

Risk factors for enteric perforation in cases of typhoid fever**Pradeep Kumar Jain^{1*}, Aekta Jain²**¹*Professor, Ananta Institute of Medical Sciences & Research Centre, Dist Siyol Udaipur, Rajasthan, India*²*Consultant, Pediatrician, Rajasthan, India***Received: 12-06-2021 / Revised: 07-08-2021 / Accepted: 27-09-2021****Abstract**

Background: Typhoid fever is a severe febrile illness caused primarily by the gram-negative bacillus *Salmonella enteritidis* serovar Typhi. The present study was conducted to assess risk factors for enteric perforation in cases of typhoid fever. **Materials & Methods:** 64 patients of enteric fever of both genders were taken. Clinical features and risk factors causing enteric perforation was recorded. **Results:** Out of 64 patients, males were 40 and females were 24. Clinical features were diarrhoea in 37, vomiting in 45, abdominal pain in 60, constipation in 21, air fluid level in 64, gas under diaphragm in 55, anaemia in 43, leukopenia in 49 and thrombocytopenia in 45. Common risk factors for enteric perforation was age (>40 years) in 54%, male gender in 70%, high fever (>38.5°C) in 80%, elevated transaminase levels in 72%, anaemia in 68%, hepatosplenomegaly in 34% and short duration of treatment in 28%. The difference was non-significant (P > 0.05). **Conclusion:** Among various risk factors, male gender and elevated transaminase levels were common.

Key words: Enteric perforation, Transaminase levels, Typhoid fever

This is an Open Access article that uses a fund-ing model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Typhoid fever is a severe febrile illness caused primarily by the gram-negative bacillus *Salmonella enteritidis* serovar Typhi. It is a global health problem that can have a devastating impact on resource-poor countries. Regions with contaminated water supplies and inadequate waste disposal have a high incidence of typhoid fever[1].

Salmonella's typhoid infection is still a serious systemic disease in developing countries and in countries where unhealthy environmental conditions prevail. Hemorrhage and enteric perforation are the most common complications of this disease[2]. The most fatal form of typhoid fever is the typhoid enteric perforation (TEP), and TEP incidence in patients with typhoid fever is between 0.5 and 78.6%. Morbidity and mortality rates of TEP are still remarkably high. TEP morbidity rates are between 50 and 81%, and TEP mortality rates are between 3 and 72%. The reasons for postoperative complications are reported to be continuing severe peritonitis, sepsis, malnutrition, and liquid electrolytes[3].

Among the various complications the most lethal are intestinal bleeding and ileal perforations, both arising from hyperplasia and necrosis of Peyer's patches in the terminal ileum usually occurring 2-3 weeks after the onset of the disease[4]. Although intestinal hemorrhage is the most common complication of typhoid fever, intestinal perforation is the complication associated with highest morbidity and mortality. Mortality rates in cases of intestinal perforation following typhoid fever are reported to be between 5% and 62%.

The management of typhoid intestinal perforation poses a diagnostic and therapeutic challenge to general surgeons practicing in resource-limited countries[5]. Surgery is considered to be the treatment of choice in these patients, who most often present late. However, there is no consensus regarding the best procedure to be performed in such a case[6]. The outcome of treatment is poor in developing countries. This is due to multiple factors including delayed presentation of the disease, poor sanitation, lack of diagnostic facilities and inadequate healthcare services especially in remote areas[7]. The present study was conducted to assess risk factors for enteric perforation in cases of typhoid fever.

Materials & Methods

The present study was conducted on 64 patients of enteric fever of both genders. All were taken after they gave their written consent with the approval from higher authorities.

Demographic data such as name, age, gender etc. was recorded. Clinical features such as abdominal pain, abdomen distension, fever, vomiting/nausea, onset and duration of presenting symptoms were recorded. Risk factors such as age (>40 years), gender, inadequate treatment, duration of symptoms, high fever (>38.5°C), elevated transaminase levels (>1.5 times normal values), hepatosplenomegaly and leukopenia was recorded. General and abdominal examination, x-ray chest PA view or x-ray abdomen upright view was done. Ultrasound (USG) of the whole abdomen was also done.

Diagnosis of enteric perforation was based upon a history of fever followed by acute onset of pain in the abdomen, signs and symptoms of perforation peritonitis and a Widal test, supplemented by radiological findings of pneumoperitoneum and intraoperative findings. Histopathological examination of tissue biopsy from the margin of the perforation was done postoperatively. Results thus obtained were subjected to statistical analysis. P value less than 0.05 was considered significant.

*Correspondence

Dr. Pradeep Kumar Jain

Professor, Ananta Institute of Medical Sciences & Research Centre,
Dist Siyol Udaipur, Rajasthan, India.

E-mail: Dr.pradeepjain18@gmail.com

Results

Table 1: Distribution of patients

Total- 64		
Gender	Males	Females
Number	40	24

Table 1 shows that out of 64 patients, males were 40 and females were 24.

Table 2: Assessment of features

Clinical features	Number	P value
Diarrhoea	37	0.15
Vomiting	45	
Abdominal pain	60	
Constipation	21	
Air fluid level	64	
Gas under diaphragm	55	
Anaemia	43	
Leukopenia	49	
Thrombocytopenia	45	

Table 2, Fig.1 shows that clinical features were diarrhoea in 37, vomiting in 45, abdominal pain in 60, constipation in 21, air fluid level in 64, gas under diaphragm in 55, anaemia in 43, leukopenia in 49 and thrombocytopenia in 45. The difference was non- significant (P> 0.05).

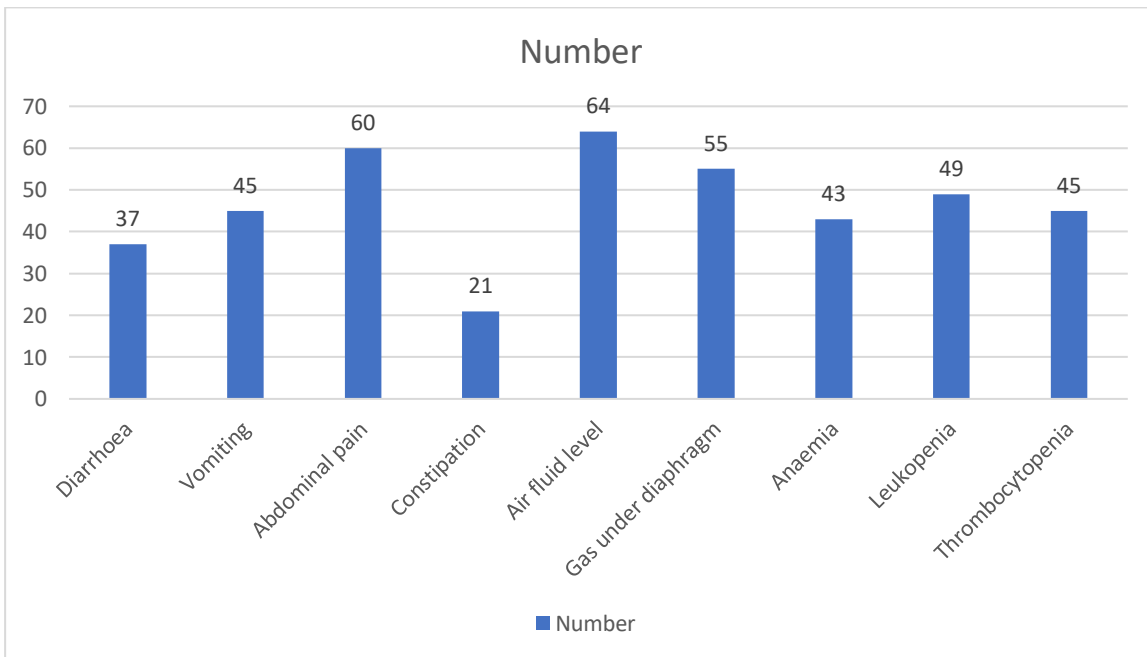


Fig 1: Assessment of features

Table 3: Risk factors for enteric perforation

Risk factors	Percentage	P value
Age (>40 years)	54%	0.17
Male gender	70%	
High fever (>38.5°C)	80%	
Elevated transaminase levels	72%	
Anaemia	68%	
Hepatosplenomegaly	34%	
Short duration of treatment	28%	

Table 3, Fig.2 shows that common risk factors for enteric perforation was age (>40 years) in 54%, male gender in 70%, high fever (>38.5°C) in 80%, elevated transaminase levels in 72%, anaemia in 68%, hepatosplenomegaly in 34% and short duration of treatment in 28%. The difference was non- significant (P> 0.05).

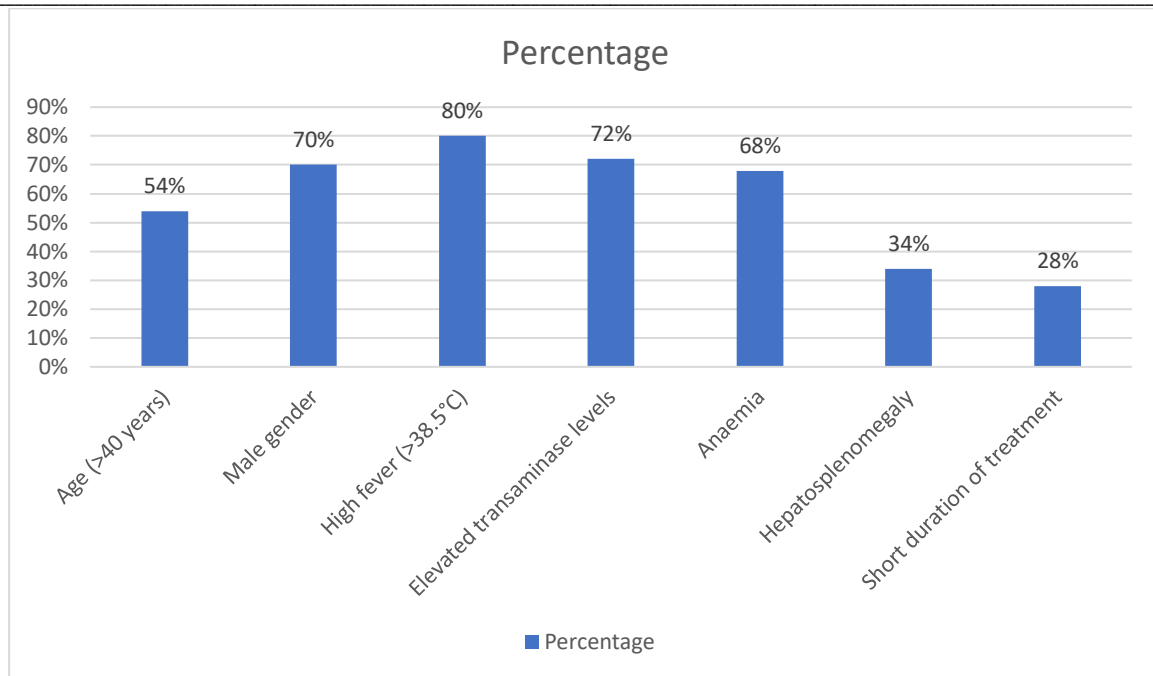


Fig 2: Risk factors for enteric perforation

Discussion

Typhoid fever is a severe febrile illness caused primarily by the gram-negative bacillus *Salmonella enteritidis* serovar typhi[8]. In developing countries, typhoid fever still remains a major health problem because of poor sanitary conditions[9]. Among the various complications the most lethal are intestinal bleeding and ileal perforations, both arising from hyperplasia and necrosis of Peyer's patches in the terminal ileum usually occurring 2-3 weeks after the onset of the disease[10]. Although intestinal hemorrhage is the most common complication of typhoid fever, intestinal perforation is the complication associated with highest morbidity and mortality. Mortality rates in cases of intestinal perforation following typhoid fever are reported to be between 5% and 62%[11]. The present study was conducted to assess risk factors for enteric perforation in cases of typhoid fever.

In present study, out of 64 patients, males were 40 and females were 24. Hosoglu et al[12] in their study risk factors for perforation were determined using logistic regression modeling. Forty case patients who had surgery because of typhoid enteric perforation were compared with 80 control patients. In univariate analyses, male sex ($p = 0.01$), age ($p = 0.01$), leukopenia ($p = 0.01$), inadequate antimicrobial therapy prior to admission ($p = 0.01$), and short duration of symptoms ($p = 0.01$) were significantly associated with perforation. In multivariate analysis, male sex (odds ratio (OR) = 4.39, 95% confidence interval (CI): 1.37, 14.09; $p = 0.01$), leukopenia (OR = 3.88, 95% CI: 1.46, 10.33; $p = 0.04$), inadequate treatment prior to admission (OR = 4.58, 95% CI: 1.14, 18.35; $p = 0.03$), and short duration of symptoms (OR = 1.22, 95% CI: 1.10, 1.35; $p = 0.001$) were significant predictors of perforation. A short duration of symptoms, inadequate antimicrobial therapy, male sex, and leukopenia are independent risk factors for enteric perforation in patients with typhoid fever.

We found that clinical features were diarrhoea in 37, vomiting in 45, abdominal pain in 60, constipation in 21, air fluid level in 64, gas under diaphragm in 55, anaemia in 43, leukopenia in 49 and thrombocytopenia in 45. Common risk factors for enteric perforation was age (>40 years) in 54%, male gender in 70%, high fever (>38.5°C) in 80%, elevated transaminase levels in 72%, anaemia in 68%, hepatosplenomegaly in 34% and short duration of treatment in 28%. Bulage et al[13] found that of the 88 TIP cases identified during

2013–2015, 77% (68/88) occurred between January and June, 2015; TIPs sharply increased in January and peaked in March, coincident with the typhoid outbreak. The estimated risk of TIP was 6.6 per 1000 suspected typhoid infections (68/10,230). The case-fatality rate was 10% (7/68). Cases sought care later than controls; Compared with 29% (13/45) of TIP cases and 63% (86/137) of controls who sought treatment within 3 days of onset, 42% (19/45) of cases and 32% (44/137) of controls sought treatment 4–9 days after illness onset, while 29% (13/45) of cases and 5.1% (7/137) of controls sought treatment ≥ 10 days after onset. 68% (96/141) of cases and 23% (23/100) of controls had got treatment before being treated at the treatment centre.

Jain et al[14] analysed surgical management of enteric perforation and to determine the prognostic factors associated with morbidity and mortality. 88 patients were studied with a male to female ratio of 6.3:1. The mean age was 36.4 years. The peak incidence was between 21 to 30 years. All the patients presented with abdominal pain and distension. More than 90% patients showed free gas under diaphragm. 71% patients had a single perforation and 97% patients had perforations confined to ileum. Debridement with double layered closure was performed in about 58% patients, ileostomy in 25% and resection anastomosis in 18% of patients. Overall complication rate was 44.3% with surgical site infection being the most common morbidity. The mortality rate was 17.1% which was significantly affected by perforation-admission interval of more than 48 hours, number of perforations and occurrence of postoperative complications.

Conclusion

Authors found that among various risk factors, male gender and elevated transaminase levels were common.

References

1. Meier DE, Imediegwu OO, Tarpley JL. Perforated typhoid enteritis: operative experience with 108 cases. *Am J Surg* 1989; 157:423–7.
2. Butler T, Knight J, Nath SK, et al. Typhoid fever complicated by intestinal perforation: a persisting fatal disease requiring surgical management. *Rev Infect Dis* 1985;7:244–56.

3. Santillana M. Surgical complications of typhoid fever: enteric perforation. *World J Surg* 1991;15:170–5.
4. Singh S, Singh K, Grover AS, et al. Two-layer closure of typhoid ileal perforations: a prospective study of 46 cases. *Br J Surg* 1995;82:1253.
5. Ceylan A, Acemoglu H, Hosoglu S, et al. Typhoid fever outbreak in Ahmetli Village, Ergani-Diyarbakir. *Mikrobiyol Bul* 2003;37:41–7.
6. Hosoglu S, Loeb M, Geyik MF, et al. Molecular epidemiology of invasive *Salmonella typhi* in southeast Turkey. *Clin Microbiol Infect* 2003;9:727–30.
7. Chatterjee H, Jagdish S, Pai D, et al. Changing trends in outcome of typhoid ileal perforations over three decades in Pondicherry. *Trop Gastroenterol* 2001;22:155–8.
8. Kaul BK. Operative management of typhoid perforation in children. *Int Surg* 1975;60:407–10.
9. Hoffner RJ, Slaven E, Perez J, et al. Emergency department presentation of typhoid fever. *J Emerg Med* 2000;19:317–21.
10. Khan M, Coovadia Y, Connolly C, et al. Risk factors predicting complications in blood culture-proven typhoid fever in adults. *Scand J Infect Dis* 2000;32:201–5.
11. Adesunkanmi AR, Ajao OG. The prognostic factors in typhoid ileal perforation: a prospective study of 50 patients. *J R Coll Surg Edinb* 1997;42:395–9.
12. Hosoglu S, Aldemir M, Akalin S, Geyik MF, Tacyildiz IH, Loeb M. Risk factors for enteric perforation in patients with typhoid fever. *American journal of epidemiology*. 2004 Jul 1;160(1):46-50.
13. Bulage L, Masiira B, Ario AR, Matovu JK, Nsubuga P, Kaharuzza F, Nankabirwa V, Routh J, Zhu BP. Modifiable risk factors for typhoid intestinal perforations during a large outbreak of typhoid fever, Kampala Uganda, 2015. *BMC infectious diseases*. 2017 Dec;17(1):1-7.
14. Jain S, Meena LM, Ram P. Surgical management and prognosis of perforation secondary to typhoid fever. *Tropical Gastroenterology*. 2017 Jun 1;37(2):123-8.

Conflict of Interest: Nil Source of support: Nil