a predefined inclusion and exclusion criteria. The study was conducted in a tertiary care medical college situated in a rural area. Informed consent was obtained from the guardians of the cases. Detailed history and demographic details were noted and thorough clinical examination was done in all the cases. Complete blood count, blood culture and sensitivity and Widal test was done in all the cases. Complications during hospital stay were also noted down. SSPE 16 version software was used for statistical analysis. P value less than 0.05 was taken as statistically significant.

**Results:** Out of 80 studied cases there were 46 (57.50%) males and 34 (42.50%) females with a M:F ratio of 1: 0.73. The most common sign was fever which was present in all (100%) the cases. The other signs and symptoms were headache (33.75%), high grade fever (28.75%), vomiting (28.75%) abdominal pain (21.25%) and chills (16.25%). On clinical examination isolated hepatomegaly and splenomegaly was present in 16 (20.00%) and 7 (8.75%) patients respectively whereas hepatosplenomegaly was present in 14 (17.50%) patients. Leukopenia was seen in 26 (32.50%) patients whereas leukocytosis was present in 7 (8.75%) patients. thrombocytopenia and deranged hepatic function tests were seen in 13 (16.25%) and 7 (8.75%) patients respectively. Blood culture was positive in 39 (48.75%) patients. Widal test was found to be positive in 41 (51.25%) patients. 75 (93.75%) patients responded well to administration of antibiotics. 5 (6.25%) patients developed complications such as meningeal signs (3.75%), bleeding diathesis (1.25%) and enteric perforation (1.25%).

**Conclusion:** Enteric fever is endemic in developing countries including India. Varied symptomatology makes its diagnosis difficult particularly in pediatric age group. Delayed diagnosis may lead to complications such as encephalopathy, bleeding diathesis and enteric perforation.

**Keywords:** Enteric Fever, Encephalopathy, Enteric perforation, Culture and Sensitivity.

## Introduction

Enteric Fever (EF) is a common health problem in developing countries of South East Asia including India. more than 2/3rd of all the cases of enteric fever come from India, china, Bangladesh, Nepal and Vietnam<sup>1</sup>. Unhygienic conditions and poor sanitation facilities are important are the most important risk factors for transmission. EF is primarily caused by gram negative enteric bacillus belonging to family enterobacteriaceae. The other common organisms which may cause EF include salmonella paratyphi A, B and C<sup>2</sup>. EF particularly in pediatric age group, may present with varied presentation and hence early diagnosis requires a high index of suspicion.

The mode of transmission is generally feco-oral route and the incubation period is usually 1-2 weeks. The patients usually present with signs and symptoms such as fever, abdominal pain, rash, splenomegaly, relative bradycardia and anorexia. Delayed diagnosis and inadequate treatment may result in life threatening complications such as encephalopathy, enteric perforations, toxemia, disseminated intravascular coagulopathy (DIC) and myocarditis. One must also be aware of atypical presentation of typhoid fever which may include severe headache, lobar pneumonia, osteomyelitis, cholecystitis, arthralgia and neurological manifestations such as altered sensorium and abnormal movements (chorea)<sup>3</sup>.

A high index of suspicion, proper history and clinical examination is most important for the diagnosis of enteric fever because the sensitivity and specificity of the available diagnostic tests vary greatly as reported by various studies across the literature. The most specific test for the diagnosis of EF is blood culture and isolation of bacteria in patients presenting with clinical picture suggestive of EF is considered diagnostic of enteric fever<sup>4</sup>. Within the first week of presentation blood culture may turn out to be positive and is diagnostic in majority of the cases. Widal test is neither sensitive nor specific and hence can't be relied upon solely<sup>5</sup>. Other serological tests such as indirect

haemagglutination test and ELISA for IgG and IgM antibodies have reported to be having varying sensitivity and specificity<sup>6</sup>. The investigations such as bone marrow culture has got high sensitivity but the invasive and painful nature of the test preclude its use as a routine investigative procedure for the diagnosis of EF. The laboratory features such as leukopenia and increased ESR may suggest EF but are non-specific. Presence of thrombocytopenia, elevated prothrombin and activated partial thromboplastin time combined with decreased fibrinogen level may suggest the possibility of potentially life threatening DIC<sup>7</sup>.

Management of EF includes general measures such as prevention of dehydration, maintenance of electrolyte balance and management of fever. An appropriate antibiotics in proper doses on the basis of culture sensitivity report is the cornerstone of therapy. Chloramphenicol and ampicillin which were used in past are hardly effective nowadays and fluoroquinolones, azithromycin and cephalosporins (ceftriaxone or cefixime) are very effective in treatment<sup>8</sup>. We conducted this prospective study to analyze clinical features, laboratory parameters, sensitivity pattern and complications in pediatric patients admitted with enteric fever.

## Materials and Methods

This was a prospective study conducted in the department of pediatrics of a tertiary care medical college situated in the rural area of Maharashtra State. The patients less than 18 years (pediatric age group) admitted with the primary diagnosis of enteric fever on the basis of a predefined inclusion and exclusion criteria. Informed consent was obtained from the guardians of the patients. The demographic details such as age, gender and address of all the patients were recorded. A detailed history about the duration of illness, presenting complaints and history of similar illness in family members was also noted down. A thorough clinical examination was done in all the cases. Any history of receiving antibiotics was asked for. Any history to drugs such as

fluroquinolnes, ceftriaxone and azithromycin was asked for. Blood samples were collected for complete blood count, electrolytes, erythrocyte sedimentation rate, WIDAL and blood culture. Antibiotics were started after collection of blood samples. Presence of electrolyte imbalance was corrected by appropriate measures. Clinical improvement was studied by repeated clinical examination. Presence of signs and symptoms suggestive of complications were specifically looked for. further specific tests were done in patients who showed signs of complications such as coagulation profile in patients presenting with bleeding manifestation and imaging in cases suspected to be having complications such as perforation. Appropriate surgical consultation was sought if needed. If required antibiotics were switched on the basis of culture and sensitivity reports. SSPE 16 version software was used for statistical analysis and p value less than 0.05 was taken as statistically significant.

**Inclusion Criteria**

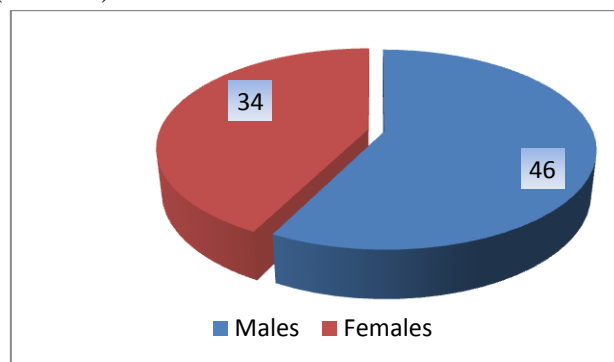
1. Patient admitted with clinical features suggestive of enteric fever.
2. Age less than 18 years.
3. Guardians have given informed consent to be part of the study.
4. Patients confirmed to be having enteric fever on the basis of investigations.

**Exclusion Criteria**

1. Age more than 18 years.
2. Patients whose guardians refused consent.
3. Patients in whom alternate diagnosis was confirmed.

**Results**

Out of the 80 pediatric patients included in this study there were 46 (57.50%) males and 34 (42.50%) females with a M:F ratio of 1:0.73



**Figure 1:** Gender Distribution of the studied cases.

The analysis of the cases on the basis of parents’ socio-economic status showed that the maximum number of patients belonged to lower socio-economic status (56.25%). This was followed by patients from lower middle class (28.75%) and middle class (15%). There was no patient belonging to upper middle and upper class.

**Table 1:** Gender wise Socio-Economic status of the studied cases

Socio-Economic Status	Male	Female	Total	%
Upper	-	-	-	-
Upper Middle	-	-	-	-
Middle	8	4	12	15.00%
Lower Middle	16	7	23	28.75%
Lower	22	23	45	56.25%
<b>Total</b>	<b>46</b>	<b>34</b>	<b>80</b>	<b>100.00</b>

The analysis of the patients on the basis of age groups showed that the most common affected age group was found to be between 5-10 years (57.50%) followed by 15-18 years (23.75%) and 11-15 years (15.00%). There were only 3(3.75%) cases diagnosed to be having enteric fever before 5 years of age. The mean age of males and

females was found to be 9.47 +/- 4.61 and 9.72 +/- 4.49 respectively. There was no statistically significant difference in the mean age of the males and females (P=0.80).

**Table 2:** Age groups of the studied cases

Age Group	Males		Females	
	No Of Patients	Percentage	No Of Patients	Percentage
Upto 5 yrs of age	2	2.50%	1	1.25%
5-10 years	26	32.50%	20	25.00%
11-15 years	7	8.75%	5	6.25%
15-18 years	11	13.75%	8	10.00%
Total	46	57.50%	34	42.50%
		Mean Age: 9.47 +/- 4.61	Mean Age: 9.72 +/- 4.49	
<b>P= 0.80 (Not Significant)</b>				

The analysis of signs and symptoms of the patients showed that the most common sign in the studied cases was fever which was present in all 80 cases (100%). The other common signs or symptoms seen in studied cases were headache (33.75%), high grade fever (28.75%), vomiting (28.75%), abdominal pain (21.25%) and chills (16.25%). isolated hepatomegaly and

splenomegaly was seen clinically in 16 (20%) and 7 (8.75%) respectively whereas hepatosplenomegaly was seen in 14 (17.50%) patients. Pallor was present in 8 (10%) patients. 5 (6.25%) patients were found to have toxic look and meningeal signs were present in 3 (3.75%) patients. Abdominal guarding and tenderness was present in 1 (1.25%) patient.

**Table 3:** Signs and Symptoms of the studied cases

Signs and Symptoms	No of Patients	Percentage
Fever	80	100 %
Headache	277	33.75%
High grade fever	23	28.75%
Vomiting	23	28.75%
Abdominal Pain	17	21.25%
Chills	13	16.25%
Hepatomegaly	16	20.00%
Splenomegaly	7	8.75%
Hepatosplenomegaly	14	17.50%
Pallor	8	10.00%
Toxic Look	5	6.25%
Meningeal Signs	3	3.75%
Abdominal guarding and tenderness	1	1.25%

The analysis of laboratory parameters showed that anemia was present in 11 (13.75%) children. The other abnormalities on complete blood count were found to be leukopenia which was seen in 26 (32.50%) patients whereas leukocytosis was seen in 7 patients (8.75%). Neutropenia and neutrophilia was present in (37.50%) and

(27.50%) patients respectively whereas eosinopenia and eosinophilia was present in (40.00%) and (26.25%) patients respectively. Evidence of thrombocytopenia was present in 13 patients (16.25%). Significantly raised Widaltiters were seen in 41 (51.25%) patients.

**Table 4:** Laboratory Parameters in studied cases

Laboratory Parameters	Values	No Of Patients	Percentage
Hemoglobin	Anemia (Hb< 11 gm %)	11	13.75%
	Normal	69	86.25%
Total Leukocyte count	Leukocytosis	7	8.75%
	Leukopenia	26	32.50%
Neutrophil Count	Neutrophilia	22	27.50%
	Neutropenia	30	37.50%

Eosinophil count	Eosinophilia	9	11.25%
	Eosinopenia	32	40.00%
Platelets	Thrombocytopenia	13	16.25%
	Normal	67	83.75%
Liver Function Test	Raised Bilirubin	3	3.75%
	Raised Liver Enzymes	7	8.75%
WIDAL titers	Significantly Raised	41	51.25%
	Not Significantly Raised	39	48.75%
Blood Culture	Positive For Salmonella	39	48.75%
	No Growth	41	51.25%

Analysis of blood culture for growth of salmonella species showed that out of 80 patients in whom blood culture was done 39 (48.75%) patients had a

positive blood culture for salmonella whereas remaining patients were found to have no growth on culture (51.25%).

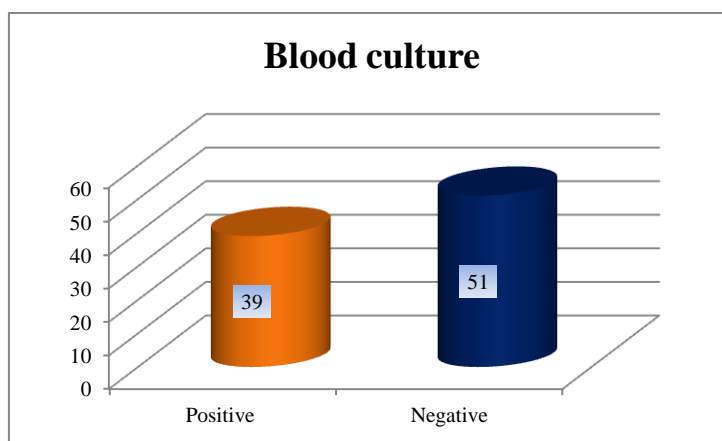


Figure 2: Blood culture for presence of salmonella

The analysis of antibiotic sensitivity patterns of the studied cases showed that all culture positive organisms were sensitive to ceftriaxone (94.87%). The other drugs to which organisms were found to be sensitive were found to be cefixime (92.31%),

ciprofloxacin (89.74%) ofloxacin (92.31%) and azithromycin (82.05%). Comparatively less cases were found to be sensitive to drugs such as amoxicillin (61.54%), chloramphenicol (38.46%) and trimethoprim-suphamethaxazole (28.21%).

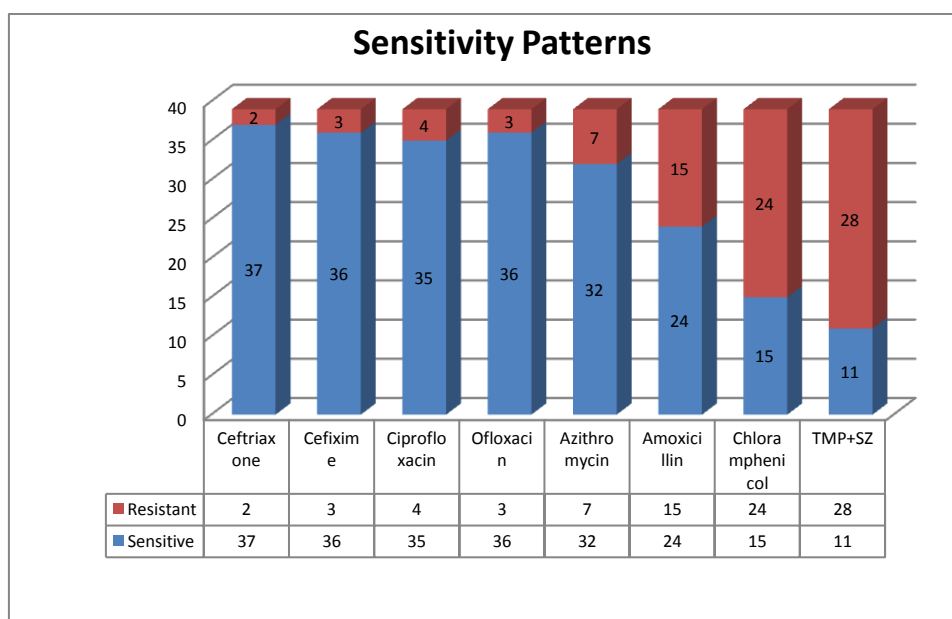
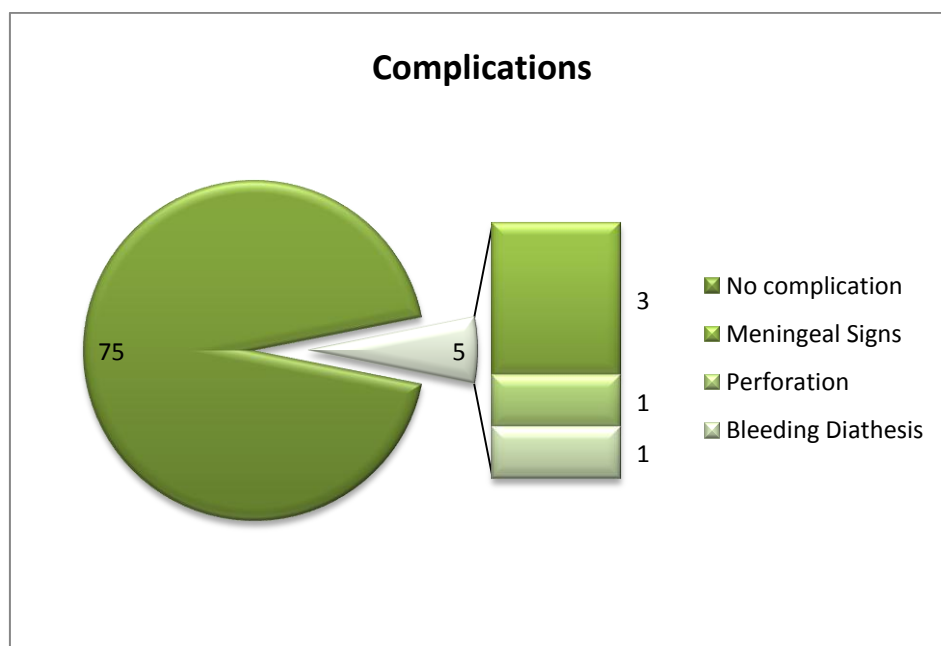


Figure 3: Sensitivity Patterns of the culture positive cases

All patients were successfully treated by appropriate antibiotics and out of 80 studied cases 75 patients could be discharged after 5 days of antibiotic therapy and asked to continue antibiotics and remain in follow up for 2 weeks. Out of remaining 4 patients 3 (3.75%) developed signs of meningeal irritation and 1 patient (1.25%) developed abdominal guarding and rigidity.

Bleeding diathesis was seen in 1 patient (1.25%) who was treated by transfusion of fresh blood and fresh frozen plasma (FFP). Erect X-ray abdomen was done which showed gas under diaphragm and hence in view of enteric perforation the patient was shifted to surgery. There was no mortality in any of the studied cases during the period of study.



**Figure 4:** Complications in the studied cases

### Discussion

This study comprised of 80 patients of pediatric age group who had been admitted with enteric fever. Out of these 80 cases there was a male predominance with a M:F ratio of 1:0.73. Maheshwari V et al conducted a cross sectional study of 163 clinically suspected patients of enteric fever<sup>9</sup>. Out of these 163 studied cases there were 89 males (54.60%) and 74 females (45.40%). Similar male preponderance was reported by Malik GM et al<sup>10</sup> and Mathura KC et al<sup>11</sup>. Though the exact cause of this male preponderance is not known the authors such as Khan M et al proposed that there are sex-linked differences in the degree of natural exposure of Peyer's patches to *S. typhi* as well as sexual dimorphism in host inflammatory response patterns which may be responsible for increased incidence and complications (perforation) of

enteric fever in males as compared to females<sup>12</sup>.

The mean age of the studied cases in our patients was found to be 9.51 years and the most common affected age group was found to be between 5-10 years. Iftikhar et al conducted a study of pediatric patients with enteric fever to find out frequency of various complications<sup>13</sup>. The authors found that Mean age of children was  $7.2 \pm 3.38$  and majority 94 (52.2%) of the children were 5-10 years old. The authors such as Akullian A et al<sup>14</sup> and Comeau JL<sup>15</sup> et al studying enteric fever in pediatric age group found the mean age of affected cases to be 8.4 years and 7.5 years. Mean age of cases in our study was found to be comparable to the mean age of cases in all these studies.

In our study fever (100%) headache (33.75%), high grade fever (28.75%), vomiting (28.75%), abdominal pain (21.25%) and chills (16.25%)

were the common presenting complaints. Dheer G et al in their study of children with enteric fever found fever, vomiting, cough anorexia, diarrhea, abdominal pain, hepatomegaly, splenomegaly and coated tongue to be common signs and symptoms of enteric fever in children<sup>16</sup>. The author recommended that enteric fever should be considered in the differential diagnosis of febrile patients with abdominal symptoms. Fever and abdominal pain were found to be common complaints in pediatric patients with enteric fever as reported by Mweu E et al<sup>17</sup>.

The investigations in studied cases showed presence of abnormalities such as leukopenia (32.50%), thrombocytopenia (16.25%), raised hepatic enzymes (8.75%) and bilirubin (3.75%). Khosla SN et al conducted a study to know the hematological abnormalities in patients with enteric fever and found that anemia, leucopenia, eosinopenia, thrombocytopenia and sub-clinical disseminated intravascular coagulation were some of the common hematological abnormalities seen in such patients<sup>18</sup>.

In our study blood culture was found to be positive in 39 (48.75%) patients and sensitivity patterns of the organisms showed that they were mostly sensitive to ceftriaxone (94.87%) cefixime (92.31%), ciprofloxacin (89.74 %) ofloxacin (92.31%) and azithromycin (82.05%). The organisms were found to be relatively resistant to antibiotics such as chloramphenicol, amoxicillin and trimethoprim-sulphamethazole combination. Similar sensitivity patterns were reported by the authors such as Gidvani CH et al who on the basis of culture and sensitivity reported that 100% cases were sensitive to ciprofloxacin followed by gentamicin (84.9%), cephalexin (83.6%), furazolidine (36.6%), trimethoprim-sulfamethoxazole (34.1%), chloramphenicol (34.0%) and amoxicillin (23.8%)<sup>19</sup>.

Finally the analysis of complication rates in our study showed that out of 80 studied cases 75 () cases recovered completely without any overt complications. 5 patients developed complication

such as meningeal signs (3/5), bleeding diathesis (1/5) and enteric perforation (1/5) and were treated accordingly. There was no mortality in any of the studied cases during study period. Similar complication rates were reported by Chiu CH et al who reported complications such as intestinal perforation (3%), rectal bleeding (3%), ascites or pleural effusion (4%), and meningitis (1%) in pediatric patients with enteric fever<sup>20</sup>.

### Conclusion

Enteric fever is one of the major health problems of developing countries including India. Possibility of EF must be considered in any patient presenting with fever and abdominal symptoms. Early diagnosis and proper antimicrobial treatment is required as delay in antimicrobial treatment may lead to severe and life threatening complications such as disseminated intravascular coagulation, meningitis and enteric perforation.

**Conflict of Interest:** None

### References

1. Date KA, Bentsi-Enchill AD, Fox KK, Abeysinghe N, Mintz ED, Khan MI, Sahastrabuddhe S, Hyde TB; Centers for Disease Control and Prevention (CDC). Typhoid Fever surveillance and vaccine use - South-East Asia and Western Pacific regions, 2009-2013.
2. Bhan MK, Bahl R, Bhatnagar S. Typhoid and paratyphoid fever. *Lancet*. 2005 Aug 27-Sep 2;366(9487):749-62.
3. Sejvar J, Lutterloh E, Naiene J, et al. Neurologic manifestations associated with an outbreak of typhoid fever, Malawi--Mozambique, 2009: an epidemiologic investigation. *PLoS One*. 2012;7(12): e46099.
4. Dance D, Richens JE, Ho M, Acharya G, Pokhrel B, Tuladhar NR. Blood and bone marrow cultures in enteric fever. *J Clin Pathol*. 1991;44(12):1038.

5. Willke A, Ergonul O, Bayar B. Widal test in diagnosis of typhoid fever in Turkey. *Clin Diagn Lab Immunol*. 2002;9(4):938-41.
6. Choo KE, Davis TM, Ismail A, Tuan Ibrahim TA, Ghazali WN. Rapid and reliable serological diagnosis of enteric fever: comparative sensitivity and specificity of Typhidot and Typhidot-M tests in febrile Malaysian children. *Acta Trop*. 1999 Mar 15;72(2):175-83.
7. Butler T, Bell WR, Levin J, Linh NN, Arnold K. Typhoid fever. Studies of blood coagulation, bacteremia, and endotoxemia. *Arch Intern Med*. 1978 Mar;138(3):407-10.
8. Thompson CN, Karkey A, Dongol S, et al. Treatment Response in Enteric Fever in an Era of Increasing Antimicrobial Resistance: An Individual Patient Data Analysis of 2092 Participants Enrolled into 4 Randomized, Controlled Trials in Nepal. *Clin Infect Dis*. 2017;64(11):1522-1531.
9. Maheshwari V, Kaore NM, Ramnani VK, Sarda S. A Comparative Evaluation of Different Diagnostic Modalities in the Diagnosis of Typhoid Fever Using a Composite Reference Standard: A Tertiary Hospital Based Study in Central India. *J Clin Diagn Res*. 2016;10(10):DC01-DC04.
10. Malik GM. Enteric Fever in asir region, southern of saudi arabia. *J Family Community Med*. 1994;1(1):35-9.
11. Mathura KC, Gurubacharya DL, Shrestha A, Pant S, Basnet P, Karki DB. Clinical profile of typhoid patients. *Kathmandu Univ Med J (KUMJ)*. 2003Apr-Jun;1(2):135-7.
12. Khan M. A plausible explanation for male dominance in typhoid ileal perforation. *Clin Exp Gastroenterol*. 2012;5:213-7.
13. Iftikhar A, Bari A, Jabeen U, Bano I. Spectrum of complications in childhood Enteric Fever as reported in a Tertiary Care Hospital. *Pak J Med Sci*. 2018;34(5):1115-1119.
14. Akullian A, Ng'eno E, Matheson AI, et al. Environmental Transmission of Typhoid Fever in an Urban Slum. *PLoS Negl Trop Dis*. 2015;9(12):e0004212. Published 2015 Dec 3.
15. Comeau JL, Tran TH, Moore DL, Phi CM, Quach C. Salmonella enterica serotype Typhi infections in a Canadian pediatric hospital: a retrospective case series. *CMAJ Open*. 2013;1(1):E56-61. Published 2013 May 2.
16. Dheer G, Kundra S, Singh T. Clinical and laboratory profile of enteric fever in children in northern India. *Trop Doct*. 2012 Jul;42(3):154-6.
17. Mweu E, English M. Typhoid fever in children in Africa. *Trop Med Int Health*. 2008;13(4):532-40.
18. Khosla SN, Anand A, Singh U, Khosla A. Haematological profile in typhoid fever. *Trop Doct*. 1995 Oct;25(4):156-8.
19. Gidvani CH, Chandar V, Raghunath D, Puri RD, Wilson CG, Nagendra A. Enteric fever - culture and sensitivity pattern and treatment outcome. *Med J Armed Forces India*. 2017;51(2):83-86.
20. Chiu CH, Tsai JR, Ou JT, Lin TY. Typhoid fever in children: a fourteen-year experience. *Acta Paediatr Taiwan*. 2000 Jan-Feb;41(1):28-32.