ORIGINAL ARTICLE

Risk Factors of Typhoid Ileal Perforation

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ABSTRACT

Objective: To determine the risk factors for typhoid Ileal perforations in cases of typhoid fever so that by the advocacy of those factors we can reduce the rate of perforations and hence the mortality and morbidity in cases of typhoid fever.
Study design: Observational & Descriptive
Place and duration: The study was carried out in the department of surgery, Sir Ganga Ram Hospital, Lahore, from 20-08-2007 to 19-08-2009
Sample size: 50 patients of Enteric perforation of Typhoid Fever.
Materials and methods: All patients were treated as a surgical emergency. Broad spectrum antibiotic (Ceftriaxone & Metronidazole) coverage, nasogastric suction, correction of fluid, electrolyte balance and anaemia done to all patients preoperatively. Exploratory laparotomy done under General Anaestheisa. Operative procedure was decided on the basis of operative findings. Postoperatively the patients were followed up for any complication like feacal fistula. Parenteral antibiotics were continued for at least 5 days. All the data were recorded on a pre-designed proforma. The data was entered and evaluated in statistical program SPSS version 16.0.
Results: Fifty cases of ileal perforation were enrolled in this study based on inclusion and exclusion criteria. The mean age±SD (range) was 25.0±12.70 years (7 to 55 years). Majority of cases 38 (76.0%) were between 13 to 45 years of age, 40 (80.0%) were males and 10(20.0%) were females. 100% patients presented with abdominal pain, 100% with history of fever, 100 with distention alongwith constipation. In 9(18.0%) patients perforations, after freshening the ulcer were closed by single layered interrupted extra-mucosal technique with vicryl 2/0 and in remaining 41(82.0%) patients loop ileostomy was made. Wound infection was present in 33(66.0%) patients, wound dehiscence in 17(34.0%), Stenosis in 3(6.0%), herniation in 5(10.0%), intra abdominal abscess in 5(10.0%) and septicemia was found in 4(8.0%). Procedure of primary repair was performed in 18(36.0%) patients, segmentation resection and end to end anastomosis procedure was done in 4(8.0%) cases and primary repair with proximal ileosotomy was performed in 28(56%) patients.
Conclusion: Typhoid fever and its complications remained an important cause of deaths in poor resources countries due to lack of proper health education. A short duration of symptom, leucopenia, inadequate treatment and male gender are independent risk factor of perforation.
Keywords: Enteric, Ileal, perforation, typhoid

INTRODUCTION

Enteric fever is endemic in developing countries, including Pakistan, typhoid fever is a prolonged disease that includes bacteremic phase with fever and chills during the first week, wide spread reticuloendothelial involvement with rash, abdominal pain and prostration in the second week, and ulceration of Payer's patches with intestinal bleeding and perforation during the third week. It is caused by salmonella typhi. There are longitudinal ulcers on antimesenteric border, situated within 45cms of ileocaecal valve in majority of patients[1]. In undeveloped countries like ours, contamination of drinking water and eatables are the major source. Infected shellfish are occasionally a source of an outbreak[2]. The bacilli may remain in the gallbladder of carriers for months or years even after the clinical cure and pass intermittently in the stool and less commonly in urine. The incubation period of typhoid fever is about 10 to 15 days.

Other complications include hemorrhage from the ulcerated peyer's patches of intestine. Septicemia, cholecystitis, myocarditis, pneumonia, arthritis, osteomylitis and meningitis represent the wide spectrum of organ involvement[3].

The incidence of TIP has been reported to be between 0.8% and 18% and in West African region the incidence has been reported to be 15% to 33%, the highest in the world[4]. The morbidity ranges between 9% to 43% with survivors having wound infection and long hospital stay. A mortality rate of 4% to 80% per cent is reported in various studies[5,7].

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Many factors such as late presentation and delayed operation have been found to have a significant effect on the prognosis[5,8]. Early diagnosis and treatment avoids extensive procedure and is associated with low morbidity and mortality[4,9].

Complications like perforation of intestine occur usually after 10 to 14 days of fever. Risk factors for perforation were determined using logistic modeling[10]. The most lethal complications of typhoid fever are intestinal bleeding and ileal perforations, both arising from necrosis of Peyer's patches in the terminal ileum[10].

Treatment depends upon the nature of complication. Surgery remains the treatment of choice in patients with typhoid perforation[11]. Various modalities of surgical options are available, these include primary closure, resection and anastomosis, resection and ileostomy, wedge resection, application of serosal or omental patch and exteriorization of the perforation. Prognosis depends upon many factors including age of the patient, duration of fever and perforation, presence of fecal peritonitis and concomitant other illnesses. On the whole patients managed with surgery, either primary repair or ileostomy do well than those kept in conservative treatments. Primary repair carries with it a significant risk of reperforation[12] and peritonitis, which may endanger the life of patients. On the other hand ileostomy while avoiding this risk carries with it problems of ileostomy and its care. Availability of second line antibiotic therapy in these third world countries would likely improve outcomes. Prospective studies on appropriate antibiotic therapy along with management in endemic areas are necessary until resources are available for preventive measurements[5].

Following are the risk factors of typhoid fever[13,14,15,16].

- Never and early washing hands before eating
- Eating unhygienic conditions specially street food
- Eating outdoor at least once a week
- Consumption of ice cubes in beverage, buying ice blocks and ice cream from street vendors
- Consumption of unboiled water and unchlorinated water
- Brushing and bathing with less clean water
- Poor housing, inadequate personal and food hygiene

Transmission: Oral transmission via food or beverages handled by an individual who chronically sheds the bacteria through stool or, less commonly, urine. Hand-to-mouth transmission after using a contaminated toilet and neglecting hand hygiene. Oral transmission via sewage-contaminated water or shellfish (especially in the developing world). An inoculum as small as 100,000 organisms causes infection in more than 50% of healthy volunteers[11].

Risk Factors of typhoid perforation

Short duration of symptoms prior to admission:

Majority of patients with typhoid fever develop perforation prior to hospital admission in emergency condition due to:

- Poor resources
- Lack of education
- Difficulty in diagnosis and most of them treated in out patient department (OPD)

Because of these factors, it is possible as the patient with perforation have a disease pathogenesis i.e. more fulminant. The mechanism of intestinal perforation in typhoid fever is hyperplasia and necrosis of Peyer's patches of the terminal ileum. The lymphoid aggregates of Peyer's patches extend from the lamina propria to the submucosa, so that in the presence of hyperplasia the distance from the luminal epithelium to the serosa is bridged by lymphoid tissue. During the course of typhoid fever, S. Typhi is found within mononuclear phagocytes of Peyer's patches, and in cases with intestinal perforation, both this tissue and surrounding tissues show hemorrhagic areas. Tissue damage in Peyer's patches occurs, resulting in ulceration, bleeding, necrosis, and, in extreme cases, full-thickness perforation. The process leading to tissue damage is probably multifactorial, involving both bacterial factors and host inflammatory response[17,18,19].

Inadequate treatment: The fact that inadequate treatment was independently associated with enteric perforation is important. In patients with typhoid fever, antimicrobial treatment needs to be started early and to be used for a sufficient amount of time. The causative organism, S. Typhi, is very sensitive to antimicrobial agents[20, 21]. The timing of antimicrobial therapy could be critical in preventing serious complications such as perforation. Enteric perforation among patients with typhoid fever has been extremely rare in developed countries during the era of antibiotic use[2].

Male gender: Being male is an independent risk factor for intestinal perforation.Iintestinal perforation occurred significantly more frequently in males than in females.[22] The male:female ratio was found to be 2.5 : 1 in one study[23] and 4:1 in another.[24] The exact reason for a higher rate of enteric perforation in males is unclear.

Leukopenia: Leukopenia was also found to be an independent risk factor for enteric perforation. Among patients with typhoid fever who do not have enteric perforation, leucopenia is known to be a very common laboratory finding[25].

The above are independent risk factors for perforation among hospitalized patients with typhoid fever. Despite this high morbidity, relatively little is known about risk factors for enteric perforation in patients with typhoid fever[26].

If liquid electrolytes, blood, antibiotics, and parenteral nutrition are applied in typhoid enteric perforation cases sufficiently, then severe peritonitis becomes an independent risk factor that affects morbidity[27].

Due to above risk factors the incidence of enteric perforation is high at our setup. This study has been conducted to find out the risk factors of typhoid ileal perforation in cases of typhoid fever so that the mortality rate can be reduced.

PATIENTS AND METHODS

This Observational & Descriptive study was done in the Department of Surgery, Sir Ganga Ram Hospital, Lahore, from 20-08-2007 to 19-08-2009 on 50 patients with typhoid ileal perforation. All patients were admitted in surgery wards through emergency department. All the data were recorded on pre-designed proforma and relevant examinations were done such as baseline investigations including CBC, chest and abdominal plain radiographs, Widal test, abdominal Ultasonogram. S. Creatinine was done preoperatively only in suspicious cases. All patients were treated as a surgical emergency. Broad spectrum antibiotic (Ceftriaxone & Metronidazole) coverage, nasogastric suction, correction of fluid and electrolyte balance and anaemia done to all patients preoperatively. Exploratory laparotomy done under General anaestheisa. Operative procedure was decided on the basis of operative findings. Postoperatively the patients were followed up for any complication like Feacal fistula. Parenteral antibiotics were continued for at least 5 days. All the data were recorded on a pre-designed proforma.

Statistical analysis: The data were entered and evaluated in statistical program SPSS version 16.0. Qualitative data (simple frequency & percentages) such as gender, age (in groups), hospital stay (in groups), Number of perforations, surgical procedures, symptomatology, specific investigations and complications etc. were presented as n(%). Numerical parameters like age (in years), hospital stay (in days) were expressed as Mean±Standard deviation. No statistical test was applied for any comparison.

RESULTS

Fifty cases of ileal perforation were enrolled in this study based on inclusion and exclusion criteria. The mean age±SD (range) was 25.0±12.70 years (7 to 55) (Table 1). Majority of cases 38 (76.0%) were between 13 to 45 years of age, 7(14.0%) ranged from 7 to 12 years and 5(10.0%) were from 46 to 55 years of age (Table 1). 40(80.0%) were males and 10(20.0%) were females (Table 1). The average hospital stay was 16.92 days (5 to 45 days). 40(84.0%) had single perforation and 8 (16.0%) had multiple perforation (Table 3). Perforations were surgically treated depending upon the number of perforations, general health status of patient and degree of fecal contamination. In 9(18.0%) patients perforations after freshening the ulcer were closed by single layered interrupted extra-mucosal technique with vicryl 2/0 and remaining 41(82.0%) loop ileostomy was made. 100% patients presented with abdominal pain, 100% with history of fever, 100% with distention alongwith constipation diarrhea and vomiting in 43(86.0%), 4(8.0%) and 26(52.0%) respectively. 11(22.0%) patients presented with dehydration (Table 2). Widal test was positive in 35(70.0%) patients Typhi dot positive in 5(10.0%).

Table 1: Demographic details of the patients (n=50)

Baseline characteristics	Frequency	%
Mean age ± SD (Range): 25.08±12.70 (7–55 years).		
Age (in groups):		
5 to 12	07	14.0
13 to 45	38	76.0
46 to 55	05	10.0
Gender:		
Male	40	80.0
Female	10	20.0
Mean hospital stay ±SD (Range): 16.92±9.0 (7–45 days).		
Hospital stay (in days):		
5 to 12 days	20	40.0
13 to 20 days	15	30.0
21 to 35 days	12	24.0
36 to 45 days	03	6.0

Table 2: Signs and symptoms of study participants (n = 50)

Symptoms	Frequency	%
Abdominal pain	50	100.0
Fever	50	100.0
Constipation	43	86.0
Diarrhoea	04	08.0
Vomiting	26	52.0
Signs		
Anaemia	39	78.0
Cyanosis	03	06.0
Pedal edema	05	10.0
Dehydration	11	22.0
Distention	50	100.0
Tenderness	50	100.0
Guarding	05	10.0

In the present study, wound infection was present in 33(66.0%) patients, wound dehiscence in 17(34.0%), Stenosis in 3(6.0%), hernition in 5(10.0%), intra abdominal abscess in 5(10.0%) and septicemia was found in 4(8.0%) (Table 4). Procedure of primary repair was performed in 18(36.0%) patients, segmentation resection and end to end anastomosis procedure was done in 4(8.0%) cases and primary repair with proximal ileosotomy was performed in 28(56%) patients in majority (Table 3).

Table 3: Number of perforations and surgical procedure (n=50)

No. of Perforations	Frequency	%
Single	42	84.0
Multiple	08	16.0
Procedure:		
Primary repair of ulcer	18	36.0
Segmental resection and end to end anstomosis	04	8.0
Primary repair with proximal ileosotomy	28	56.0

Table 4: Post operative complications (n = 50)

Complications	Frequency	%
Wound infection	33	66.0
Wound dehiscence	17	34.0
Ileostomy:	03	6.0
- Retraction	03	6.0
- herniation	05	10.0
Intra abdominal abscess	05	10.0
Septicemia	04	8.0
Death	04	8.0

DISCUSSION

Typhoid fever is recognized as a serious global health problem by WHO[28]. A worldwide annual incidence of 16–33 million cases, with 500,000 to 600,000 annual deaths in endemic areas has been reported. The incidence of disease varies considerably in different parts of the world, 15-33% in West Africa and 1-3% in Egypt and Iran.[29] The exact incidence in Pakistan is not known. Perforation of a typhoid ulcer usually occurs during the third week and is occasionally the first sign of the disease.[30] The incidence of disease varies considerably in different parts of the world, 15- 33% in West Africa and 1-3% in Egypt and Iran.[31] The time of perforation was determined based on the onset of acute abdominal pain preceded by symptoms and signs of typhoid fever.[32,33]

In this study the incidence was found to be highest 38(76.0%) in young people ranging from 13 to 45 years, this observation is comparable with the study of Shaikh GS et al[34] conducted at Chandka Medical college Larkana; who showed 80% incidence ranging from 13 to 30 years of age. Ali S. et al.[35] also reported highest incidence in young age group i.e. 64% ranging from 21 to 30 years. Regarding number and location of perforations, in this study 84.64% had single perforation 16.0% had multiple perforations whereas Shaikh GS et al.[36] and his collea.gues reported 80.64% had single perforation 14.5 % had two perforations and 04.83 % patients had multiple perforations. In another local study of Ansari AG et al.[37] conducted in Nawabshah, 36 (81.81%) patients had single perforation & 8 (18.18%) patients had more than one perforation, these figures correlate well with this study. All perforations were 18 cm away from ileocaecal junction along the antimesenteric border of the ileum this is similar to previous reports.[38]

In the present study the 100% patients presented with abdominal pain and history of fever respectively, These figures are comparable with study of Shaikh GS et al [34] and his colleagues they reported that 93% patients presented with abdominal pain and 85% with history of fever while according to Ansari AG et al.[37] fever and abdominal pain was present in 100% patients he showed the same observation. Hosoglu S et al.[39] conducted in Turkey Abdominal pain was seen in 100% and high fever was 92.5% cases, these observations are similar to this study.

Furthermore Widal test was positive in 70% patients in this series, whereas typhidot was positive in 10% of cases postoperatively. This observation correlates with the study of Gedik E et al.[40] he showed that the Widal test was positive in 73% cases. Shaikh GS et al[34] proved that widal test was positive in 66% patients, whereas typhidot was positive in rest of cases. Ali S et al[41] reported in his study that widal test was positive in 64%.

The most common complication in this series was wound infection which accounted for 33(66.0%) cases, Ansari AG et al.[37] revealed that wound infection was present in 68.2% while Gedik E et al[40] reported 76.6% wound infection and this is also similar to a Nigerian study[42].

Wound dehiscence was noted in 17(34.0%) patients, this figure is comparable with the study of Ansari AG et al.[37] he reported 27.3% wound dehision in his study. Rashid A et al[43] showed 27.6% wound dehision. These figures are similar to this study.

Intra abdominal abscess was in 5(10.0%) while Ansari AG et al[37] showed the Intra abdominal abscess in 9.1% cases in his study. Naaya HU et al. [44] reported 11.3% and Rashid A et al[43] revealed 12.5% cases.

In this series, out of 50 cases, septicemia was occurred in 8.0% cases due to heavy abdominal contamination, delayed surgery. This observation is

comparable to the study of Siddiqui FG et al.[45] who revealed 7.84% septicemia out of 51 cases in his study. In an other local study conducted in Liaquat University Hospital Jamshoro by Malik AM et al. [46] who reported 4.0% septicemia out of 112 cases which is lower to our result because of less number of patients. Internally it is observed in the study of Cooper MR et al.[47] 14.9% patients developed septicemia which is slightly higher than the present study.

Present study performed three different surgical operations in patients depending upon the general condition of the patient, preoperative resuscitation, delayed operation, degree of contamination of the peritoneal cavity and the number of perforations at laparotomy. It is generally claimed in the literature that the mortality and morbidity associated with typhoid ileal perforation is not related to the surgical technique employed but rather on the general status of the patient and duration of the illness and this necessitates an aggressive pre-operative resuscitation[48].

In the present study, patients died who underwent segmentation resection end to end anastomosis without ileostomy procedure was done in 4(8.0%) cases. Mortality rate in this study was 8.0% (n=50) followed by septicemia whereas Malik AM[46] showed the 6.25% mortality rate in his study which is similar to this study while in the study of Siddiqui FG et al[45] death was seen in 8.3% patients.

Incisional hernia occurred at the site of an intestinal stoma on the abdominal wall usual causes are, too large opening in the abdominal wall and stoma site lateral to the rectus muscle. In this study, 5(10%) patients developed incisional Hernia, this is near to the Nigerial study[49].

In the present study, all patients 50(100%) were managed surgically. Of these, 18(36%) patients by primary repair, 4(8%) by segmental resection and end to end anastomosis while other remaining patients 28(56%) were managed by primary repair with proximal ileostomy. The frequency of these procedures were observed in the study of Chowdhury JUA et al[50] conducted in Bangladesh, who managed 40% patients by primary closure in two layer, 50% patients by primary repair with proximal ileostomy in his study out of 100 patients.

CONCLUSION

Typhoid fever and its complications remained an important cause of deaths in poor resources countries due to lack of proper health education. A short duration of symptom, leucopenia, inadequate treatment and male gender are independent risk factor of perforation. I would like to recommend that primary ileostomy should be given priority over the surgical options especially in those patients who presented late in the course of their illness with massive fecal contamination of the abdominal cavity. Segmental resection and end-to-end anastomsis is recommended for patients with multiple perforations. Primary repair of ulcer is a preferable technique in clinical stable patients with single perforation. Early diagnosis, effective resuscitation in the pre operative period, proper antibiotic, surgery and post operative care are the key to the successful management of patients with typhoid perforation. All above safety measures leads to decrease the mortality rate.

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