PROGNOSTIC FACTORS IN TYPHOID ENTERIC PERFORATION

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ABSTRACT
Objective: To analyze and predict the significance of various factors on the outcome in typhoid enteric perforation in a Surgical Unit of Teaching Hospital in Karachi.
Study Design: Case series.
Setting & Duration: Surgical Unit II and VI of Civil Hospital Karachi from March 2007 to February 2009.
Methodology: This study was conducted in sixty two consecutive patients clinically diagnosed as having typhoid perforation were included in this study. Diagnosis was mainly clinical and supplemented by Widal test, radiological findings of free gas under diaphragm, per operative findings of ileal perforation on anti mesenteric border. All the patients had exploratory laparotomy after adequate resuscitation. Operative findings were noted, and the amount of pus and fecal material drained were estimated, and perforation was exteriorized as ileostomy. The postoperative outcome was closely monitored, and the data on each patient were entered into a proforma.
Results: Fifty (80%) patients were males and twelve (20%) patients were females. Fifty two (84%) patients had single perforation while ten (16%) patients had multiple perforations. Fifty (80%) patients developed various postoperative complications, in which included wound infection, burst abdomen, residual intra-abdominal abscess, septicemia and fecal fistula. The age and sex had no effect on the prognosis. Late presentation, delay in operation, multiple perforations, and drainage of copious quantities of pus and fecal material from the peritoneal cavity adversely affected the mortality rate. Overall mortality rate was 17.7% (11/62).
Conclusion: Mortality in typhoid perforation is significantly affected by duration of illness, perforation-operation interval, multiple perforations, copious peritoneal fluid, septicemia, fecal fistula and burst abdomen; and some of the survivors with fecal fistula, wound infection and wound dehiscence are faced with prolonged hospital stay.

KEY WORDS: Enteric Perforation, Mortality, Prognostic Factors, Typhoid

INTRODUCTION
Perforation of the bowel is the most serious complication of typhoid fever. The resulting peritonitis in such a seriously ill patient may be rapidly fatal unless it is treated promptly and vigorously. These patients constitute a difficult therapeutic problem, and surgery, although associated with a high morbidity and mortality, offers the greatest hope of survival.1 Nowadays, this mortality rate, although decreasing but still remains very high, ranging from 1 to 39%,2 with a significant morbidity rate in spite of therapeutic progress. The mortality rate could be improved with the use of better supportive care, including parenteral nutrition and invasive monitoring. Such measures are beyond the reach of many hospitals in the developing world and management remains difficult in developing countries, which are frequently located in typhoid endemic areas such as Pakistan, India, South America and Africa.3 Various factors affect the prognosis and outcome of surgical treatment such as delayed presentation, inadequate preoperative resuscitation, delay in surgery, number of perforations and degree of fecal contamination.4-6 Intestinal perforation from typhoid fever is an extensive and continuing disease and should not be handled like a localized or limited perforation such as perforated ulcer, appendicitis or trauma.7

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This study was carried out to analyze and predict the significance of various factors on the outcome in typhoid enteric perforation in a Surgical Unit of teaching hospital in Karachi and to compare our findings to that of other parts of the world. The identification of the outcome factors will help in decision making, prioritizing management and improving the quality of care.

**METHODOLOGY**

This study was done on sixty two consecutive patients with typhoid ileal perforation were admitted in the Surgical Unit II and VI of Civil Hospital, Karachi during the period of two years from March 2007 to February 2009. All patients were above the age of 12 and ranged up to 60 years. Since typhoid fever is endemic in this region, for all practical purposes it was assumed that patients with a fever of 1-3 weeks duration who developed a clinical picture consistent with intestinal perforation were cases of typhoid enteric perforation. Diagnosis was mainly clinical and supplemented by Widal test, radiological findings of free gas under diaphragm, per operative findings of ileal perforation on anti mesenteric border and an acutely inflamed and edematous terminal ileum. Traumatic perforation was excluded by absence of a history of trauma; tubercular perforations were excluded by typical operative findings and biopsy.

Perforation was heralded by exacerbation of abdominal pain associated with tenderness, rigidity and guarding, most pronounced over right iliac fossa, however for some patients in a severe toxic state, these signs were obscured with resultant delay in diagnosis and adequate surgical intervention.

All patient was resuscitated before operation for 12 to 24 hours until the circulatory volume was restored and the patients had exploratory laparotomy after adequate resuscitation. Operative findings were noted, and the volume of pus and fecal material drained were estimated.

The edge of the ileal perforation was excised along with mesenteric lymph node for histopathology, and perforation was exteriorized as ileostomy. In case of multiple perforations distal perforation primarily closed while proximal exteriorized. Copious peritoneal lavage was done with warm saline, with a drain in the pelvis, and mass closure of the abdomen was done.

The postoperative outcome was closely monitored, and the data on each patient were entered into a pro forma prepared for the study. All data were analyzed using Fisher Exact test to determine the influence of the studied variables on the outcome. The differences were taken as significant only if the p-value is <0.05.

**RESULTS**

Fifty (80%) patients were males and twelve (20%) patients were females. Their age ranged from 12 to 60 years with maximum number of patients 37(60%) belonged to 25 to 40 years age group. The period between the first prodromal sign and the estimated perforation time ranged 4 to 28 days with a mean of 10.3 days. Fifty one (82%) patients presented within two weeks of onset of illness with a mortality of 11.7% (six out of 51 patients), and 11(18%) presented after two weeks with 45% mortality (5 out of 11 patients). Fourteen (22.5%) patients were operated within 24 hours estimated time of perforation with no recorded deaths, while 48 patients (77.4%) were operated after 24 hours had a mortality rate of 23% (eleven out of 48 patients).

Fifty two (84%) patients had single perforation while 10(16%) patients had multiple perforations. The mortality rate in single and multiple perforation groups was 7.7% and 70% respectively while morbidity was 77% and 100% respectively. The perforations all were located on the anti-mesenteric border of the ileum, ranging from the ileocecal valve to 80 cm proximally, with a mean location of 25 cm proximal to the ileocecal valve. The effect of number of perforations on post-operative complications and outcome can be noticed in Table I. The quantity of peritoneal fluid ranged from 200-2,300 ml with a mean of 718 ml. Thirty four (54.8%) patients had volumes <1,000 ml and three died (8.8%); and twenty eight (45.1%) had >1,000 ml and a significant effect on mortality with eight (28.5%) deaths.

Fifty (80%) patients developed various postoperative complications, which included wound infection in 50 (80%), wound dehiscence in 24(38.7%) and septicemia in 14(22.5%), out of which 07 already had septicemia at the time of admission. Others included residual intra-abdominal abscess in seven (11%) patients and enterocutaneous fistula in five (8%). Duration of illness, perforation-operation interval, number of perforations, burst abdomen, septicemia and fecal fistula have significant effects on mortality. Morbidity and mortality are detailed in Table I and Table II. Overall mortality rate was 17.7% (11/62). The duration of hospital stay for survivors was 8-62 days with a mean of 15.1 days.

**DISCUSSION**

Typhoid fever remains a public health problem in the developing world with gut perforation the major complication. This complication is almost invariably fatal but with the development of specific antibiotics and safe anesthesia techniques, surgery is increasingly used to manage perforations and offers the best hope of survival.
Table I. Effect of number of perforation on outcome

DF = Degree of Freedom

Primarily, the mortality and the morbidity rate do not depend on the surgical technique, but rather on the general status of the patient, the virulence of the germs and the duration of disease evolution before surgical treatment. That is why it is so important to provide adequate pre-operative management associating aggressive resuscitation with antibiotic therapy.1,2,8 This study has been undertaken in order to contribute to the improvement in the knowledge of prognostic factors of this disease.

Typhoid ileal perforation is still seen frequently in our environment, with a preponderance among males as

Table II. Variables associated with prognosis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mortality</th>
<th>DF</th>
<th>(P-Value)</th>
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<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>9/50</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>2/12</td>
<td>1</td>
<td></td>
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<tr>
<td>Age</td>
<td></td>
<td></td>
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<tr>
<td>≤ 40 years</td>
<td>8/50</td>
<td>1</td>
<td></td>
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<tr>
<td>&gt; 40 years</td>
<td>3/12</td>
<td>1</td>
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<tr>
<td>Duration of symptoms</td>
<td></td>
<td></td>
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<tr>
<td>&lt; 2 weeks</td>
<td>6/51</td>
<td>1</td>
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<tr>
<td>&gt; 2 weeks</td>
<td>5/11</td>
<td>1</td>
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<tr>
<td>Perforation-operation interval</td>
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<tr>
<td>&lt; 24 hours</td>
<td>0/14</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>&gt; 24 hours</td>
<td>11/48</td>
<td>1</td>
<td></td>
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<tr>
<td>Number of perforations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>4/52</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Multiple (&gt; 2)</td>
<td>7/10</td>
<td>1</td>
<td></td>
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<tr>
<td>Amount of peritoneal fluid</td>
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</tr>
<tr>
<td>&lt; 1000 ml</td>
<td>3/34</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>&gt; 1000 ml</td>
<td>8/24</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Burst abdomen</td>
<td>9/24</td>
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<td></td>
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<tr>
<td>Septicemia</td>
<td>8/14</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Fecal fistula</td>
<td>3/5</td>
<td>1</td>
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</tbody>
</table>

DF = Degree of Freedom
seen in our study with male to female ratio of 4:1, similar to other’s studies. Most of the patients in our study belonged to 25-40 years which is also same as other studies, while Aziz and Aajo reported second and third decades of life in their studies.

Symptoms and signs were not different from those in other studies, with a mean duration of symptoms before presentation being 11.8 days, and 82% of the patients presenting within 14 days of onset of symptoms, with fever, vomiting, abdominal distension and generalized abdominal pain being the major complaints. All patients belonged to low socioeconomic class and 70% came from rural areas or slum areas, where water supply and sewerage systems are not proper. Although many factors affect the prognosis of typhoid perforation but the most important are the duration of illness and the time interval between perforation and surgery. The need for adequate resuscitation resulted in further delay before operation in some of our patients who had presented in a poor state, which was also found to affect the outcome adversely. The effect of duration of illness and perforation operation interval on mortality can be seen in Table II, which is also reported by others in their studies.

No differences were found in survival between male and female patients; neither were the patients ages found to be an important prognostic factor, and same is reported by others in their studies.

The volume of peritoneal fluid/pus and the number of perforation in the gut have adverse affect on the outcome in terms of survival. Less volume of fluid/pus (less than 1000ml) and single perforation were associated with complication like wound infection, wound dehiscence, and residual abscess, while much fluid/pus (more than 2 liters) in the peritoneal cavity and multiple perforations were associated with fecal fistula and increased mortality (Table I and II).

Enterocutaneous fistula, which has been shown to adversely affect the postoperative outcome and mortality. Over all rate of Fecal fistula in our study was 4.8% of cases, which is low when compared with 10%, 8% and 8.3% in other studies, respectively. Postoperative burst abdomen contributed significantly to mortality, as 37.5% of those who developed this complication died. Burst abdomen was associated with fecal fistula, severe peritoneal contamination and wound infection in this study. Intra-abdominal residual abscess was found in 7 (11.2%) patients while Aziz reported 25% and 21.8% by Talwar Septicemia was found in 14(22.5%) patients, over whelming septicemia was the major cause of mortality in this study resulted due to late presentation of patient leading to delay in operation associated with multiple perforation and copious amount of peritoneal fluid/pus (more than 2 liter), while Aziz reported septicemia 22.2% and Akgun reported 25.5% in their studies.

Over all mortality rate was 17.7% which is comparable to other studies as 28% reported by Adesunkami and Aajo, 16.4% by Talwar13.8% by Aziz and 48% by Ameh. These figures are much higher than the rates reported from other tropical countries such as 6.8% from Nepal, and 10.5% from India. However, mortality rates of 1.5-2% have been reported from some parts of the developed world, where socioeconomic infrastructures are well developed. Most patients died in the early post-operative period and survival beyond the 10th post-operative day was associated with a high chance of complete recovery. Survivors of typhoid perforation were faced with various postoperative complications, such as wound infection and wound dehiscence, with prolonged hospitalization and increased cost of management. The over all wound infection was observed 80.6%. In the literature wound infection had been observed 33-100%. Attempts have been made at reducing the incidence of wound infection by delayed primary closure, but they have not been quite effective.

CONCLUSION

This study has shown that mortality in typhoid perforation is significantly affected by duration of illness, perforation-operation interval, multiple perforations, copious peritoneal fluid, septicemia, fecal fistula and burst abdomen; and some of the survivors with fecal fistula, wound infection and wound dehiscence are faced with prolonged hospital stay.

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