



## A prospective cohort study of patients with peptic perforation to identify high-risk clinical characteristics

Ahmed Ziarra Khalaf<sup>1,\*</sup>, Mazin A. Abdulla<sup>2</sup>, Ahmed AR Issa<sup>1</sup>

### ABSTRACT

**Introduction:** Peptic ulcer perforation is the most common complication in peptic ulcer disease and can lead to serious complications and mortality; however, despite the widespread use of antisecretory agents and eradication of *Helicobacter pylori*, the incidence of peptic ulcer perforation remains largely unchanged. This study aimed to evaluate the risk factors for perioperative morbidity and mortality in patients with peptic ulcer perforation.

**Methods:** This was a prospective, observational study involving patients with perforated peptic ulcer disease admitted to the Al-Basra Teaching Hospital from January 2017 to December 2019. A total of 100 patients were followed for 4 weeks. Patients' demographic data, history of chronic diseases, American Society of Anesthesiologist (ASA) score, nonsteroidal anti-inflammatory drug (NSAID) and steroid use, duration before surgery, preoperative shock status, previous symptoms of peptic ulcer disease, smoking habits, and fasting status were evaluated, and significant correlations with postoperative complications were analyzed statistically.

**Results:** A total of 100 patients aged 16–87 years were included in the study, and the male-to-female ratio was 3:1. Sixty-seven (67%) patients underwent surgery within 12 h after admission, 41% of patients had a history of chronic disease, 54% of patients had an ASA score of 1, 57% of patients were smokers, 45% of patients reported previous peptic ulcer symptoms, and 22% of patients had preoperative shock status. Thirty-seven (37%) patients developed postoperative complications, and 8% of patients died.

**Conclusion:** This study confirmed that advanced age, a high ASA score, preoperative shock, comorbidities, and delayed presentation before surgery were all risk factors for postoperative complications and mortality in patients with perforated peptic ulcer disease. Habitual smoking, fasting status, and NSAID and steroid use were not correlated with mortality.

**Keywords:** risk factors, morbidity and mortality, perforated PUD

<sup>1</sup>Al-Basra Teaching Hospital, Basrah, Iraq

<sup>2</sup>Department of Surgery, Basrah College of Medicine, Basrah, Iraq

\*Email:  
Ahmed.Khalaf@uobasrah.edu.iq

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## INTRODUCTION

At present, it is widely accepted that infection with *Helicobacter pylori* and consumption of nonsteroidal anti-inflammatory drugs (NSAIDs) are the two most important factors in the development of peptic ulceration. *H. pylori* and NSAIDs act synergistically to promote ulcer development and other complications such as bleeding. Cigarette smoking predisposes to peptic ulceration and increase the relapse rate after treatment with either gastric antisecretory agents or past elective surgery. Multiple factors may be involved in the transition between superficial and deep penetrating chronic ulcer, but they are of lesser importance [1].

Peptic ulcer perforation is the most common complication in peptic ulcer disease. Despite the widespread use of antisecretory agents and eradication therapy, the incidence of perforated peptic ulcer disease remains largely unchanged [1–3]. This study aimed to evaluate the risk factors for perioperative morbidity and mortality in patients with perforated peptic ulcer disease in Al-Basra Teaching Hospital.

## METHODS

This was a prospective, observational study of patients with perforated peptic ulcer admitted to the Department of surgery in the Al-Basra Teaching Hospital from January 2017 to December 2019. A total of 100 patients were followed for 4 weeks from the time of admission. Informed consent was obtained from each patient enrolled in this study, and the study was approved by the ethics committee. Patients' demographic data, the time elapsed before surgery, history of chronic diseases, smoking habits, preoperative shock status at the time of presentation, history of peptic ulcer symptoms and American Society of Anesthesiologist score (ASA) scores, and NSAID and steroid use were evaluated, and all data were transferred to the SPSS software program, version 16 (SPSS Inc. Released 2007, SPSS for Windows, Version 16.0. Chicago) for data interpretation, and statistical analysis of the association of these data with postoperative complications and mortality was evaluated statistically. All patients underwent surgery in the emergency operating room under general anesthesia and were followed from admission until 4 weeks after hospital discharge.

### Exclusion criteria

All patients with gastric malignancy confirmed by histopathology were excluded. Shock was defined as systolic blood pressure <90 mmHg or a decrease in systolic blood pressure > 40 mmHg from baseline with dehydration.

## RESULTS

A total of 100 patients with perforated peptic ulcer disease were enrolled in this study. The male-to-female ratio was 3:1. The mean age was 44.53 years, and the age range was from 16 to 87 years. Moreover, 54 (54%), 33 (33%), and 12 (12%) patients had ASA scores of 1, 2, and 3, respectively; 1 (1%) patient had an ASA score of 4; and no patients had an ASA score of 5. Furthermore, 41 (41%) patients had various chronic diseases, 45 (45%) patients had different peptic ulcer symptoms before admission, 67 (67%) patients underwent surgery within 12 h of presentation, and 33 (33%) patients underwent surgery 12 h after presentation. Fifty-seven (57%) patients were smokers, 25 (25%) patients were fasting, 22 (22%) patients had preoperative shock, and 57 (57%) patients were using nonsteroidal anti-inflammatory drugs (NSAIDs) or steroids (Table 1).

Forty-one patients had chronic medical diseases that are mostly observed in elderly patients (Table 2). Thirty-seven (37%) of patients had different early postoperative complications (Table 3).

Regarding mortality, 8% of patients died, and their mean age was 70.8 years. Death occurred in patients with comorbidities and a high ASA score; more than half of them were admitted > 12 h after pain onset, and five of eight patients developed shock (Table 4).

## RESULTS OF CORRELATION ANALYSIS

All studied factors showed a significant impact on postoperative comorbidity, except pre-perforation symptoms and patients' fasting status (Table 5).

The spearman correlation (R) of the studied risk factors showed a significant relationship between some of these factors and mortality (Table 6).

**Table 1. Clinical characteristics in relation to morbidity and mortality**

Variables		n.	%	Morbidity n.	%	Mortality n.	%
sex	Male	75	75	21	28	5	6.7
	Female	25	25	16	64	3	12
Age	16–48	69	69	12	17.4	0	0
	49–80	31	31	25	80.6	8	25.8
Chronic diseases	Present	41	41	25	60.9	6	14.6
	Absent	59	59	12	20.3	2	3.38
NSAID + steroids	Present	57	57	16	28	2	3.5
	Absent	43	43	21	48.8	6	13.9
ASA score	1	54	54	9	16.6	2	3.7
	2	33	33	17	51.5	2	6
	3	12	12	10	83.3	3	25
	4	1	1	1	100	1	100
Duration before surgery	< 12 h	78	78	13	16.6	3	3.8
	> 12 h	22	22	17	77.2	5	22.7
Preoperative shock	Present	22	22	17	77.3	5	22.7
	Absent	78	78	20	25.6	3	3.84
Smoking	Yes	57	57	16	28	2	3.5
	No	43	43	21	48.8	6	13.9
Preoperative peptic symptoms	Present	45	45	15	33.3	3	6.6
	Absent	55	55	22	40	5	9
Fasting state	Present	25	25	6	24	1	4
	Absent	75	75	31	41.3	7	9.3

**Table 2. Chronic medical diseases**

Chronic diseases	No. (%)
Hypertension	9(21.95)
Cardiac diseases	6(14.64)
OA + HYPERTENSION	6(14.64)
Disc prolapse	5(12.19)
Diabetes	5(12.19)
CRF	3(7.33)
Asthma	2(4.87)
Liver cirrhosis	2(4.87)
Epilepsy	1(2.44)
Psoriasis	1(2.44)
CVA	1(2.44)
Total	41(100)

**Table 3. Postoperative complications**

Postoperative complications	No. (%)
Wound sepsis	16(43.24)
Lung collapse	4(10.81)
Leakage	3(8.10)
Pneumonia	3(8.10)
Pulmonary embolism	2(5.41)
DVT	2(5.41)
Acute renal failure	2(5.41)
Wound dehiscence	2(5.41)
Ileus	2(5.41)
Intra-abdominal fluid collection	1(2.70)
Total, n (%)	37(100)

## DISCUSSION

Peptic ulcer disease has a worldwide distribution, and it can be treated by the use of antisecretory agents and eradication of *H. pylori* infection. In this way, the need for surgical treatment has greatly declined [1,3,4]. However, despite the widespread use of antisecretory agents and eradication of *H. pylori*, the incidence of perforation is still high, and it carries with it the risk of serious perioperative morbidity and mortality [1,3].

**Table 4. Clinical characteristics of deceased patients**

Age in years	Sex	Comorbidity	Preoperative shock	ASA score	Duration before surgery (hours)
67	Female	Present	Absent	3 E	> 12
75	Female	Present	Present	2 E	> 12
80	Male	Present	Present	3 E	> 12
55	Male	Present	Present	1 E	> 12
87	Male	Present	Present	3 E	> 12
75	Male	Present	Absent	4 E	< 12
78	Male	Present	Present	1 E	< 12
50	Female	Present	Absent	2 E	< 12

**Table 5. Spearman's correlation (R) of sample variables with postoperative complications**

Variables	Postoperative complications	
	R value	P value
Sex	- 0.323**	0.001
Age	0.492**	0.000
Chronic diseases	0.414**	0.000
ASA score	0.531**	0.000
Time before surgery	0.443**	0.000
Preoperative shock	0.443**	0.000
NSAID + steroids	- 0.213*	0.033
Pre-perforation symptoms	- 0.069	0.497
Fasting state	- 0.155	0.122
Smoking	- 0.213*	0.033

\*\* Correlation is significant at the 0.01 level (2-tailed).

\* Correlation is significant at the 0.05 level (2-tailed).

**Table 6. Spearman's correlation (R) of sample variables with postoperative complications**

Variables	Mortality	
	R value	P value
Sex	- 0.085	0.400
Age	0.387**	0.000
Chronic diseases	0.204*	0.042
ASA score	0.241*	0.016
Time before surgery	0.185	0.065
Preoperative shock	0.288**	0.004
NSAID + steroids	- 0.191	0.033
Pre-perforation symptoms	- 0.044	0.661
Fasting state	- 0.085	0.400
Smoking	- 0.191	0.033

\*\* Correlation is significant at the 0.01 level (2-tailed).

\* Correlation is significant at the 0.05 level (2-tailed).

In this study, men outnumbered women, a pattern similar to that seen in other studies [5–9]. Advanced age was significantly correlated to both postoperative complications and mortality [7–10]. Additionally, the sex of the patients had a significant impact on morbidity but not mortality, as reported by Kim et al. [8].

Seventy-six (76%) patients underwent surgery within 12 h, while for others surgery was performed > 12 h after presentation for different reasons, such as living in far rural areas and taking a long time to reach the hospital. Moreover, many patients were of advanced age and would therefore not have displayed the classical clinical picture at presentation. The timing of surgery showed a significant effect on both morbidity and mortality, as reported by other studies [12–14]. We found that a long period before surgery, > 12 h, had a negative impact on patients, which is comparable to the results of other studies [5,6,13,14].

In this study, 57% of patients were smokers; it is known that smoking is an important risk factor in peptic ulcer disease, as it increases the rate of complications such as perforation [15,16]. We found smoking to be significantly associated with postoperative morbidity rather than mortality, in agreement with Kocer et al. [5]. However, other researchers confirmed the presence of a strong association of smoking with mortality [11,19].

We observed that 41% of our patients had chronic diseases, which is an important risk factor for postoperative complications and mortality. The same findings were also reported by other similar studies [14,18,19].

In the present study, the ASA score was found to be a valuable risk factor for postoperative morbidity and mortality in patients with perforated peptic ulceration, and the higher the ASA score, the higher the morbidity and mortality. Similar results were reported by other studies [19–21].

Half of our patients had a history of NSAID and steroid use in different periods before surgery for diverse reasons; this represents a significant effect on postoperative morbidity, but it had a weaker association with patient mortality because most deceased patients were older, had multiple comorbidities, and were not chronic users of such medications. The same results were reported by Unver et al. [19].

The patient's medical history was suggestive of peptic ulcer symptoms, such as epigastric pain, heart burn, and nausea in 45% of patients. Some of them had been treated by H<sub>2</sub> blockers and proton-pump inhibitors before the occurrence perforation. However, there was no significant association with either postoperative morbidity or mortality; this is may be related to patients' concerns about their health, which drives them to seek help earlier.

One quarter of patients were found to be fasting, either as part of Ramadan (when Muslims abstain from eating and drinking fluids from dawn to sunset) or for other religious occasions, and the incidence of peptic perforation is known to increase in the daytime during fasting [22–24]. We did not find fasting to be a significant risk factor in postoperative morbidity and mortality; our explanation for this is that patients who want to fast during Ramadan are supposed to be fit and healthy to sustain the required long fasting hours.

This study reported that 37% of patients had postoperative complications, such as simple wound infection, which were managed conservatively with proper antibiotics and daily dressing. Other patients who developed more serious complications, such as postoperative leakage, needed reoperation for new repair and drainage, whereas patients with pulmonary embolism, renal shutdown, and postoperative pneumonia were managed in the ICU for observation and proper medical therapy until they subsequently improved and were referred to the ward.

Eight patients died, and all of them were aged >50 years. They had multiple comorbidities, half of them had high ASA scores, and close findings were reported by other similar studies [5,6]. Moreover, although there is a difference of opinion regarding the association of the delay before surgery and the mortality rate [12], we found that 5% of patients died when there was a >12-h delay in presentation and a preoperative shock state, which is claimed to be crucial in the increase in mortality [25].

## CONCLUSION

This study clearly demonstrates that advanced age, a high ASA score, preoperative shock, the presence of comorbidities, and a delayed presentation before surgery are all relevant risk factors for postoperative complications and mortality in patients with perforated peptic ulcer disease. Thus, early treatment, correction of shock state, and control of chronic medical diseases may play a vital role in decreasing complication and mortality rates. Smoking, fasting, and NSAID and steroid use had no correlation with mortality. Further studies in multiple centers with larger sample sizes are recommended in the future.

## Conflict of interests

the authors declare there is no conflict of interests.

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### Authors' contributions

Mazin A. Abdulla, Ahmed A. R. Issa, and Ahmed Ziarra Khalaf contributed to the design and implantation of the research, to the analysis of the results and the writing of the manuscript.

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### REFERENCES

- [1] The Underwood and John N. Primrose. The stomach and duodenum, by Norman S. Williams. Christopher J.K. Bulstrode P. Ronan O'Connell. Bailey and Love's Short Practice of Surgery 27edition. London, U.K. Hodder Arnold, 2008: 1121-1123.
- [2] Svanes C. Trends in perforated peptic ulcer: incidence, aetiology, treatment and prognosis. *World J Surg.* 2000; 24:277–283.
- [3] Towfigh S, Chandler C, Hines OJ, McFadden DW. Outcomes from peptic ulcer surgery have not benefited from advances in medical therapy. *Am Surg.* 2002; 68(4):385–389.
- [4] Neuhaus P, Lemmens HP. Ulkuserkrankheit. Die Rolle des Chirurgen [Ulcer disease. The role of the surgeon]. *Ther Umsch.* 1992; 49(11):776–781.
- [5] Kocer B, Surmeli S, Solak C, et al. Factors affecting mortality and morbidity in patients with peptic ulcer perforation. *J Gastroenterol Hepatol.* 2007; 22(4):565–570. doi:10.1111/j.1440-1746.2006.04500.x.
- [6] Ozalp N, Zulfikaroglu B, Bilgic I, Koc M. Evaluation of risk factors for mortality in perforated peptic ulcer in Ankara Numune Teaching Hospital, Ankara, Turkey. *East Afr Med J.* 2004; 81(12):634–637. doi:10.4314/eamj.v81i12.9249.
- [7] Taş İ, Ülger BV, Önder A, Kapan M, Bozdağ Z. Risk factors influencing morbidity and mortality in perforated peptic ulcer disease. *Ulus Cerrahi Derg.* 2014;31(1):20-25. Published 2014 Oct 20. doi:10.5152/UCD.2014.2705.
- [8] Kim JM, Jeong SH, Lee YJ, et al. Analysis of risk factors for postoperative morbidity in perforated peptic ulcer. *J Gastric Cancer.* 2012; 12(1):26–35. doi:10.5230/jgc.2012.12.1.26.
- [9] Hamby LS, Zweng TN, Strodel WE. Perforated gastric and duodenal ulcer: an analysis of prognostic factors. *Am Surg.* 1993; 59(5):319–324.
- [10] Bodner B, Harrington ME, Kim U. A multifactorial analysis of mortality and morbidity in perforated peptic ulcer disease. *Surg Gynecol Obstet.* 1990; 171(4):315–320.
- [11] Svanes C. Trends in perforated peptic ulcer: incidence, etiology, treatment, prognosis. *World J. Surg.* 2000; 24:277–283.
- [12] Nogueira C, Silva AS, Santos JN et al. Perforated peptic ulcer. Main factors of morbidity and mortality. *World J. Surg.* 2003; 27:782–787.
- [13] Testini M, Portincasa P, Piccini G, Lissidini G, Pellegrini F, Greco L. Significant factors associated with fatal outcome in emergency open surgery for perforated peptic ulcer. *World J. Gastroenterol.* 2003; 9:2338–2340.
- [14] Chan WH, Wong WK, Khin LW, Soo KC. Adverse operative risk factors for perforated peptic ulcer. *Ann Acad Med Singapore.* 2000; 29(2):164–167.
- [15] Svanes C, Soreide JA, Skartein A, et al. Smoking and ulcer perforation. *Gut.* 1997; 41:177–180.
- [16] Duggan JM, Zinsmeister AR, Kelly KA. Long-term survival among patients operated on for peptic ulcer disease. *J Gastroenterol Hepatol.* 1999; 14:1074–1082.
- [17] Doll R, Peto R, Wheatly K, Gray R, Sutherland I. Mortality in relation to smoking: 40 years' observation on male British doctors. *BMJ.* 1994; 309:901–911.
- [18] Arveen S, Jagdish S, Kadambari D. Perforated peptic ulcer in South India: an institutional perspective. *World J Surg.* 2009; 33(8):1600–1604.
- [19] Unver M, Firat Ö, Ünalp ÖV, et al. Prognostic factors in peptic ulcer perforations: a retrospective 14-year study. *Int Surg.* 2015; 100(5):942–948.
- [20] Makela JT, Kiviniemi H, Ohtonen P, Laitinen SO. Factors that predict morbidity and mortality in patients with perforated peptic ulcers. *Eur. J. Surg.* 2002; 168:446–451.
- [21] Kujath P, Schwandner O, Bruch HP. Morbidity and mortality of perforated peptic gastroduodenal ulcer following emergency surgery. *Langenbecks Arch Surg.* 2002; 387:298–302.
- [22] Torab FC, Amer M, Abu-Zidan FM, Branicki FJ. Perforated peptic ulcer: different ethnic, climatic and fasting risk factors for morbidity in Al-ain medical district, United Arab Emirates. *Asian J Surg.* 2009; 32(2):95–101.
- [23] Dönderici O, Temizhan A, Küçükbaş T, Eskioğlu E. Effect of Ramadan on peptic ulcer complications. *Scand J Gastroenterol.* 1994; 29(7):603–606.
- [24] Kocakusak A. Does Ramadan fasting contribute to the increase of peptic ulcer perforations? *Eur Rev Med Pharmacol Sci.* 2017; 21(1):150–154.
- [25] Boey J, Choi SKY, Alagaratnam TT, Poon A. Risk stratification in perforated duodenal ulcers, a prospective validation of predictive factors. *Ann. Surg.* 1987; 205:22–26.