Non-malignant perforations: a study of various risk factors

Khamar Jaha Banu*

Department of General surgery, K S Hegde medical academy, Mangalore, Karnataka, India

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*Correspondence:
Dr. Khamar Jaha Banu,
E-mail: khamar.banu@gmail.com

ABSTRACT

Background: Patients with peritonitis are among the most complex patients encountered in surgical practice. Despite advances in the management of gastrointestinal perforation, mortality remains high. Various studies have accessed the association of various risk factors with the outcome, but either with the single risk factor or an isolated post-operative complication. But there are additional risk factors that influence the outcome either directly or in a synergism. Thus there is a need to analyze the various determinants which can help us to plan the treatment strategy.

Methods: 50 patients were studied over a period of two years. All the patients were closely monitored till discharge or death. The association between the various risk factors and the outcome were correlated statistically using Pearson correlation co-efficient and its significance test.

Results: The overall mortality was 16% and multi organ dysfunction syndrome was seen in 44% of the patients. The morality rate was higher in older individuals and longer the preoperative duration. Mannheim prognostic index was significantly higher in patients who developed multi organ dysfunction syndrome, though higher score was not significantly associated with mortality.

Conclusions: The association between various risk factors studied and multi organ dysfunction and mortality did not achieve statistical significance. Multi organ dysfunction syndrome was associated with higher Mannheim peritonitis prognostic index but was not significantly associated with mortality. Mortality can be reduced by identifying the patients at risk and initiating immediate intensive approach in such patients.

Keywords: Gastrointestinal perforation, Risk factors, Mortality, MODS

INTRODUCTION

Gastrointestinal perforation is a common surgical emergency encountered. Patients with peritonitis are among the most complex patients encountered in surgical practice. Thus there is a need to stratify the various determinants which can help us to plan the treatment strategy.1 Various studies have accessed the association of various risk factors with the outcome, but either with the single risk factor or an isolated post-operative complication. But there are additional risk factors that influence the outcome. Known since the days of Hippocrates, transmigration of bacteria from the gut causes peritonitis, which may be fatal or cause profound morbidity. Contamination of peritoneal cavity can cause sepsis, multisystem organ failure and death if not treated timely.

Objectives: The objectives are to establish an association between various risk factors and the possible outcomes in gastrointestinal perforations either independently or in synergism. The secondary objective was to correlate the results with existing Mannheim peritonitis prognostic index.
METHODS

Patients admitted to medical teaching hospitals with diagnosis of gastrointestinal perforation were included in the study.

In this study, perforations of esophagus, stomach, small intestine, colon and rectum were included. Total number of patients was 50. Study period was 2 years. All patients above 16 years of age included in the study.

Exclusion criteria were (i) Perforations due to malignancies (ii) traumatic perforations with associated solid organ injury (iii) immunocompromised patients and (iv) patients with comorbid medical illness

The diagnosis of gastrointestinal perforation was made by history and physical examination and confirmed by radiological examinations.

All the patients underwent following laboratory investigations on admission: 1) Complete blood count. 2) Renal function tests 3) Liver function test 4) Coagulation profile 5) Arterial blood gas analysis and serum electrolytes. The following radiological investigations were done: 1) Chest X-ray 2) Ultrasononography 3) Computed tomography of the abdomen- in few cases.

All the patients after initial resuscitation were taken up for surgery. The peritoneal fluid was sent for culture. Depending on site of perforation, patients underwent perforation closure with Graham’s omentoplasty, minimal resection and end to end anastomosis, or appendicectomy.

All patients were given thorough peritoneal lavage and abdomen was mopped dry. Mannheim prognostic index was calculated for all the patients.

All the patients were followed up daily till discharge or death. Mortality defined as death during hospital stay. Patients who needed ventilatory support or who needed inotropic support to maintain life were treated in intensive care unit. Rests of the patients were monitored in post-operative ward.

Laboratory and radiological investigations were done as per requirement of individual patients.

All the patients were treated with broad spectrum antibiotics for 5 days post operatively; antibiotics were continued if patient had fever or leukocytosis.

Data was entered in Microsoft excel and analyzed using SPSS (Statistical Package for Social Science, Ver.20.0) package. Proportions were compared using Chi-square test of significance. A “P” value of less than 0.05 was accepted as indicating statistical significance.

RESULTS

Gastrointestinal perforations were common among middle age patients. Men were most commonly affected in 84% of patients. There were eight deaths. Mortality rate was 16%. The patients older than 60 years had higher mortality. Patients younger than 20 years and older than 60 years had about 50% mortality, which was an independent risk factor.

The most common site for perforation was duodenum, comprising of 44%. Next common site was ileum. There was no significant difference in mortality rate with various sites of perforation.

The most common etiological factor was acid peptic disease followed by typhoid fever. Despite the better diagnostic tools and good medical treatment available for these diseases, it makes up 60% of all the causes of gastrointestinal perforation in our study. Trauma and NSAID usage were seen in 16% of the patients.

The duration of perforation in our study varied from 1 to 10 days. The mean duration of perforation was 3 days. The mean duration of perforation in discharged patients was 2.8 days and among dead patients was 4.25 days, which was not statistically significant though was an independent factor for poor outcome.

The most common investigation used was chest X-ray, which diagnosed gastrointestinal perforation in 96% of our patients. The only situation where there was no evidence of pneumoperitoneum in Chest X-ray in our study was in appendicular perforation.

Peritoneal fluid microbial culture showed E. coli most common organism. In 32% of patients there was no growth. This may also signify the resurgence of rare microbes, which need special media for culture, like fungi. But among the patients who died, 87.5% of patients had no growth, which was statistically significant. The number of days of hospital stay was 2 to 45 days.

The mean duration of hospital stay for discharged patients was 14.7 days and that for dead patients was 7.5 days. Most of the patients, who died, did so within 2 to 5 days of admission. The mean number of ICU stay was 4.28 days. The mean duration of ICU stay for discharged patients was 3.1 days and that for dead patients was 7.1 days, which is statistically significant.

Multi-organ dysfunction syndrome was observed in 22%. The mortality rate among patients with multi-organ dysfunction syndrome was 78%.

Mannheim peritonitis index score was calculated. Patient with MPI score of more than 21 had higher incidence of MODS and mortality which was statistically significant.
Table 1: Association of risk factors with MODS.

| Age (years) | Patients (%) | MODS (%) | Pearson Chi-square | Likelihood ratio | Linear-by-linear association |
|-------------|--------------|----------|--------------------|------------------|-----------------------------|
| <20         | 10           | 8        | 0.008              | 0.005            | 0.410                       |
| 21-40       | 44           | 14       |                    |                  |                             |
| 41-60       | 30           | 8        |                    |                  |                             |
| >61         | 16           | 14       |                    |                  |                             |

| Gender      | Patients (%) | MODS (%) | Pearson Chi-square | Likelihood ratio | Linear-by-linear association |
|-------------|--------------|----------|--------------------|------------------|-----------------------------|
| Male        | 84           | 40       | 0.768              | 0.762            | 0.771                       |
| Female      | 16           | 4        |                    |                  |                             |

| Site        | Patients (%) | MODS (%) | Pearson Chi-square | Likelihood ratio | Linear-by-linear association |
|-------------|--------------|----------|--------------------|------------------|-----------------------------|
| Gastric     | 10           | 8        |                    |                  |                             |
| Duodenum    | 44           | 12       |                    |                  |                             |
| Jejunum     | 4            | 2        | 0.037              | 0.014            | 0.103                       |
| Ileum       | 30           | 14       |                    |                  |                             |
| Appendix    | 8            | 8        |                    |                  |                             |
| Colon       | 4            | 0        |                    |                  |                             |

| Duration (days) | Patients (%) | MODS (%) | Pearson Chi-square | Likelihood ratio | Linear-by-linear association |
|-----------------|--------------|----------|--------------------|------------------|-----------------------------|
| <1              | 12           | 4        | 0.113              | 0.102            | 0.084                       |
| 2-4             | 76           | 30       |                    |                  |                             |
| >4              | 12           | 10       |                    |                  |                             |

| Etiology       | Patients (%) | MODS (%) | Pearson Chi-square | Likelihood ratio | Linear-by-linear association |
|----------------|--------------|----------|--------------------|------------------|-----------------------------|
| APD            | 34           | 12       |                    |                  |                             |
| NSAIDs         | 16           | 10       |                    |                  |                             |
| Trauma         | 16           | 14       | 0.033              | 0.011            | 0.449                       |
| Typhoid        | 26           | 4        |                    |                  |                             |
| Appendicitis   | 4            | 0        |                    |                  |                             |
| Others         | 4            | 4        |                    |                  |                             |

| Culture        | Patients (%) | MODS (%) | Pearson Chi-square | Likelihood ratio | Linear-by-linear association |
|----------------|--------------|----------|--------------------|------------------|-----------------------------|
| E. coli        | 34           | 8        | 0.102              | 0.040            | 0.109                       |
| Klebsiella     | 14           | 6        |                    |                  |                             |
| Streptococcus  | 6            | 2        |                    |                  |                             |
| Enterococcus   | 8            | 8        |                    |                  |                             |
| Pseudomonas    | 2            | 2        |                    |                  |                             |
| Proteus        | 2            | 0        |                    |                  |                             |
| Candida species| 2            | 0        |                    |                  |                             |
| No growth      | 32           | 18       |                    |                  |                             |

Table 2: Association of Mannheim peritonitis index with occurrence of MODS and mortality.

| MPI score | MODS (%) | DEATH (%) | P value | DEATH (%) | P value |
|-----------|----------|-----------|---------|-----------|---------|
| <13       | 2        |           | 0.003   |           | 0.111   |
| 14-21     | 8        |           | Linear by linear association 0.001 |           | Linear by linear association 0.087 |
| 22-29     | 18       |           |         | 0         |         |
| >29       | 16       |           |         | 6         |         |
Table 3: Association of risk factors and mortality.

|                         | Patients (%) | MODS (%) | Pearson Chi-square | Likelihood ratio | Linear-by-linear association |
|-------------------------|--------------|----------|--------------------|------------------|------------------------------|
| **Age (years)**         |              |          |                    |                  |                              |
| <20                     | 10           | 4        |                    |                  |                              |
| 21-40                   | 44           | 2        |                    |                  |                              |
| 41-60                   | 30           | 2        | 0.007              | 0.014            | 0.216                        |
| >61                     | 16           | 8        |                    |                  |                              |
| **Gender**              |              |          |                    |                  |                              |
| Male                    | 84           | 14       |                    |                  |                              |
| Female                  | 16           | 2        | 0.768              | 0.762            | 0.771                        |
| **Site**                |              |          |                    |                  |                              |
| Gastric                 | 10           | 4        |                    |                  |                              |
| Duodenum                | 44           | 4        |                    |                  |                              |
| Jejunum                 | 4            | 2        |                    |                  |                              |
| Ileum                   | 30           | 6        | 0.310              | 0.302            | 0.862                        |
| Appendix                | 8            | 0        |                    |                  |                              |
| Colon                   | 4            | 0        |                    |                  |                              |
| **Duration (days)**     |              |          |                    |                  |                              |
| <1                      | 12           | 4        |                    |                  |                              |
| 2-4                     | 76           | 30       | 0.113              | 0.102            | 0.084                        |
| >4                      | 12           | 10       |                    |                  |                              |
| **Etiology**            |              |          |                    |                  |                              |
| APD                     | 34           | 4        |                    |                  |                              |
| NSAIDs                  | 16           | 4        |                    |                  |                              |
| Trauma                  | 16           | 4        |                    |                  |                              |
| Typhoid                 | 26           | 2        |                    |                  |                              |
| Appendicitis            | 4            | 0        | 0.717              | 0.747            | 0.472                        |
| Others                  | 4            | 2        |                    |                  |                              |
| **Culture**             |              |          |                    |                  |                              |
| E. coli                 | 34           | 6        |                    |                  |                              |
| Klebsiella              | 14           | 0        |                    |                  |                              |
| Streptococcus           | 6            | 2        |                    |                  |                              |
| Enterococcus            | 8            | 2        |                    |                  |                              |
| Pseudomonas             | 2            | 0        |                    |                  |                              |
| Proteus                 | 2            | 0        |                    |                  |                              |
| Candida species         | 2            | 0        |                    |                  |                              |
| No growth               | 32           | 6        |                    |                  |                              |

**DISCUSSION**

Peritonitis is defined as an inflammatory process of the peritoneum caused by any irritant/agent such as bacteria, fungi, virus, talc, drugs, granulomas, and foreign bodies. Intra-abdominal infection is defined as the local manifestations that occur as a consequence of peritonitis. Intra-abdominal sepsis entails a systemic manifestation of a severe peritoneal inflammation. The mortality of an intra-peritoneal infection in the early 1900s was close to 90%. This condition was managed nonoperatively until Kishner introduced the basic principles of surgery in intra-abdominal infections: (1) elimination of the septic foci, (2) removal of necrotic tissue, and (3) drainage of purulent material. By the 1930s, mortality had been reduced to 50%. With the introduction of antibiotics, the mortality continued to decrease slowly. The use of cephalosporins by the early 1970s was associated with a reduction of mortality to less than 30% to 40%. Subsequent advances in the understanding of physiology, the monitoring and support of the cardiopulmonary systems, the rational use of new drugs, and ICU care aided in stabilizing mortality at around 30%.

The diagnosis of peritonitis is usually clinical. Pain abdomen, initially dull and is poorly localized (visceral peritoneum) and then progresses to steady, severe and more localized pain (parietal peritoneum). Later the pain...
becomes diffuse. Anorexia, nausea and vomiting may occur. On physical examination patients are in acute distress. Fever or hypothermia may be present. Tachycardia is caused by release of inflammatory mediators. Hypovolemia is due to vomiting and third space loss into the peritoneal cavity. With progressive dehydration, patients may become hypotensive and may have oliguria. On abdominal examination all patients demonstrate tenderness on palpation. In most patients the point of maximum tenderness or rebound tenderness overlies the pathological process. All patients demonstrate abdominal wall rigidity. Patients with severe peritonitis often avoid all motion and keep their hips flexed to relieve abdominal wall tension. The abdomen is often distended with hypoactive or absent bowel sounds. The findings of generalized ileus may not be present if infection is well localized.

Primary or spontaneous peritonitis can occur as a diffuse bacterial infection without an obvious intra-abdominal source commonly caused by pneumococcus and hemolytic streptococcus. Commonly occurs in children and in adults with ascites. The most common secondary peritonitis results from perforation, infection and gangrene of intra-abdominal organs usually of gastrointestinal tract. Gastrointestinal secretions, pancreatic secretions, bile, blood, urine and meconium cause chemical peritonitis. Tertiary peritonitis is seen in patients with severe sepsis, cause of sepsis being extra abdominal. It is a syndrome of abdominal infection, altered microbial flora and progressive organ dysfunction. Mortality with tertiary peritonitis is 30-60%. 1,3,6

Gastrointestinal perforations are common in young males younger than 50 years of age. Upper gastrointestinal perforations are common in developing countries. Gastrointestinal perforation can occur anywhere between esophagus and rectum. Most common site for perforation was the duodenum, followed by ileum. 5

The most common etiology for gastrointestinal perforation is acid peptic disorders. 5 Other important causes include typhoid, trauma, diverticular diseases and ischemic bowel disease. Overall incidence for admission with peptic ulceration is falling. The number of perforated ulcers remains unchanged. 80% of perforated duodenal ulcers are H. pylori positive. As many as 4-10% of patients on daily therapeutic-dose NSAIDs develop a duodenal ulcer within 3 months of initiation of therapy, and up to 1% of these duodenal ulcers are clinically significant. A clear dose-response relationship exists, with high doses associated with increased risk of duodenal mucosal damage.

Typhoid is most common cause of small bowel perforation in resource-poor countries. Regions with contaminated water supplies and inadequate waste disposal have a high incidence of typhoid. The most lethal complications of typhoid are intestinal bleeding and ileal perforations, both arising from necrosis of Peyer’s patches in the terminal ileum. The majority of patients with typhoid who develop perforation do so within the first 2 weeks of the illness. 7,8 Tuberculosis accounts for 5-9% of small intestinal perforations in India and is the second commonest cause after typhoid. 9

Both penetrating and blunt injuries can cause gastrointestinal tract perforations. Injuries to the GIT may be clinically subtle and are more common with penetrating than blunt trauma. GIT injuries occur in 30% of stab wounds and in 80% of gunshot wounds to the abdomen. In blunt trauma, an abdominal wall bruise or seat-belt sign should raise the level of suspicion since the finding is associated with a GIT injury in up to 21% of cases. Perforation of the gastrointestinal tract is relatively infrequent sequel of blunt abdominal trauma. Incidence of hollow visceral injury varies from <1%-8.5%. 10

Most common microorganism isolated from peritoneal fluid culture is E.coli, followed by Klebsiella and Enterococcus. In many of the earlier studies also, there was no organism isolated which may signify the resurgence of rare microbes, which need special media for culture, like fungi. Routine intraoperative peritoneal fluid cultures in GI perforation are controversial. Several studies have found no significant difference in patients with appendicitis, diverticulitis, and other common etiologies for bacterial peritonitis with regard to postoperative complication rates or overall outcomes. 11-13 The antibiotic regimen was altered only 8-10% of the time based on operative culture data. In patients who had previous abdominal operations or instrumentation (e.g., peritoneal dialysis catheter, percutaneous stents) and patients with prolonged antibiotic therapy, critical illness, and/or hospitalization, these cultures may reveal resistant or unusual organisms that should prompt alteration of the antibiotic strategy.

Mannheim prognostic index: It is a specific score with good accuracy to predict the individual prognosis in patients with peritonitis. The risk factors included are age >50 years, female sex, organ failure, malignancy, duration of peritonitis >24 hours, non-colonic origin of sepsis, diffuse peritonitis and type of exudates. Depending on the score the patients are categorized into various levels of risk. In patients with score of 0-5 the expected mortality is zero, 6-13 expected mortality is 2%, 14-21 expected mortality is 13%. 22-29 expected mortality is 26% and in score of 30-39 expected mortality is 64%. 14

CONCLUSION

The association between various risk factors studied and multi organ dysfunction and mortality did not achieve statistical significance. Multi organ dysfunction syndrome was associated with higher Mannheim peritonitis prognostic index but was not significantly associated with mortality. Mortality can be reduced by
identifying the patients at risk and initiating early intensive approach in such patients.

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