

Original Research Article

Morbidity and mortality in peptic ulcer perforations-an insights from a tertiary care center in upper Assam, India

Bidya Sing Bey, Kewithinwangbo Newme*, Raguangjienglungle Newme, Keyikawangbo Newme

¹Department of General Surgery, Diphu Medical College & Hospital, Diphu, Assam, India

²Department of General Surgery, All India Institute of Medical Sciences (AIIMS), Guwahati, India

³Department of Obstetrics & Gynaecology, Diphu Medical College & Hospital, Diphu, Assam, India

⁴Department of Orthopaedics, Guwahati Medical College & Hospital, Guwahati, Assam, India

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*Correspondence:

Dr. Kewithinwangbo Newme,

E-mail: adinewme@gmail.com

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ABSTRACT

Background: Perforated peptic ulcer (PPU) is a severe and feared complication, presenting as an acute abdomen. While acid-reduction medications have contributed to a decline in perforated peptic ulcer cases. Although the incidence persists in a few rural regions in our North-East part of India. PPU significantly increases morbidity and mortality of patients. Early recognition can prevent mortality associated with delayed presentation.

Methods: In the prospective observational study, 73 patients were evaluated. A detailed clinical history and examination were performed. The data was analysed using descriptive analysis(n, number of patients, in percentage % and p-value)

Results: A significant increase in morbidity and mortality associated with age($p=0.03$, $p=0.001$), shock ($p=0.005$, $p=0.0001$), ASA ($p=0.0001$, $p=0.0001$), peritoneal contents ($p=0.005$, $p=0.001$), associated illnesses ($p=0.03$, $p=0.001$) and time of surgery ($p=0.04$, $p=0.01$) was observed respectively.

Conclusions: The study highlights the significance of specific parameters in managing peptic ulcer perforation, which typically presents as an acute abdomen.

Keywords: Acute abdomen, Perforated peptic ulcer, Peptic ulcer

INTRODUCTION

Perforated peptic ulcer is one of the causes of acute abdomen. 'Acute abdomen' means-an acute attack of abdominal pain that occurs suddenly or gradually over several hours and presents a symptom complex that suggests a disease that potentially threatens life and demands an immediate or urgent diagnosis and early treatment.¹ Perforation occurs in 2–10% of patients with Peptic ulcer disease (PUD).² As per the literature, the complication is more common with increasing age.³ The majority of perforations, 60% typically occur on the anterior wall of the duodenum, while a significant proportion also occur in antral (20%) and lesser-curvature

gastric ulcers (20%).⁴ Moreover, it continues to inflict high morbidity and mortality (5%-25%).⁵ The main factors responsible for the development of peptic ulceration include cigarette smoking and the use of NSAIDs. It is now widely acknowledged that *Helicobacter pylori* (*H. pylori*) infection is the primary contributing factor to the development of peptic ulceration.⁶ There has been a marked decrease in elective surgery for peptic ulcer disease following the introduction of medical therapies including H₂-receptor antagonists and more recently proton pump inhibitors with or without antibiotics for *H. pylori* eradication.⁶ Despite advances in treatment, the incidence of perforation appears to remain unchanged and even in

some cases, it rises, particularly among older age group patients.^{7,8} In developing countries, the majority of patients are young males who often delay seeking medical attention and there is a strong association between the condition and smoking habits.⁹ Mortality rates are impacted by a combination of factors, including patient age and sex, ulcer location, initiation of early treatment, presence of concurrent diseases, preoperative shock and anaesthesia type. Notably, several of these factors are interrelated, with treatment delays being a significant contributor to increased mortality.¹⁰

Elderly patients are more likely to experience delayed pre-treatment and age has been shown to have a direct correlation with increased mortality.¹¹ Although numerous studies have investigated perforated peptic ulcers, the understanding of factors influencing postoperative morbidity and mortality still remains incomplete. Nevertheless, advancements in disease understanding, resuscitation methods and prompt surgery under modern anaesthesia hold promise for significantly reducing morbidity and mortality rates.

Here in the study the impact of various factors on morbidity and mortality of patients with PPU are analysed and presented in suitable representations.

METHODS

Study design

A prospective observational study.

Study place

The prospective observational study was conducted in the Assam Medical College, a Tertiary Care Centre of Upper Assam, India.

Study duration

This hospital-based study was conducted over a two-year period from 2021 to 2023.

Population

All patients presenting to the emergency department with suspected perforation were screened, and intraoperatively confirmed cases of gastric or duodenal perforation were included in the study.

Sample size

Patients who presented to the emergency department with clinical symptoms and imaging-confirmed perforation within the two-year study period were included.

Sample technique

Consecutive sampling was used as the study technique.

The Institute Ethics Committee (IEC) approval was taken for the study.

Study participants

The study included patients who met the following criteria.

Inclusion criteria were patients diagnosed with duodenal or gastric perforation due to peptic ulcer disease. Exclusion Criteria were a) Patients with perforations in the jejunum, ileum or Meckel's diverticulum b) Pediatric patients (≤ 14 years old) with peptic ulcer disease c) cases of perforation due to stomach cancer d) Patients with traumatic perforations e) Patients are managed with conservative treatment.

Diagnosis and study parameters

The X-ray imaging was done to detect hollow viscus perforation and then during the intraoperative period (Figure 1), the perforation site, i.e., gastric or duodenum, was confirmed. The proper history and clinical examination were conducted during the presentation in the outpatient and emergency departments. The patients data (history and investigations) were collected at the time of presentation and during follow-up for 6 months.

The study analyzed various parameters, i.e., demographic profile, smoking, alcohol, NSAID intake, shock, peritoneal contents, site of perforation, co-morbidities, history of PUD and postoperative complications, which may influence the morbidity (the condition of being unwell due to a disease or disorder i.e., wound infection, respiratory infection, renal failure, cardiac failure etc.) and mortality in patients presented with a perforated peptic ulcer (PPU). It also assessed the importance of the time frame for surgery and the American Society of Anesthesiologists (ASA) grading regarding the outcome of surgery in a tertiary Center.

Statistical analysis

Statistical analyses were carried out by using the Software Statistical Package for Social Sciences (SPSS) for MacOS (version 26.0, IBM Corp., Armonk NY). All categorical variables were summarized as absolute frequencies i.e., number of patients (n) and percentages (%), while the p-value, was based on the normal or non-normal distribution. Differences were considered significant when $P < 0.05$.

RESULTS

A total of 81 patients were presented with hollow viscus perforation, but 8 patients were not included in the study due to other etiologies, incomplete data and not satisfying an inclusion criterion. The 73 patients were analyzed; accordingly, the clinico-demographics profile was presented in terms of the number of patients (n),

percentages (%) and p value. It was observed that postoperative morbidity and mortality were seen more in elderly patients. In our study 7 patients were above 65 years and out of them, 3 (42.8%) expired and 6 (85.7%) experienced post-operative morbidity. Good post-operative recovery (patient recovering without any complication) was observed to be better in younger age groups, with a good recovery of 82.4% in the 15 -24 age group (Table 1 and 2). Perforated peptic ulcers were more common in males compared to females. In the present study, out of 73 cases, 62 (84.9%) were males and 11 (15.1%) were females with a male: female ratio of 5.6:1.

In the study, 10 (13.7%) patients had a history of regular use of NSAIDs. It was observed that NSAID use was more common in the elderly age group, with 8 of our patients above 39 years of age. The other two were both 22 years old. One of them gave a history of regular intake of NSAID for body ache, as he was a manual laborer. 3 patients developed post-operative complications in patients with a history of NSAID use, but no mortality was noted. Morbidity and mortality rates of 28.6% and 14.3%, respectively, were observed in patients with no history of NSAID use.

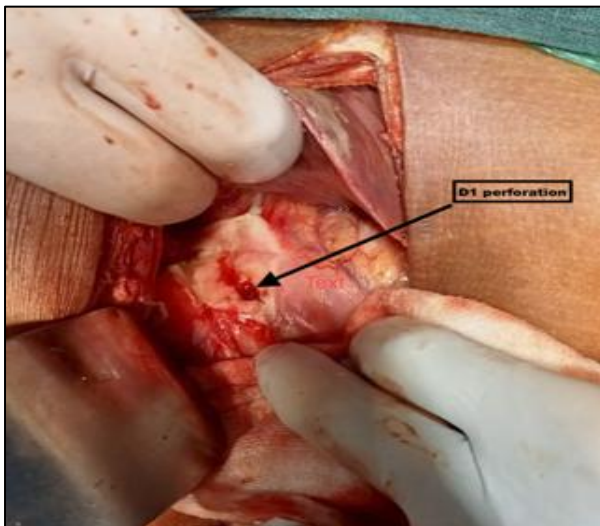


Figure 1: A perforation in the first part of the duodenum.

Among the patients, 35 (48%) had a history of regular smoking. Of these, 10 (28.7%) experienced postoperative complications and 5 patients died postoperatively. In non-smokers, the morbidity and mortality rates were 28.9% and 10.5% respectively. A history of regular alcohol consumption was noted in 31 patients (42.5%), where 7 patients (22.6%) subsequently developed postoperative complications and 1 patient (3.2%) unfortunately expired during the postoperative period.

For those patients who did not have a history of regular alcohol intake, the morbidity and mortality were 33.3% and 10.9% respectively. 7 patients (9.6%) had associated co-morbid conditions. Hypertension was present in 3

patients; 3 patients were known to be asthmatic and 1 patient had a history of Congestive Heart Failure (CHF). 6 patients developed postoperative complications and 3 patients expired in the postoperative period. The morbidity (22.7%) and mortality (9.1%) rate in patients with no associated illness was found to be lower compared to those with associated illness.

Of the total patients, 50 (69%) underwent surgery more than 24 hours after perforation, while the remaining patients received surgery within 24 hours. Among those with delayed surgery, 19 (38%) developed postoperative complications and 9 (18%) succumbed to their condition. In those patients who were operated within 24 hours from onset of symptoms, there was no mortality; only 2 (8.7%) patients developed post-operative complications. Upon admission, 23 patients (31.5%) presented with shock, defined as a systolic blood pressure of 90mmHg or less. This subgroup experienced a high incidence of postoperative complications (73.9%, n=17) and mortality (30.4%, n=7) during the postoperative period. However, in hemodynamically stable patients, we observed low morbidity (8%) and mortality (4%) rates. A prior history of dyspepsia or peptic ulcer symptoms was noted in 26 individuals, constituting 36% of the total 73 participants patients. 11 (42.3%) patients developed post operative complications and 4 (15.4%) patients expired. In those patients without a history of PUD, the morbidity and mortality were found to be 21.3% and 10.6% respectively.

The preoperative American Society of anesthesiologists (ASA) grade was evaluated for all patients in collaboration with anesthesiologists. The distribution of ASA grades was as follows: Grade II: 43 (58.9%), Grade III: 23 (31.5%), Grade IV: 7 (9.6%). Notably, the incidence of morbidity and mortality increased with higher ASA grades: ASA Grade II: 1 (2.3%) morbidity, 0% mortality, ASA Grade III: 13 (56.5%) morbidity, ASA Grade IV: 7 (100%) morbidity, 100% mortality. On exploration 55 (75.3%) patients had bilious peritoneal collection and 18 (24.7%) were purulent. Out of 55 patients who had bilious peritoneal collection 10 (18.2%) developed post-operative complications and 3 (5.5%) patients expired during the postoperative period. Of the 18 patients with the purulent peritoneal collection, 11 (61.1%) developed post-operative complications and 6 (33.3%) patients expired post-operatively.

In the study, 69 (94.5%) had duodenal perforations and 4 (5.5%) had gastric perforation. Out of 69 patients who had duodenal perforations, 21 (30.4%) patients developed post-operative complications and 9 (13.04%) patients expired post-operatively. 21 (28.8%) patients developed post-operative complications.

The most common postoperative complication was wound infection-found in 11 patients (33.3%), followed by septicemia in 9 (27.3%), respiratory failure in 6 (18.2%), renal failure in 3 (9%) and coronary artery

disease in 1 (3%) patient, (Table 3). In the present study, sepsis was found to be the most common cause of

mortality accounting for 66%, followed by respiratory failure (22.2%) and renal failure (11.1%).

Table 1: The relations of variables and morbidity /mortality in number of the patients, percentage of the patients and p value respectively.

Parameter		Total number N (%)	Morbidity N (%)	Mortality N (%)	P value (Morbidity)	P value (Mortality)
Sex	Male	62 (85)	16 (25.8)	6 (9.7)	0.12	0.27
	Female	11 (15)	5 (45.5)	3 (27.3)		
Age in years	<65	66 (90)	15 (23.1)	6 (9.1)	0.03*	0.001*
	≥65	7 (10)	6 (85.7)	3 (43)		
NSAID intake history	Present	10 (13.7)	39 (30)	0 (0)	0.34	-
	Absent	63 (86.3)	18 (28.6)	9 (14.3)		
H/O smoking	Present	35 (48)	10 (28.7)	5 (14.3)	0.72	-
	Absent	38 (52)	11 (29)	4 (10.5)		
H/O Alcohol	Present	31 (43)	7 (22.6)	1 (3.2)	0.06	0.43
	Absent	42 (58)	14 (33.3)	8 (19.1)		
Associated illness	Present	7 (9.6)	6 (85.7)	3 (43)	0.03*	0.001*
	Absent	66 (90.4)	15 (22.7)	6 (9.1)		
Time of surgery	<24	23 (32)	2 (8.7)	0 (0)	0.04*	0.01*
	≥24	50 (69)	19 (38)	9 (18)		
Shock	Present	23 (32)	17 (73.90)	7 (30.4)	0.005*	0.0001*
	Absent	50 (69)	4 (8)	2 (4)		
H/o PUD	Present	26 (36)	11 (42.3)	4 (15.4)	0.71	0.06
	Absent	47 (64.4)	10 (21.3)	5 (10.6)		
ASA	I	0	0 (0)	0 (0)	0.0001*	0.0001*
	II	43 (59)	1 (2.3)	0 (0)		
	III	23 (32)	13 (53.5)	2 (8.7)		
	IV	7 (9.6)	7 (100)	7 (100)		
Peritoneal content	Bilious	55 (75.3)	10 (18.2)	3 (5.5)	0.005*	0.001*
	Purulent	18 (24.7)	11 (61.1)	6 (33.3)		
Site of perforation	Duodenal	69 (94.5)	21 (30.40)	9 (13)	-	-
	Gastric	4 (5.5)	0 (0)	0 (0)		

H/O- history of, PUD-peptic ulcer disease, ASA- American Society of Anesthesiologists, *signify the significant difference of the parameters for morbidity and mortality of the patients.

Table 2: Shows age-related morbidity and mortality in patients with perforated peptic ulcer.

Age group (in years)	Number of cases	Good recovery N (%)	Morbidity N (%)	Mortality N (%)
15-24	17	14 (82.4)	3 (17.4)	2 (11.8)
25-34	8	4 (50)	4 (50)	2 (25)
35-44	10	9 (90)	1 (11.1)	0
45-54	21	18 (85.7)	3 (14.3)	1 (4.8)
55-64	10	6 (60)	4 (40)	1 (10)
>65	7	1 (14.3)	6 (85.7)	3 (42.8)

Table 3: Postoperative complications and cause of mortality in patients with perforated peptic ulcer.

Complications	Number (N)	(%)	Cause of mortality N (%)
Wound infection	11	33.33	-
Septicaemia	9	27.27	6 (66)
Respiratory failure	6	18.2	2 (22.2)
Renal failure	3	9.09	1 (11.1)
Wound dehiscence	3	9.09	-
Coronary artery disease	1	3.03	-

DISCUSSION

Peptic ulcers are localized lesions in the stomach or duodenum lining that penetrate into the submucosa or deeper tissues. These ulcers can be acute or chronic in nature and their development is ultimately attributed to a disruption in the delicate balance between the protective mechanisms of the mucosa and the damaging effects of stomach acid and digestive enzymes. The pathogenesis of peptic ulceration is multifactorial, but increasingly understood to be a consequence of *H. pylori* infection.¹²

PPU is a serious complication of peptic ulcer disease, posing a significant risk of severe and potentially life-threatening consequences. Although the treatment of PUD is conservative usually with medication, despite a decline in the overall incidence of peptic ulcer disease in recent decades, the rate of complications has remained steady.¹⁰ Peptic ulcer perforation is common in the second and third decades.¹³ Kim et al in their study for analysis of risk factors for postoperative morbidity in perforated peptic ulcer stated that age above 60 years is a significant factor affecting the morbidity.¹⁴ In our study, a notable 9.6% of our patients were elderly above (65 years). This age group exhibited significantly higher complications and mortality compared to younger counterparts (Table 1).

In a study by Taş et al with a ratio of 6.8:1.¹⁵ In the study, 85% were males, 15% were females and the male-to female ratio was 5.6:1. Male predilection is higher in various works of literature. The literature has reported conflicting data concerning the impact of gender in terms of surgical mortality and morbidity. A 2015 study in Turkey found that female patients had a significantly higher mortality rate compared to their male counterparts. However, they did not find the same in the case of morbidity.¹⁶ Following the study by Chalya et al, the present study showed no significant sex-related mortality (p value is 0.129) and morbidity (p value is 0.27) in operated cases of perforated peptic ulcer.¹⁷

In contrast to other studies, the present study found a relatively low incidence of NSAID use among the patients. Consistent with previous research, the present study also found no evidence that a history of NSAID use influences morbidity and mortality rates.¹⁷ Smoking is a causal factor for ulcer perforation. Smokers have a three-fold higher mortality rate from peptic ulcer than non-smokers.¹⁸ Marsoumi et al determined that smoking influences the mortality in operated cases of the perforated peptic ulcer.¹⁹ However, on the contrary, another study by Noguera et al did not find regular smoking to influence morbidity and mortality.²⁰ Operative delays exceedingly more than 24 hours significantly escalate mortality and morbidity rates. The duration of perforation is directly correlated with the risk of postoperative complications and death.^{20,21} Here, in our set-up as a Tertiary center, we encountered most of the patients referred from peripheral hospitals and a few

neglected cases were on the part of patients and attendants. Hemodynamic instability and purulent peritoneal collection were seen in delayed cases, which contributed to higher mortality (18%) and morbidity (38%). The long-standing perforation (≥ 24 hours) was an important risk factor for postoperative morbidity and mortality following a perforated peptic ulcer. ASA scores proved to be a reliable predictor of mortality in the management of perforated peptic ulcers. Notably, higher ASA scores (III and IV) were associated with increased mortality. Each incremental increase in ASA score corresponded to a 2-fold rise in morbidity and a 4.5-fold increase in mortality.²¹ In our study, there were 100% and 8.7% mortality in patients with ASA Grade 4 and 3 respectively with a p-value of 0.0001 which is statistically significant.

Most of the studies showed that wound infection is the most common complication, followed arbitrarily by respiratory infection, septicemia, wound dehiscence, renal failures, development of coronary artery disease and death.^{17,22} The present study found that most postoperative complications (about 34%) occurred on the 4th postoperative day. 61.9% of patients were above 50 years of age. 90.1% of complicated patients presented to the hospital after 24 hours of the onset of symptoms. Post-operative complications were seen in 21 patients. The most common complication was wound infection (33.3%) followed by septicemia (27.3%), respiratory failure (18.2%), renal failure (9.09%), wound dehiscence (9.09%) and newly diagnosed coronary artery disease (3.03%) (Table 2).

Out of 73 patients operated for perforated peptic ulcer, 9 (12.3%) patients expired in the post-operative period. It was observed that most of the patients (66.7%) expired within the 5th postoperative day. In the present study, sepsis was found to be the most common cause of mortality accounting for 66%, followed by respiratory failure (22.2%) and renal failure (11.1%). Works of literature suggest a strong association between regular alcohol consumption and peptic ulcer complications. However, a history of regular alcohol consumption does not influence the outcome of surgery in perforated peptic ulcers.^{17,20,21,23} The present study did not find the history of regular alcohol consumption to influence postoperative morbidity and mortality.

There are studies indicating that associated premorbid illness influences the outcome of patients with PPU.^{19,20,24} Similarly, we identified that our patients who had concomitant diseases had higher morbidity and mortality rates. In the present study, associated premorbid illness was documented in 7 patients (9.6 %). 3 patients who developed a postoperative wound complication had a previous history of chronic obstructive pulmonary disease. A possible explanation for the development of wound-related complications could be the reduced tissue oxygenation resulting in damage to the post-surgical wound healing process.

There is no history of previous PUD in approximately 64% and those with a known history often received irregular treatment. Although the existing literature reported that about 60% of cases had a previous history of peptic ulcer disease.²⁵⁻²⁷ Our study revealed that 64.4% of patients with perforation had no prior diagnosis or treatment for PUD. This lack of prior diagnosis significantly increases the risk of PPU. A likely explanation is that patients with a known history of ulcers are more likely to take preventative measures and seek medical attention sooner, thereby reducing their risk of complications.¹⁹ The present study also did not find previous history of peptic ulcer disease, to influence the morbidity (p value 0.06) and mortality (p value 0.7) in perforated peptic ulcer.

The presence of shock on presentation increases mortality.²¹ Tas et al in their study, did not identify any association between the presence of shock and morbidity. However, the presence of shock on admission and pre-operative period is an important risk factor to influence the mortality rate if associated with a medical disease.^{15,28} If shock is not corrected properly preoperatively, it reflects on mortality but not on morbidity.²⁹ In this study, shock upon admission was defined as a systolic blood pressure of 90 mmHg or less. The results showed that patients admitted in shock had significantly higher morbidity and mortality rates.

The morbidity (61.11% vs. 18.2%) and mortality rate (33.3% vs 6.8%) in patients with purulent and bilious peritoneal collection, respectively, were statistically found to be significant. 33.3% of patients with purulent peritoneal collection expired, whereas in those with bilious peritoneal collection, the mortality rate was 5.5%. Similarly, 61.11% of patients with purulent peritoneal collection developed complications as compared to 18.18% in patients with bilious peritoneal collection (Table 1).

However, Arveen et al and Hannan et al did not find any significant association between the nature of peritoneal contamination and postoperative complications.^{24,29} However, the present study found the nature of peritoneal collection to influence the morbidity and mortality in perforated peptic ulcers with a p value of 0.0018 and 0.0055, respectively. This finding may be due to the fact that purulent peritoneal collection is usually found in the late stage of perforation with associated septicemia and shock attributing to the high morbidity and mortality rate. As the institute is a tertiary medical college, most of our patients (68.5%) presented to our college more than 24 hours i.e., mostly from peripheral villages, from the onset of symptoms with associated shock, attributing to the high mortality and morbidity rate. Thus, the type of peritoneal collection as a cause of high mortality and morbidity needs further evaluation and there is further scope for study.

The study has certain limitations in that the sample size is small, as the patients suffering from complications of peptic ulcer diseases is declining due to the indiscriminate use of Proton Pump Inhibitor medication. Nevertheless, the study in its scope has identified several prognostic markers that may aid in the management of PPU.

CONCLUSION

The study revealed that delayed hospital admissions (beyond 24 hours and most of them were referred from remote centres) and patients with shock significantly increase morbidity and mortality rates. Additionally, advanced age, shock, higher ASA grades, pre-existing disease and purulent peritoneal collection also substantially impact outcomes for emergency perforated peptic ulcer surgeries. Consequently, healthcare providers in peripheral centres should maintain a high index of suspicion for PPU in acute abdomen cases until proven otherwise while prioritizing timely resuscitation and referral to specialized centres to optimize patient outcomes and, at the same time, prognostication considering the above-mentioned factors.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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