

ORIGINAL ARTICLE**Perforated Peptic Ulcer Disease in a Tertiary Hospital, Addis Ababa, Ethiopia: Five Year Retrospective Study****Henok Teshome^{1*}, Mekbib Birega², Mekdim Taddese¹****OPEN ACCESS**

Citation: Henok Teshome, Mekbib Birega, Mekdim Taddese. Perforated Peptic Ulcer Disease in a Tertiary Hospital, Addis Ababa, Ethiopia: Five Year Retrospective Study. *Ethiop J Health Sci.* 2020;30(3): 363. doi:<http://dx.doi.org/10.4314/ejhs.v30i3.7>

Received: December 27, 2019

Accepted: February 10, 2020

Published: May 1, 2020

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Funding: Nil

Competing Interests: The authors declare that this manuscript was approved by all authors in its form and that no competing interest exists.

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ABSTRACT

BACKGROUND: Peptic ulcer perforation is one of the two major acute complications of peptic ulcer disease with significant morbidity and mortality.

METHODS: Institution based retrospective review was done to determine patient presentation, management and postoperative complications of perforated peptic ulcer disease (PPUD) at a tertiary hospital in Addis Ababa, Ethiopia. Patients operated on from January 2013 to December 2017 were included. Univalent analysis was used to determine the influence of patient and operative events on postoperative outcomes.

RESULT: Totally, 136 patients were studied. Males outnumbered females by a ratio of 5.5:1. The mean age of patients was 36.05 ± 16.56 years. Seventy-one (52.2%) patients presented after twenty-four hours of onset of symptoms. Most perforations were located on the first part of the duodenum (117,86%). There were 73 postoperative complications recorded in 31(22.8%) patients. Old age, being female, presence of comorbidity, hypotension, tachycardia, and delayed presentation were significantly associated with postoperative morbidity ($P < 0.05$). Nine (6.6%) patients died at the hospital. Mortality was significantly associated with old age, comorbid illness, tachycardia, and development of post-operative complications ($P < 0.05$). The postoperative hospital stay of the patients with complications was 18.6 ± 14.7 days which was significantly higher than that of patients without complication 6.7 ± 2.7 days ($P = 0.001$).

CONCLUSION: Old age, being female, presence of comorbidity, hypotension, tachycardia, and delayed presentation were significantly associated with postoperative morbidity. Old age, comorbid illness, tachycardia and development of post-operative complications were found to increase the risk of mortality.

KEYWORDS: Peptic ulcer disease, Perforated Peptic ulcer disease, Morbidity and Mortality

INTRODUCTION

Peptic Ulcer Disease (PUD) is associated with potentially life-threatening complications, including bleeding, perforation, and obstruction. Perforation is the second most frequent complication after bleeding (1).

Perforation due to peptic ulcer is a serious complication that affects an average of 2-10% of peptic ulcer patients and having an overall mortality of 10%, although some authors report ranges between 1.3 and 20%. Thirty day mortality rate reaching 20% and 90-day mortality rate of up to 30% have also been reported. Being a life-threatening complication of PUD, it needs special attention with prompt resuscitation and appropriate surgical management if morbidity and mortality are to be avoided (2).

The pattern of perforated PUD has been reported to vary from one geographical area to another depending on the prevailing socio-demographic and environmental factors. In the developing world, the patient population is young with male predominance, patients present late, and there is a strong association with smoking. In the west, the patients tend to be elderly and there is a high incidence of ulcerogenic drug ingestion (2,3). Delay in diagnosis and initiation of surgical treatment for perforated PUD has been reported to be associated with high morbidity and mortality after surgery for perforated PUD (4).

Though perforated peptic ulcer disease (PPUD) is one of the most common surgical emergencies at Saint Paul's Hospital Millennium Medical College (SPHMMC), there was no study conducted about it. To our knowledge, there are only two studies in the country, which are done six and thirteen years ago. This study tries to fill this gap and helps to understand the burden of the disease and to propose strategies that improve patient outcomes. The objective of the study was to determine patient presentation, management and postoperative complications of PPUD.

MATERIALS AND METHODS

A retrospective review was done at SPHMMC, Addis Ababa, Ethiopia, from January 2018 to August 2018. St. Paul's Hospital Millennium Medical College is a teaching hospital for both

undergraduate and postgraduate studies with 110 surgical beds. All patients who were operated on for Perforated Peptic Ulcer Disease (PPUD) from January 2013 to December 2017 were included in the study. Patients with perforations caused by pathologies other than Peptic Ulcer Disease (PPUD), pediatrics patients and missed or incomplete charts were excluded from the study.

The operation theater logbook was used to identify patients and individual patients' medical records were reviewed to extract data. Trained surgical residents in a pretested data collection format collected data on patients' socio-demographic characteristics, comorbidities, risk factors, intraoperative finding, management, morbidities, and mortalities. Data collection was supervised, and the quality of data was checked every day.

The data was analyzed using SPSS version 23. Univariate analysis was used to determine the influence of patient factors and operative events on postoperative outcomes. P-value of < 0.05 was used as a cut-off for determining statistical significance. A written ethical clearance letter was given from SPHMMC's Institutional Review Board. Data acquired was used only for the study, and patients' information used in the research was kept confidential.

In this study, early operation is when patients are operated within 24 hours after the onset of symptoms and late operation is after 24 hours. The duration of symptoms is the period between the initial pain perception due to perforation and visit to SPHMMC.

RESULTS

During the study period, 146 patients underwent emergency laparotomy for perforated peptic ulcers; of these, 10 patients were excluded from the study due to incomplete data and failure to meet the inclusion criteria making the response rate 93%. One hundred thirty six patients, 115(84.6%) men, with 5.5:1 male to female ratio were enrolled in the study. The mean and median age of patients was 36.05 ± 16.56 and 30 years respectively. The peak incidence was between 15 and 30 years. The majority of patients, 105 (77.2%), were younger than 45 years. Half (50.7%) of the patients were

from an urban area and the rest were from a rural area.

Eighty-two (60.0%) patients reported previous history of dyspepsia or a history of treatment for peptic ulcer disease. Twenty four (47.05%) patients reported a history of recent ingestion of alcohol among 51 documents with the record. Other risk

factors included chewing chat and smoking in 12 (48%) and 16 (34.7%) patients among 25 and 46 documents with the record respectively (Table 1). Five (3.7%) patients had comorbidities; these include diabetes mellitus, bronchial asthma, chronic liver disease, congestive heart failure and retroviral infection (RVI).

Table 1: Potential risk factors identified among patients operated for perforated peptic ulcer disease at St. Paul Hospital Millennium Medical College, Addis Ababa, Ethiopia from January 2013 to December 2017

| Risk factors | Present No.(%) | Absent No.(%) | Undocumented No.(%) |
|----------------------|-------------------|------------------|------------------------|
| Smoking | 16(11.8) | 30(22.1) | 90(66.2) |
| Chewing chat | 12(8.8) | 13(9.6) | 111(81.6) |
| Alcohol ingestion | 24(17.6) | 27(19.9) | 85(62.5) |
| NSAIDS use | 2(1.5) | 13(9.6) | 121(89.0) |
| History of dyspepsia | 82(60.3) | 18(13.2) | 36(26.5) |
| Dyspepsia treatment | 68(50.0) | 29(21.3) | 39(28.7) |

Presentation: The duration of symptoms ranged from 1 to 8 days making the mean and median 2.11 ± 1.67 days and 1.75 days respectively. Seventy one (52.2%) of the patients presented after twenty-four hours of onset of symptoms; the rest 65(48.7%) of the patients presented within 24 hours of onset of symptoms. All of the patients presented with sudden onset of severe abdominal pain, nausea, and vomiting. Eighteen (13%) and 87(64%) patients presented with systolic BP<90mmHg and with PR>100beats/minute respectively. All of the patients with systolic BP<90mmHg came after 24 hours of onset of symptoms. Abdominal tenderness was demonstrable in all of the patients.

WBC count was normal in 67 patients (49.3%), 5(40.3%) of the patients had leukocytosis (WBC> 11,000 /mm³), 9(6.6%) patients had leucopenia of WBC less than 4000/mm³ and in the rest 5 patients (3.7%), the WBC count was not found in the chart.

Intraoperative: Most (121, 89%) perforations were located on the first part of the duodenum, whereas the remaining 15(11%) ulcers were on the stomach. The duodenal to gastric ulcer ratio was 8.1:1. The median size of the ulcers was 5 mm. Eighty-eighth (64.7%) of the perforations were ≤ 5

mm and 8(5.9%) were >10 mm, the rest 35 (25.7%) were between 5 and 10mm. The amount of peritoneal fluid varied from 100 to 6000 milliliters with a mean and median of 1293 and 1000 milliliters respectively.

The majority, 126(92.6%), of the patients had Graham's omental patch. Four patients had spontaneously sealed duodenal perforations and just had peritoneal lavage with warm saline. Another four patients with gastric ulcer had simple closure with G-J; the rest two patients had simple closure of the perforation. Subhepatic drain was put for 84(61.8%) patients.

Complications: Seventy-three post-operative complications were recorded in 31(22.8%) patients. Of these, superficial surgical site infection (20, 27.4%) was the commonest. The other complications were wound dehiscence (10, 13.7%), Hospital-acquired pneumonia (16, 21.9%), post-operative collections (12, 16.4%), acute kidney injury (7, 9.7%) and repair site failure (8, 10.9%) (Table 4).

Old age, being female, presence of comorbidity, hypotension, tachycardia, and delayed presentation were significantly associated with postoperative morbidity ($P<0.05$). The mean age of the patients who developed complications was

40.18 ± 17 years, whereas the mean age of patients without complications was 34.7 ± 16.2 years (P=0.25). Thirty five percent of the patients who presented after 24 hours of their illness developed postoperative complications as compared to only

9% of the patients who presented within the first 24 hours (P=0.000). Forty four percent of the patients with hypotension developed complications as compared to only 19% of patients without hypotension (P=0.019) (Table 2).

Table 2 Factors associated with Post-operative complications among patients operated for perforated peptic ulcer disease at St. Paul Hospital Millennium Medical College, Addis Ababa, Ethiopia from January 2013 to December 2017

| Factors | Total No.(%) | Complications No.(%) | No Complications No.(%) | P value |
|-------------------------|----------------|----------------------|-------------------------|---------|
| Sex | Male | 115(84.6) | 21(18.3) | 0.003 |
| | Female | 21(15.4) | 10(47.6) | |
| Comorbid Illness | Yes | 5(3.7) | 4(80.0) | 0.001 |
| | No | 131(96.3) | 27(20.6) | |
| Pre-Operative stay | <24 hours | 65(47.8) | 6(9.2) | 0.000 |
| | >24 hours | 71(52.2) | 25(35.2) | |
| Pulse Rate | >100 beats/min | 87(69.0) | 28(32.2) | 0.001 |
| | <100 beats/min | 49(36.0) | 3(6.1) | |
| Systolic Blood Pressure | <90mmHg | 18(13.2) | 8(44.4) | 0.019 |
| | >90mmHg | 118(86.7) | 23(19.5) | |

Of the five patients with comorbid illness, four developed postoperative complications (P=0.001). The first patient with diabetes developed SSSI, wound dehiscence, post-operative collection and repair site leak and the patient died after four days of hospital stay. The other patients with RVI and CLD developed post-operative collection, wound dehiscence and HAP; both of them died at nine and eleven days of hospital stay. The patient with asthma developed SSSI; he was discharged improved after nine days of hospital stay. Only the patient with CHF was discharged without complications.

A total of 9 patients (6.6%) died at the hospital postoperatively. MOF secondary to severe sepsis was the most common cause of mortality (88.9%). Old age, comorbid illness, tachycardia and development of post-operative complications were significantly associated with mortality.

The mean age of the mortality group (52±14.2 years) was higher than the survivors (mean 34.9 ±16 years). The average age of patients with mortality was significantly higher (P=0.04).

Among the nine patients who died postoperatively, three patients (33.3%) had comorbidities (P=0.001). Except for one, all patients who died (88.9%) had postoperative complications (P=0.001). Even though late presentation (>24hrs) had no statistically significant association with mortality (P=0.36), 66.6% of the deaths occurred on patients who presented 24 hours after the onset of symptoms. Hypotension and perforation size has no statistically significant association with mortality (Table 3).

All the complications except superficial surgical site infections were significantly associated with mortality. Around 6(86%) of the patients with acute kidney injury, 4(50%) with repair site leak and 7(43.8%) who developed hospital-acquired pneumonia died (P=0.000, 0.002, 0.000 respectively) (Table 4).

The postoperative hospital stay of the patients with complications was 18.6 ± 14.7 days which is significantly higher than that of the patients without complication 6.7±2.7 days (P=0.001).

Table 3: Factors associated with Mortality among patients operated for perforated peptic ulcer disease at St. Paul Hospital Millennium Medical College, Addis Ababa, Ethiopia from January 2013 to December 2017

| | | Total No.(%) | Death No.(%) | Discharged Improved No.(%) | P-Value |
|--------------------|----------------|--------------|--------------|----------------------------|---------|
| Comorbid Illness | Yes | 5(3.7) | 3(60.0) | 2(40.0) | 0.001 |
| | NO | 131(96.3) | 6(4.6) | 125(95.4) | |
| Pre-operative stay | <24 hours | 65(47.8) | 3(4.6) | 62(95.4) | 0.36 |
| | >24 hours | 71(52.2) | 6(8.5) | 65(91.5) | |
| Pulse Rate | >100 beats/min | 87(64.0) | 9(10.3) | 78(89.7) | 0.02 |
| | <100 beats/min | 49(36.0) | 0 | 49(100) | |
| Systolic BP | <90mmHg | 18(13.2) | 3(16.7) | 15(83.3) | 0.066 |
| | >90mmHg | 118(86.7) | 6(5.1) | 112(94.9) | |
| Morbidities | Yes | 31(22.8) | 8(25.8) | 23(74.2) | 0.001 |
| | No | 105(77.2) | 1(1.0) | 104(99.0) | |

Table 4 Association between postoperative complications and mortality among patients operated for perforated peptic ulcer disease at St. Paul Hospital Millennium Medical College, Addis Ababa, Ethiopia from January 2013 to December 2017

| Complications | | | Total No.(%) | Death No.(%) | Discharged Improved No.(%) | P-Value |
|--------------------------------|-----|------|--------------|--------------|----------------------------|---------|
| Acute Kidney Injury | Yes | | 7(5.1) | 6(85.7) | 1(14.3) | 0.000 |
| | No | | 129(94.9) | 3(2.3) | 126(97.3) | |
| Superficial Surgical Infection | Yes | Site | 20(14.7) | 3(15.0) | 17(85.0) | 0.103 |
| | No | | 116(85.7) | 6(5.2) | 110(94.8) | |
| Wound Dehiscence | Yes | | 10(7.4) | 3(30.0) | 7(70.0) | 0.002 |
| | No | | 126(92.6) | 6(4.8) | 120(95.2) | |
| Post-Operative Collection | Yes | | 12(8.8) | 3(25.0) | 9(75.0) | 0.007 |
| | No | | 124(91.2) | 6(4.8) | 118(95.2) | |
| Repair Site Leak | Yes | | 8(5.9) | 4(50.0) | 4(50.0) | 0.002 |
| | No | | 128(94.1) | 5(3.9) | 123(96.1) | |
| Hospital Acquired Pneumonia | Yes | | 16(11.8) | 7(43.8) | 9(56.2) | 0.000 |
| | No | | 120(88.2) | 2(1.7) | 118(98.3) | |

DISCUSSION

We found that males were affected 5.5 times higher than females by PPU disease. This is consistent with several other studies done locally and in Africa which found a variable male predominance, 7.2, 6.6, 1.3 and 9 times in Black Lion Hospital (BLH), Zewditu Memorial Hospital (ZMH), Tanzanian and Nigerian studies respectively (5,6,7, 8). However this is contrary to the common depiction in western series as a disease of the elderly female (9).

In this study, 52.2% of the patients presented after twenty-four hours of onset of symptoms. Other studies done in Tanzania, BLH and ZMH found similar delayed presentations, where more than 35%, 95% and 92.1% of the patients presented after 48 hours respectively (4,5,6). This can be due to lack of nearby healthcare facilities since around half of our patients were from rural areas. It can also be due to lack of skill by health professionals to detect peritonitis early.

Our study has found that delayed presentation has significantly affected patients' outcomes. All of the patients with systolic BP < 90 mmHg had come after 24 hours of the onset of symptoms, and 44% of them developed complications ($P=0.019$). Thirty five percent of patients who presented after 24 hours of their illness developed postoperative complications as compared to only 9% of patients who presented within the first 24 hours ($P=0.000$). Two third (66.6%) of the deaths occurred on patients who presented within 24 hours after the onset of symptoms. Similar studies done in Turkey, Singapore and Ivory Coast also showed presentation after 24 hours of the onset of symptoms increased both post-operative complications and mortality (10,11,12).

In our study, duodenal ulcer perforations were 8 times more common than gastric ulcer perforations. This is comparable to studies done in Tanzania, ZMH, and Singapore, which reported a duodenal to gastric ulcer ratio of 12.7:1, 8.5:1, 7.7 respectively. Another study done Iru, Nigeria, found that gastric ulcer perforations were two times more common than duodenal ulcer perforations (4,6,11,13). We could not explain this disparity.

We have found that a subhepatic drain was left for 61.8% of the patients. Another similar study conducted in India showed that post-operative wound infection, wound dehiscence and intraperitoneal collection were significantly lower in the no-drain group as compared to drain groups. There was no significant difference between the no-drain and drain groups with respect to the postoperative intra-abdominal sepsis, leak, and mortality. Drain-related complications were recorded in 36.8% of the patients with tube drain(s) (14). Other studies had also shown that drain placement increases the risk of infection by 10% and does not decrease the rate of intra-abdominal abscess (40% with drains vs 34% without drains), nor the rate of suture line leak (15).

The overall complications rate in this series was 22.8% which is comparable to other African studies, 27.5% in Côte d'Ivoire and 29.8% in Tanzania. The complication rate in some western series is found to be higher than this (around 35% in a German study). This can be due to the fact that most western PPU patients were older, and definitive ulcer surgeries were done more

frequently. In our study and the other African studies mentioned above, none of the patients had definitive ulcer surgery (4,16).

Being female, presence of comorbidity, hypotension with SBP < 90 mmHg, tachycardia, and delayed presentation of > 24 hours were significantly associated with postoperative morbidity in our study ($P < 0.05$). Similarly, studies done in Tanzania and Côte d'Ivoire showed delayed presentation (> 24 hours), systolic BP < 90 mmHg at admission, and presence of comorbid illnesses had increased complication rate (4,12).

The mortality rate in our study was 6.6%, which is lower than other studies done in Tanzania (10.7%), BLH (19%), India (14%), Germany (13%), Nigeria (17.3%) and America (10.6%) (4,5, 8,16,17,18). Younger patients and the lower number of patients with comorbidity in this study can explain this. In our study, only 3.7% of the patients had a comorbid illness and 91.1% of the patients were younger than 60 years. A study conducted in Norway had shown that in PPU patient's age ≥ 60 years increases postoperative mortality by more than 50-fold (19).

Our study showed that patients that are old age, with comorbidity, late presentation, and who developed complications had a higher rate of mortality. The study done by Phillip L in Tanzania had a similar finding (4).

The postoperative hospital stay of the patients with complications is 24.16 ± 26 days which is significantly higher than that of the patients without complication 6.7 ± 22 days ($P=0.001$). A similar finding was in the study conducted at ZMH, patients with post-operative complications have significantly increased hospital stay (24 days) as compared to patients without complication (6.7 days) (6). Another study conducted at SPHMMC to assess the pattern of general surgery admissions showed that the average total hospital stay for emergency patients was 7.08 days, which is 3.4 times lower than the hospital stay of the patient with complications (20).

Generally, among the analyzed parameters, old age, being female, presence of comorbidity, hypotension, tachycardia, and delayed presentation were significantly associated with postoperative morbidity. Postoperative mortality was significantly associated with old age, comorbid

illness, tachycardia, and development of post-operative complications.

As this is a retrospective study, all the limitations of such type of study should be expected. Also, some of the patients lacked properly registered data and complete investigations.

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