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Original Research Article

Factors affecting morbidity and mortality in peptic ulcer perforation

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ABSTRACT

Background: Peptic ulcer disease is very common disease in developing countries and so are its complications. With the introduction of H_2 receptor antagonists and proton pump inhibitors, the incidence of elective surgery for peptic ulcer (PU) disease has decreased dramatically, although complications of peptic ulcer disease such as perforation and bleeding have remained fairly constant.
Methods: A prospective study was conducted on43 patients presenting to KIMS Hospital, Hubli with features suggestive of hollow viscus perforation and intraoperative findings suggestive of peptic ulcer perforation from January 2015 to June 2016.
Results: In this study, there were 43 cases of peptic ulcer perforation. Peptic ulcer perforation was common in third decade of life(n=12) with the mean age(SD) 39.88 years. Perforation is more common in males as compared to the female population 7.6:1. Post-operative morbidity is seen in 31 (72.1%) of patients and mortality in 4 (9.3%). Smoking, Alcohol beverage consumption, regular ingestion of NSAIDs were commonly seen in patients with peptic ulcer perforation but these factors were not significant risk factors for postoperative mortality and morbidity. Age ≥60 years (p-value 0.051), Female gender (p-value 0.012), Presence of co-morbid conditions (p-value 0.055), Shock on admission (p-value 0.029, perforation-surgery interval >24 hours (p-value 0.001), preoperative higher-grade ASA, purulent intraperitoneal collection (p-value 0.002) were statistically significant predictors of mortality.
Conclusions: Perforated peptic ulcer (PPU) is a life-threatening disease with historically reported high morbidity and mortality rates. Age ≥60 years, female gender, presence of co-morbidities, preoperative shock, higher ASA grade, perforation-surgery interval >24 hours, Purulent intraperitoneal collection are inter-related statistically significant predictors of mortality. Therefore, proper resuscitation from shock, improving ASA grade and decreasing delay in surgery is needed to improve overall results.

Keywords: Morbidity, Mortality, Peptic ulcer, Perforation-surgery interval, Risk factors

INTRODUCTION

Perforated peptic ulcer is one of the most common surgical emergencies in South India.[1] Peptic ulcers occur due to mucosal damage and subsequent ulceration due to increased aggressive factors, decreased protective factors, or both.[2,3] The estimated prevalence of peptic ulcer disease in the western population ranges from 5 to 15%, with a lifetime incidence of almost 10%.[2]

With the introduction of H_2 receptor antagonists and proton pump inhibitors, the incidence of elective surgery for peptic ulcer (PU) disease has decreased dramatically, although complications of peptic ulcer disease such as perforation and bleeding have remained fairly constant.[4] However, there has been a considerable change in the epidemiology of perforated peptic ulcer in the west over the last two decades. Daniel TD mentions that the three most common complications of peptic ulcer disease, in

decreasing order of frequency, are bleeding, perforation and obstruction.[5,6]

Perforation remains a major life-threatening complication. The current treatment of perforated peptic ulcer is surgical repair. It has the highest mortality rate of any complication of ulcer disease.[2,6] Therefore, early identification of perforated peptic ulcer patients with a high risk of adverse outcomes following surgery is important for clinical decision-making. This can assist in risk stratification and triage, e.g. timing and extent of pre-operative respiratory and circulatory stabilization, post-operative admission to a high dependency unit (HDU), the level and extent of monitoring, and inclusion in specific perioperative care protocols.[1,4,7,8]

Duodenal, antral and gastric body ulcers account for 60%, 20% and 20% ulcers among the peptic ulcer perforations respectively.[9]

Mortality and morbidity following perforated peptic ulcer (PPU) are substantial, and mortality rates of up to 25-30% have been reported in population-based studies.[7] A large number of prognostic factors for morbidity and mortality following PPU have been reported, this study tries to analyze such factors affecting mortality and morbidity in patients with peptic ulcer perforation.

METHODS

A prospective study was conducted on 43 patients presenting to KIMS Hospital, Hubli with features suggestive of hollow viscus perforation and intraoperative findings suggestive of peptic ulcer perforation from January 2015 to June 2016.

Inclusion criteria

- All patients with duodenal or gastric perforations of peptic ulcer origin.
- Patients with peptic ulcer perforation of age more than 14 years
- Patients who undergo surgery for the management

Exclusion criteria

- Patients with perforation of peptic ulcer origin at jejunum, ileum adjacent to Meckel's diverticulum.
- Patients managed conservatively.
- Patients who underwent vagotomy with gastrojejunostomy with simple closure or partial gastrectomy or pyloroplasty.
- Paediatric patients of age <14 years presenting as peptic ulcer perforation.
- Patients presenting as recurrent perforation or stomas ulcer perforation.

A de Inclusion criteria tailed history of suspected patients of peptic ulcer perforation regarding age, sex, previous use of steroids or NSAIDs, smoking, alcohol intake, any active malignant disease and other associated illnesses was taken. The diagnosis was made on clinical findings supported by investigations like plain X-ray of the erect chest and ultrasound abdomen. Preoperatively ASA grading of patients and time frame of surgery were assessed, immediate resuscitation was done with nasogastric suction, intravenous fluids, antibiotics, and urine output monitoring. Patients with peptic ulcer perforation were operated as simple closure with Graham's omental patch. Patients were followed-up every day with continuous bedside monitoring of vital data in the immediate postoperative period and evaluated on daily ward rounds to note the development of any complications like wound infection, wound dehiscence, pleural effusion, paralytic ileus, septicemia, respiratory infections, renal failure etc., and appropriate treatment was instituted promptly according to the needs of the patients

After satisfactory improvement, patients were discharged from the hospital with counselling regarding diet, anti-ulcer drugs and quitting of smoking/alcohol etc.

A detailed structured proforma was used to collect this information. The results were discussed and compared with available published literature in the form of tables and charts.

Statistical methods

The data was entered in Microsoft excel and analyzed using Epi-Data analysis software. The continuous variables like age, serum creatinine value was expressed mean and standard deviation. The categorical variables like the site of perforation, perforation - surgery interval, gender, alcohol use, smoking status, tobacco use, PPI/H_2 blocker use, steroid use, ASA grade scoring, complications and outcome of surgery were expressed as proportions. The association between categorical variables such as age category, site of perforation, perforation surgery interval, gender, alcohol use, smoking status, tobacco use, PPI/H_2 blocker use, steroid use, ASA grade scoring, heart rate, creatinine category, pre-operative shock with complications (morbidity) and outcome of surgery (mortality) was tested using chi-square test. The p value of <0.05 was considered for statistical significance. Kaplan-Meier curve was used to denote the survival of the patient over a period of time.

RESULTS

The highest incidence was observed in the third decade of life (n=12). The youngest patient was 17 years old and oldest was 75 years old. The mean age (SD) of patient was 39.88 years. All the four patients who expired were >60 years of age. All the 8 patients in the age group ≥60 years had one or more postoperative complications. Perforation is more common in males as compared to the female population. The ratio in this study was 7.6:1.

Table 1: Comparison table.

Patient risk factors	Mortality (N=4)	P value	Morbidity (N=31)	P value
Age (years)				
≥60	4 (50)	1.000	8 (100)	0.051
<60	0(0)		23 (65.7)	
Gender				
Female	2 (40)	0.012	4 (80.0)	0.675
Male	2 (5.3)		27 (71.1)	
NSAID use of the study participants				
Yes	1 (5.9)	0.532	14 (82.4)	0.225
No	3 (11.5)		17 (65.4)	
PPI use of the study participants				
Yes	0 (0.0)	1.000	10 (71.4)	0.946
No	4 (13.8)		21 (72.4)	
Alcohol use of the study participants				
Yes	1 (6.7)	0.663	12 (40)	0.397
No	3 (10.7)		19 (67.9)	
Smoking habits of the study participants				
Smoker	2 (14.3)	0.663	9 (64.3)	0. 428
Non-smoker	2 (6.9)		22 (75.9)	
Tobacco habits of the study participants				
Tobacco user	1 (11.1)	0.836	3 (33.3)	0.213
Non-smoker	3 (8.8)		8 (23.5)	
Creatinine value				
≥1.5	1 (12.5)	0.730	7 (87.5)	0.281
<1.5	3 (8.6)		24 (68.6)	
Presence of preoperative shock				
Shock present	2 (33.3)	0.029	5 (83.3)	0.508
No shock	2 (5.4)		26 (70.3)	
Perforation-surgery interval (hours)				
≥24	2 (11.8)	0.653	17 (100)	0.001
<24	2 (7.7)		14 (53.8)	
Presence of co-morbidities				
Present	2 (28.6)	0.055	6 (85.7)	0.380
No	2 (5.6)		25 (69.4)	
ASA score				
2	0	1.000	26 (74.3)	0.314
3	0		2 (100)	
4	4 (66.6)		3 (50)	
Intraperitoneal collection				
Bilious discharge	0	1.000	3 (42.9)	0.002
Purulent	2 (9.1)		21 (95.5)	
Seropurulent discharge	2 (14.3)		7 (50)	
Heart rate of the study participants				
<100	1 (4)	0.730	19 (76)	0.595
101-140	3 (17.6)		11 (64.7)	
>140	0 (0)		1 (100)	
Site of the ulcers				
Proximal	4 (12.9)	1.000	22 (71)	0.791
Distal	0 (0)		9 (75.0)	
C-reactive protein				
Negative	3 (15.8)	0.193	16 (84.2)	0.115
Positive	1 (4.2)		15 (62.5)	

(N-number of patients with morbidity or mortality)

Out of 43 cases, we had 38 males and 5 female patients. Out of 5 female patients 2(40%) patients expired.

In this study 17(39.5%) patients had history of ingestion of NSAIDs. History of alcohol consumption was present in 15 (34.9) patients. History of regular smoking was present in 14(32.6%) and tobacco chewing in 9 (20.9%) patients. A previous history of dyspepsia or peptic ulcer symptoms was present in 14 (32.6) patients who were on H_2/PPIs.

Table 2: Outcome of surgery.

Outcome of surgery	Total no. of study participants N (%)
Discharged from hospital	39 (90.7)
Expired	4 (9.3)
Day 1 of surgery	1(25)
Day 2 of surgery	2 (50)
Day 12 of surgery	1 (25)
Total	43

Three patients (16.3%) had associated comorbid conditions. Hypertension and left ventricular hypertrophy in 1 patient, ischemic heart disease (IHD) in 1 patient. Both patients expired in the postoperative period.

At the time of admission shock (systolic BP less than 90) was present in 6(14%) patients. Out of 6 and other 5 developed postoperative complications and 2 patients expired in postoperative period.

Thirty-one (72.1%) patients had pre-pyloric perforation and 12(27.9%) patients had duodenal perforation. All the 4 patients who expired in postoperative period had pre-pyloric perforation, but site of perforation had no effect on outcome of the patient.

Out of 22 patients with purulent intraperitoneal collection, 21 developed postoperative complications and 2 expired in postoperative period. All 11 people who had wound complications in the postoperative period had a purulent intraperitoneal collection.

Eight (18.6%) patients had deranged RFT with raised serum creatinine values. Seventeen (39.5) patients underwent surgery after 24 hours of perforation, the rest were seen before 24 hours. All the patients 17(100%) who underwent surgery after 24 hours developed postoperative complications and 2 expired in postoperative period.

The smallest size of perforated ulcer seen in the study group measured subjectively by operating surgeon is 0.3cm^2 and the largest was 2cm^2. Size of perforation had no significance on mortality (p-value 0.738) and morbidity (p-value 0.093).

Preoperative ASA (American society of anesthesiologists) grade was assessed for all patients.35 (81.4%) were grade 2; 2(4.7%) were grade 3, and 6 (14.0%) were grade 4. Morbidity was 26 (74.3) in grade 2, 2 (100%) in grade 3 and 3 (50%) in grade 4. Out of 6 patients in ASA grade 3, 4 (66.6%) patients expired in postoperative period.

Out of 43 patients 31 patients had one or more postoperative complications. 13 patients needed ICU care out of which 9 patients required ventilator support in postoperative period. Elven patients had surgical site infection out of which 2 patients developed wound dehiscence. Eleven patients developed postoperative respiratory infection most common being pleural effusion. Seven patients had abdominal complications (Distension, loose stools, and pelvic collection). Two patients were diagnosed with cardiac comorbidity and both patients expired in postoperative period.

Out of 43 patients, 4(9.3%) expired in postoperative period (Table 2). In the analysis of 43 patients, age ≥60 years, (p-value 0.051); perforation- surgery interval >24 hours (p-value 0.001), purulent intraperitoneal contamination (p-value 0.002) were statistically significant predictors of morbidity.

Delayed surgery (after 24 hours), and purulent Intraperitoneal collection increased morbidity by 2 times. Female gender (p-value 0.012). Preoperative shock (p-value 0.029), presence of co-morbidities (p-value 0.055) were statistically significant predictor of mortality.

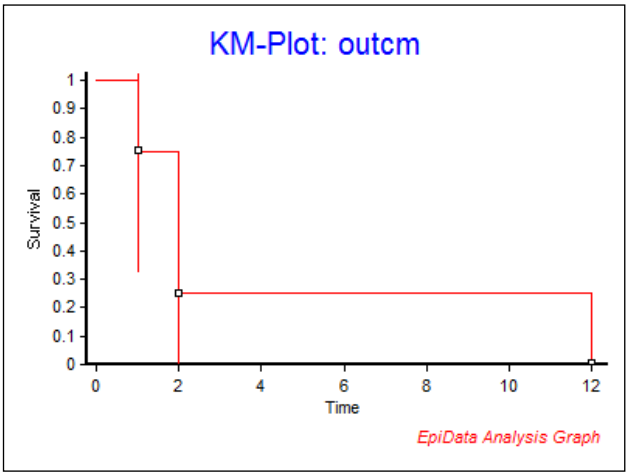

Figure 1: Survival curve for the death event and time since admission.

DISCUSSION

Although the incidence and hospitalization rate for PUD have been decreasing since the 1980s, it remains one of the most prevalent and costly GI diseases. The role of surgery in the treatment of ulcer disease has also decreased, primarily caused by a marked decline in elective surgical therapy for chronic disease because the percentage of patients who require emergent surgery for the complicated disease has remained constant.

Mortality and morbidity following perforated peptic ulcer (PPU) are substantial, and mortality proportions of 25-30% have been reported in population-based studies.[7]

While age is no bar for peptic ulcer perforation, we observed in present study that the youngest patient was 17 years and oldest was 75 years old. Peptic ulcer perforation was found to be most common in the fourth decade of life and accounted for 28% of the study population.[8,10,11]

The mean age of patients with peptic ulcer perforation in the study by Kocer et al was 43 years and in the study by Dakubo et al, it was 41 years.[10,11] However, Mishra et al in an Indian study showed a mean age of 39 years.[12] Recent studies like Moller et al and Thorsen et al showed that older age group patients (median age 71 and 67 years respectively) are most commonly affected.[7,13] The present study matches with studies by Mishra et al and Ranjusingh et al with a mean age of 39.8.[8,14] In 1987-Boeys and Wong found that age itself has no effect on patient's outcome, but they did find concurrent medical illness to have a significant detrimental effect.[15] This indicates that higher mortality in old age might be due to associated medical illness.

In present study population out of 43 cases, we had 38 male and 5 females patients with a ratio of 7.6:1 Present study results match with those of Kocer et al with a ratio of 8:1 and Boey et al with a ratio of 6.6:1.[10,15]

In present study 31(72.1%) patients had pre-pyloric perforation and 12(27.9%) patients had duodenal perforation with a ratio of duodenal perforation: Prepyloric perforation being 1:2.6. Present study result match with those of Kim JM et al with ratio of 1:2 and Tas et al with ratio of 1:2.1.[16,17] All the 4 patients who expired in postoperative period had pre pyloric perforation but site of perforation had no effect on outcome of the patient.

In a study by Testini et al, mortality was 9.8% in case of delayed surgery, whereas in the study by Kocer et al, it was 20% and in the study by Dakubo JC et al, it was 11.8% (Table 3).[10,11,18]

In a study by Testini et al, mortality was 55.6% in patients with shock on admission, whereas in the study by Kocer et al, it was 68.8% and in the study by Dakubo et al, it was 20.6% (Table 4).[10,11,18]

Four patients expired in present study, 2 of them had undergone surgery 24 hours after the onset of symptoms and 2 patients were in shock at the time of admission. In present study, mortality was 11.8% in patients who underwent surgery 24 hours after the onset of symptoms

and 33.3% in patients with shock on admission. Time of surgery and shock on admission significantly affected postoperative mortality as a 2 out of 4 of the patients who expired had undergone surgery 24 hours after onset of symptoms and 2 of them had shock on admission. Delay in surgery caused increased bacterial peritonitis and led to septicemic shock and deranged renal parameters in the postoperative period. In a study by İlhan Taş et al, the most common complication was wound infection. Mortality was observed in 18.2%.[17] The most common cause of mortality was sepsis.

In the study by Kocer et al, each increase in ASA score increased mortality by 4.5 times in their patients. In present study, there were only 4 deaths and all of them were ASA grade 4.[10] Hence ASA grade is a highly important predictor of postoperative mortality. This helps us to explain the amount of risk to the patient's attenders.

Table 3: Morbidity based on time of surgery and shock on admission in patients with PPU.

Study	Parameters		Time of surgery		Shock	
			<24 hrs	>24 hrs	Present	Absent
Kocer et al[10]	No. of patients		189	80	16	253
	Morbidity	No	30	35	15	50
		%	15.9	43.8	93.8	19.8
Dakubo et al[11]	No. of patients		118	136	34	220
	Morbidity	No	17	45	13	39
		%	14.4	33.1	38.2	17.7
Present study	No. of patients		26	17	6	37
	Morbidity	No	14	17	5	26
		%	53.8%	100%	83.3%	70%

Table 4: Mortality based on time of surgery and shock on admission in patients with PPU.

Study	Parameters		Time of surgery		Shock	
			<24 hrs	>24 hrs	Present	Absent
Testini et al[18]	No. of patients		41	108	9	140
	Mortality	No	5	11	5	1
		%	1.9	9.8	55.6	0.7
Kocer et al[10]	No. of patients		189	80	16	253
	Mortality	No	7	16	11	12
		%	3.7	20	68.8	4.7
Dakubo et al[11]	No. of patients		118	136	34	220
	Mortality	No	8	16	7	14
		%	6.8	11.8	20.6	6.4
Present study	No. of patients		26	17	6	37
	Mortality	No	2	2	2	2
		%	7.7%	11.8%	33.3%	5.4%

CONCLUSION

Perforated peptic ulcer (PPU) is a life-threatening disease with historically reported high morbidity and mortality rates. It is much more common in third decade and males as compared to females (7.6:1 in the present study).

Multiple studies showed evidence for an association between mortality and older age, comorbidity, and the use of medications such as Non-Steroid Anti-Inflammatory Drugs (NSAIDs), steroids and immunosuppressive agents. Further predictive factors associated with a poor prognosis included shock upon admission, pre-operative metabolic acidosis, tachycardia, elevated respiratory rate, acute renal failure, low serum albumin level, high ASA score, and a pre-operative time-delay >24 hours. Notably, several of the scoring systems proposed include one or several of these factors, but usually not all. Postoperative morbidity is seen in 31 (72.1%) of patients and mortality in 4 (9.3%). As per our mortality and morbidity analysis following risk factors are significant i.e. age ≥60 years, Female gender, presence of co-morbidities, preoperative shock, higher ASA grade, perforation-surgery interval >24 hours, purulent intraperitoneal collection. All these factors are inter-related.

Therefore, proper resuscitation from shock, improving ASA grade and decreasing delay in surgery is needed to improve overall results.

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