

## Original Article

## Impact Of Modifiable Risk Factors On Outcome In Patients With Perforated Peptic Ulcers: A Local Experience

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### Abstract

**Objective:** This study aims to determine the impact of modifiable factors in perforated peptic ulceration on reducing mortality at our local setting of Benazir Bhutto Hospital, Rawalpindi, over two years.

**Methods:** All the patients who were admitted and managed for perforated duodenal ulcer at the emergency department of the Surgical Unit 1 at Benazir Bhutto Hospital, Rawalpindi, from 01-11-2021 to 31-10-2023 were included in the study. The possible causes, co-morbidities, and complications were noted, and data were recorded on a specified proforma.

**Results:** Among thirty-two patients of perforated duodenal ulcers, 63% were smokers, a history of NSAIDs use was present in 37.5% patients, and co-morbidities were present in 25.00% patients. All patients underwent exploratory laparotomy and repair of perforation. The average hospital stay was 5 days, with a range of 1-15 days. The mortality rate in our study was 28.12%.

**Conclusion:** Perforation is still a prevalent complication of peptic ulcer disease. Smoking, increased NSAIDs use, and stressful life play an important role in such cases. Mortality rate is very high in perforated duodenal ulcer cases despite increased understanding of post-operative care.

**Keywords:** Peptic ulcer perforation, exploratory laparotomy and Graham patch repair, mortality

### Introduction

Peptic ulcer disease (PUD) is very common. In this disease, the natural balance between the acid and pepsin production and defence barriers in the mucosa of the stomach is lost. Peptic ulcer disease (PUD) affects about four million people annually around the globe, with a cumulative incidence of 1.5% to 3.0%.<sup>1,2,17</sup> Among others, perforated peptic ulcer (PPU) is a very grave complication which occurs in about 5% of patients with peptic ulcer disease.<sup>3</sup> It presents as a sudden onset of upper abdominal pain, tachycardia and abdominal rigidity.<sup>4,5</sup> The major risk factors for PPU are smoking, decreased physical activity, abnormal use of steroids and NSAIDs, physiological stress, H.pylori association and the previous history of peptic ulcer disease.<sup>1,6-11</sup> Gastronist and Zollinger-Ellison syndrome (ZES) also increase the production of gastric acid.<sup>12</sup> In almost 85% of the clinically suspected patients, a Chest X-ray in the erect position can show free gas under the diaphragm. A CT scan abdomen with contrast can diagnose other patients.<sup>13</sup> It can also exclude acute pancreatitis. Hyperamylasemia can be found in many cases of PPU, acute pancreatitis, and gut perforation due to other reasons.<sup>14</sup> All the patients should be adequately resuscitated. A central venous line is maintained to gauge the fluid intake. Broad-spectrum antibiotics like Ceftriaxone, Amoxicillin and Metronidazole are started on an empirical basis along with good systemic analgesics.

Once the diagnosis of perforated peptic ulceration is confirmed, the patient is shifted to the emergency operation theatre for exploratory laparotomy and surgical treatment is performed on merit.<sup>15</sup> Incidence of mortality after perforation of a peptic ulcer is about 1.3% to 30%.<sup>3,4,6-10</sup>

The objective of this study is to determine the correlation of modifiable risk factors in perforated peptic ulcer patients at our local setting of Benazir Bhutto Hospital, Rawalpindi, for two years.

#### Operational definitions.

##### 1. Perforated peptic ulceration

A peptic ulcer is an open sore in the stomach lining or the upper part of the small intestine (Duodenum). An ulcer can go through all the layers of the digestive tract and form a Hole (perforation). This is called a perforated ulcer.<sup>3</sup>

2. **Modifiable risk factors for peptic ulcer disease (PUD)** are lifestyle and behavioural factors that can be changed to reduce the risk of developing ulcers and their complications. These include smoking, excessive alcohol consumption, regular use of NSAIDs, stress, and potentially even diet.<sup>5</sup>

#### Contributions:

MI, MNZ, - Conception, Design  
MI, MNZ, SI - Acquisition, Analysis, Interpretation  
MI, AAK, MSC, S.I, MAK - Drafting  
MI, MNZ, - Critical Review

All authors approved the final version to be published & agreed to be accountable for all aspects of the work.

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#### Institutional Review Board

##### Approval

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## Materials And Methods

This descriptive observational study was performed at surgical unit 1, Benazir Bhutto Hospital, Rawalpindi, from 01-11-2023 to 31-10-2023. This hospital is a teaching hospital affiliated with Rawalpindi Medical University, a public sector university in Punjab, Pakistan. Keeping the proportion size of 2%, confidence interval 95 and margin of error of 5, the sample size was 31 according to the WHO formula.<sup>16, 34</sup> Non-probability consecutive technique was used for sampling. Approval from the ethical committee of the Rawalpindi Medical University was obtained before the commencement of the research. Informed consent was acquired from all participants involved in the study. The research was conducted with respect for participant privacy, confidentiality, and autonomy. All the patients admitted to the emergency department of the Benazir Bhutto Hospital with a diagnosis of acute peritonitis due to perforated peptic ulcer were included in the study. Patients of acute peritonitis due to other causes like perforated appendix, enteric perforation, tuberculous intestinal perforation and perforation due to gut malignancy were excluded. Patients in the pediatric age group (less than 12 years old) were also excluded from the study.

Diagnosis of PPU was made clinically with history of severe abdominal pain associated with previous history of PUD, NSAIDs and Steroid intake and smoking and having tachycardia, hypotension, and abdominal tenderness with guarding on examination. Blood Complete picture, serum amylase level, serum electrolytes, liver function tests (LFTs) and blood group were checked in all the patients. ECG was performed in all the elderly and patients having a family history or personal history of IHD (ischemic heart disease). X-ray chest PA view was performed in all the patients to see free gas under the diaphragm, indicative of gut perforation (Fig. 1). All patients were managed in the emergency department according to the ATLS guidelines. Relevant advice regarding comorbidities was taken from the departments concerned. After optimisation, all patients underwent midline exploratory laparotomy under general anaesthesia in the emergency operation theatre. Operative findings were noted. All the debrinuous material was washed out. Perforated peptic ulcer was repaired with absorbable suture Vicryl using Graham patch technique. Abdomen washed thoroughly with normal saline, and en masse abdominal closure done with non-absorbable suture Prolene 1.

All postoperative patients were initially managed in the ICU/HDU and later on shifted to the surgical ward once stable hemodynamically. They were treated with broad-spectrum antibiotics, analgesics, I/V fluids with strict vitals charting. Later, they were allowed orally once gut sounds were audible. Wounds are managed according to surgical merits.

Data regarding age, sex, history of smoking, NSAIDs and steroid intake, previous history of PUD, co -co-morbidities, any complications like surgical site infection, wound dehiscence, chest infections were noted on a specified proforma. Biochemical and radiological findings were also recorded. Once stable hemodynamically and tolerated orally, they were discharged from the ward with H Pylori eradication therapy and proper follow-up advice.

Data regarding age, gender, percentage of patients with perforated peptic ulcers, association with smoking, NSAIDs use, steroid use and previous history of peptic ulcer disease were collected. And analysed on SPSS version 22. Frequencies of numerical data, like symptoms and causative factors of PPU, were measured. P value for correlation between mortality and intra-abdominal collection, leakage of repair, PUD history, smoking and steroid use was measured, and a value less than 0.05 was considered significant. Quantitative variables are presented as mean /SD or median.

## Results

Twenty-six (81.25%) were male, and six (18.75%) patients were female. In our study, all the patients (100%) presented in the emergency department. The average age was 46 years (SD+ 15.495) with a range of 19-85 years. The main symptoms were pain abdomen and fever present in all of the patients, followed by other features as shown in Table 1.

The average pulse was 116 bpm with a range of 92-153bpm. Mortality in our study was 28.12% (nine patients), which is quite high (Table 2).

**Table 1: Main clinical features**

S. No	Feature	Present	Absent
1	Pain abdomen	32 (100%)	0
2	Fever	31 (96.9%)	1
3	Constipation	28 (87.5%)	4(12.5%)
4	Vomiting	17(53.12%)	15(46.87%)

**Table 2: Outcome of a Perforated peptic ulcer**

Serial no	Total	Survived	Mortality
1	32 (100%)	23 (71.87%)	09 (28.1%)

Most of the expired patients were more than 50 years of age. The most important associated factors were smoking, NSAIDs use, and previous history of PUD, followed by other factors, are shown in Table 3 and Figure 2.

**Table 3: Correlation between mortality and associated factors**

Serial number	Associated factor	Yes (Number & percentage of patients)	No (Number & percentage of patients)	P value
1	Smoking	20 (62.5%)	12 (37.5%)	-0.233 Pearson 0.199 2-tailed
2	NSAID use	12 (37.5%)	20 (62.5%)	0.090 Pearson 0.625 2-tailed
3	Previous History of PUD	11(34.37%)	21 (65.62%)	0.864 Pearson 0.000 2-tailed**
4	Steroid use	6 (18.75%)	26 (81.25%)	0.590 Pearson 0.000 2-tailed**
5	Comorbidities like hypertension and diabetes mellitus	8 (25%)	24 (75%)	0.227 Pearson 0.211 2-tailed
6	Old age (= or >50 years)	09 (28.12%)	23 (71.87%)	0.493 Pearson 0.004 2-tailed**

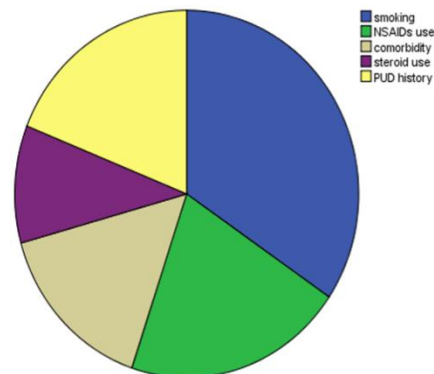
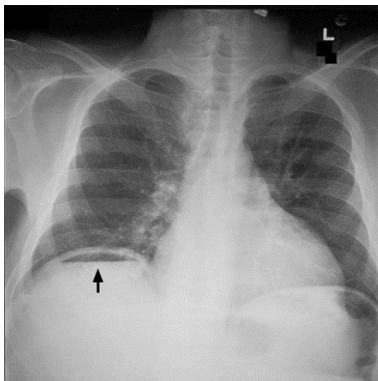
Correlation is significant at the 0.01 level (2-tailed). \*\*

**Table 4: Complications of perforated peptic ulcer**

Complication	Patients number (out of 32)	Percentage	P value
Chest infection	11	34.37%	0.664 Pearson 0.000 2-tailed**
Wound infection	8	25.00%	0.173 Pearson 0.343 2-tailed
Both chest and wound Infection	02	06.25%	0.056 Pearson 0.762 2-tailed
Leakage	02	06.25%	0.126 Pearson 0.493 2-tailed
Intra-abdominal collection	01	03.12%	0.037 Pearson 0.840 2-tailed

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

Mostly, the patients belonged to the middle social class (68.75%). Free gas under the diaphragm was present in 29 patients (about 90%). Serum amylase was in the range of 75 to 200 mg/dl in seventy-five per cent of the patients. Average hospital stay was 5 days (ranged 1-15days). The most important post-operative complications were chest and wound infections, as shown in Table 4. At two weeks follow-up, the wound was healthy in 56.25% patients while infected in 15.62%. Similarly, oral intake was much better in 53.12% patients and poor in 18.75%.



**Figure 1: Arrow showing free gas under the right dome of the diaphragm, indicating gut perforation**

**Figure 2: Causative factors of perforated peptic ulcer**

## Discussion

In our study, the male population was more than the female population (81.25% vs 18.75%). It might be because males are more smokers than females. They are more stressed than females and use more NSAIDs than females. In their study, Li et al reported the male incidence of 64.7%.<sup>18</sup>

The average age in our study was 46 years. Other studies, like Huang L et al, also found middle age preponderance.<sup>19</sup>

In our study, nearly all the patients had a history of abdominal pain and fever, while constipation and vomiting were present in 87.5% and 46.87% of the patients, respectively. While Ali AM., Mohamed AN, Mohamed YG et al found that pain and fever were present in 82.40% of their study population.<sup>20</sup> 46.15% patients developed constipation in a study by Lin, TY. Chuang, YC. Kao, FC. Et al.<sup>21</sup>

Smoking is one of the causative factors which leads to PPU. Nicotine in cigarette smoking is thought to inhibit pancreatic bicarbonate secretion as well as decrease prostaglandin secretions in the stomach mucosa, which makes it susceptible to ulceration.<sup>10</sup> In our study, about 62.5% patients had a history of smoking. Xie X., Ren K., Zhou Z. Et al also found a very high relationship between PUD and smoking.<sup>22</sup>

NSAIDs use increases the incidence of PPU in PUD patients. In our study, about 37.5% patients had a positive history of NSAIDs use mainly because of musculoskeletal and joint pains. Most NSAIDs are now available over the counter in Pakistan. In their study, L. McEvoy, D. F. Carr, and M. Pirmohamed found that about 40% NSAID users develop mild dyspeptic symptoms.<sup>23</sup>

The presence of a previous history of PUD also increases the risk of PPU. In our study, about 34.37% patients had such a history. In their study, Ali AM, Mohamed A.N, Mohamed YG ET al found that nearly fifty per cent of patients had a history of dyspepsia.<sup>20</sup> Similarly, steroid use also increases the development of PPU. In our study, about 18.75% patients used steroids for their chest infections and joint pains.

Comorbidities like hypertension and diabetes mellitus increase the risk of perforation due to their immunosuppressive effect. Comorbidities were present in about 28% of our study population. In their study, Sivaram P, Sreekumar A. noted that Diabetes Mellitus was present in 20.8% and systemic Hypertension in 13.9% patients.<sup>24</sup>

Ninety per cent of patients in our study showed free gas under the diaphragm on their Chest X-ray.

Despite advancements in different modalities, the time-tested treatment of perforated peptic ulcer is early exploratory laparotomy and repair of the perforation on merit. Unnecessary delay in surgical treatment can increase post-operative mortality due to chemical and septic peritonitis and their sequelae.<sup>15, 25</sup>

All thirty-two patients in our study underwent exploratory laparotomy after resuscitation and optimisation. Most of the patients got their perforation repaired with absorbable Vicryl 1 suture employing Graham's technique.

Mortality in our study was 28.12%. Previous history of PUD, steroid use, and old age were the main associated factors leading to death. All these factors had a significant correlation, as the p-value of all these factors was less than 0.05. Other factors like history of NSAIDs use, hypertension, diabetes mellitus and smoking were also the contributory factors. In a similar study, Kurniawan E and Danardono E reported mortality as high as 48.5%.<sup>28</sup> In their studies, Buck DL, Møller MH et al and Søreide K, Thorsen K, Søreide JA et al reported 30-d mortality rate reaching 20% and 90-d mortality rate of up to 30%.<sup>3,4</sup> Incidence of post-operative mortality in the elderly is 3 to 5 times higher than in adults.<sup>26</sup> This may be due to the presence of comorbidities, delayed presentation leading to severe sepsis, atypical presentation or delay in diagnosis of more than twenty-four hours.<sup>27</sup> Surgical delay should be limited as much as possible in patients with perforated peptic ulcer.<sup>32</sup> Optimal perioperative sepsis control can decrease mortality in such patients.<sup>31, 32, 34</sup>

Of the surviving 23 patients, ten (31.25%) developed other postoperative complications in our study. In their study, Liu J, Zhou S, Wang S, et al found a complication rate of twenty-eight per cent.<sup>29</sup> Comorbidities harmed the post-operative course of the patient.<sup>30</sup> In our study, the most common complications were chest infection (34.37%) and wound infection (25.0%). Two patients had both chest and wound infections. Chest infection was very significant as the p-value was less than 0.01. Two patients (6.25%) developed leakage, which needed re-laparotomy, abdominal wash and repair of the leak. In a study by Shreya A, Sahla S et al, 17.0% patients developed wound infection and chest infection each, 4.2% cardiac complications, 4.2% urinary tract infection and 4.2% intra-abdominal collection.<sup>31,33</sup>

Two weeks postoperative follow-up in OPD showed that 15(65.21%) patients were completely cured of their diseases with good oral intake, while 08 (34.78%) patients still had some problems in the form of low oral intake, wound infection and some anxiety. Although a lot of international data regarding PPU and its complications is present on the internet but in our local set-up at Rawalpindi Medical University, such data is scarce. So this study will help our postgraduate resident surgeons pay more attention to the preventive aspects of PUD, given the international guidelines. Moreover, the need for adequate and prompt resuscitation can reduce the mortality in such cases of PPU disease. There are a few limitations in our study. Firstly, the sample is taken from one surgical unit. Its size is too small to be externalised to other institutions. Secondly, we did not address the association of H pylori infection, as detection of this organism is not done in the emergency department in our resource-limited hospital.


## Conclusions

Results of our study and the relevant other national and international studies show that, despite the wide use of highly developed proton pump inhibitors and many other medicines, the incidence of peptic ulcer disease is still very high. In addition to many other complications, the perforated peptic ulcer is a very grave complication of PUD. Many factors like previous history of PUD, smoking, NSAIDs and steroid overuse, hypertension, diabetes mellitus and stressful lifestyle play a major role in the development of PPU. Mortality after PPU is as high as 28.12% in our study.

It is recommended that morbidity and mortality in patients with PPU can be decreased by prompt diagnosis by surgical experts, reducing the time of early surgical intervention, optimal perioperative fluid resuscitation and addressing the comorbidities well in time.

## Author Information

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## References

1. Coco D, Leanza S. A Review on Treatment of Perforated Peptic Ulcer by Minimally Invasive Techniques. *Maedica (Bucur)*. 2022 Sep; 17(3):692-698. <https://doi.org/10.26574/maedica.2022.17.3.692>.
2. Khan MS, Singh V. Peptic Ulcer Disease (PUD): An overview of the History, Risk factors, Symptoms, Diagnosis Considerations and Conventional Management, *Asian Journal of Pharmaceutical Research and Development*. 2021; 9(5):111-114. <http://dx.doi.org/10.22270/ajprd>.
3. Buck DL, Möller MH; Danish Clinical Register of Emergency Surgery. Influence of body mass index on mortality after surgery for perforated peptic ulcer. *Br J Surg*. 2014 Jul; 101(8):993-9. <https://doi.org/10.1002/bjs.9529>.
4. Søreide K, Thorsen K, Søreide JA. Strategies to improve the outcome of emergency surgery for perforated peptic ulcer. *Br J Surg*. 2014 Jan; 101(1):e51-64. <https://doi.org/10.1002/bjs.9368>.
5. Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG Clinical Guideline: Treatment of *Helicobacter pylori* Infection. *Am J Gastroenterol*. 2017 Feb; 112(2):212-239. Doi: 10.1038/ajg.2016.563. Epub 2017 Jan 10. Erratum in: *Am J Gastroenterol*. 2018 Jul; 113(7):1102. <https://doi.org/10.1038/s41395-018-0132-6>.
6. Georgopoulos SD, Michopoulos S, Rokkas T, Apostolopoulos P, Giamarellos E, Kamberoglou D, et al. Hellenic consensus on *Helicobacter pylori* infection. *Ann Gastroenterol*. 2020 Mar-Apr; 33(2):105-124. <https://doi.org/10.20524/aog.2020.0446>.
7. Guo CG, Zhang F, Wu JT, Cheung KS, Li B, Law SYK, et al. Divergent trends of hospitalizations for upper and lower gastrointestinal bleeding based on population prescriptions of aspirin, proton pump inhibitors and *Helicobacter pylori* eradication therapy: Trends of upper and lower gastrointestinal bleeding. *United European Gastroenterol J*. 2021 Jun; 9(5):543-551. <https://doi.org/10.1002/ueg2.12067>.
8. Jung YS, Park JH, Park CH. Impact of proton pump inhibitors on the risk of small bowel or colorectal bleeding: A systematic review and meta-analysis. *United European Gastroenterol J*. 2023 Nov; 11(9):861-873. <https://doi.org/10.1002/ueg2.12448>.
9. Lewis JD, Strom BL, Localio AR, Metz DC, Farrar JT, Weinrieb RM, Nessel L, Brensinger C, Kimmel SE. Moderate and high-affinity serotonin reuptake inhibitors increase the risk of upper gastrointestinal toxicity. *Pharmacoepidemiol Drug Saf*. 2008 Apr; 17(4):328-35. <https://doi.org/10.1002/pds.1546>.
10. Seyoum N, Ethicha D, Assefa Z, Nega B. Risk Factors that Affect Morbidity and Mortality in Patients with Perforated Peptic Ulcer Diseases in a Teaching Hospital. *Ethiop J Health Sci*. 2020 Jul 1; 30(4):549-558. <https://doi.org/10.4314/ejhs.v30i4.10>.
11. Chung KT, Shelat VG. Perforated peptic ulcer - an update. *World J Gastrointest Surg*. 2017 Jan 27; 9(1):1-12. <https://doi.org/10.4240/wjgs.v9.i1.1>.
12. Sayehmiri K, Abangah G, Kalvandi G, Tavan H, Aazami S. Prevalence of peptic ulcer in Iran: Systematic review and meta-analysis methods. *J Res Med Sci*. 2018 Jan 29; 23:8. [https://doi.org/10.4103/jrms.JRMS\\_1035\\_16](https://doi.org/10.4103/jrms.JRMS_1035_16).
13. Itama EP, Tran K, Patel P, Patel Y, Saifollahi A, Dushkin N, Tiesenga F. Graham Patch Repair of a Prepyloric Ulcer Complicated by Recurrent Abdominal Abscesses and Leukocytosis: A Case Report. *Cureus*. 2024 Feb 21; 16(2):e54646. <https://doi.org/10.7759/cureus.54646>.
14. Coco D, Leanza S. A Review on Treatment of Perforated Peptic Ulcer by Minimally Invasive Techniques. *Maedica (Bucur)*. 2022 Sep; 17(3):692-698. <https://doi.org/10.26574/maedica.2022.17.3.692>.
15. Coco D, Leanza S. A Review on Treatment of Perforated Peptic Ulcer by Minimally Invasive Techniques. *Maedica (Bucur)*. 2022 Sep; 17(3):692-698. <https://doi.org/10.26574/maedica.2022.17.3.692>.
16. Naing L, Nordin RB, Abdul Rahman H, Naing YT. Sample size calculation for prevalence studies using Scalex and ScalaR calculators. *BMC Medical Research Methodology*. 2022 Jul 30;22(1):209. <https://doi.org/10.1186/s12874-022-01694-7>.
17. Butt N, Usmani MT, Mehak N, Mughal S, Qazi-Arisar FA, Mohiuddin G, Khan G. Risk factors and outcomes of peptic ulcer bleed in a Pakistani population: A single-center observational study. *World J Gastrointest Pharmacol Ther*. 2024 May 28; 15(3):92305. <https://doi.org/10.4292/wjgpt.v15.i3.92305>.
18. Li R, Wang W, Ma Y, Chen H. Analysis of risk factors for ulcer recurrence and upper gastrointestinal bleeding in children with peptic ulcer treated with *Helicobacter pylori* eradication therapy. *Transl Pediatr*. 2023 Apr 29; 12(4):618-630. <https://doi.org/10.21037/tp-23-155>.

19. Huang L, Li R, Wang T, Wang S, Yu C, Gong J et al. Comparison of Secular Trends in Peptic Ulcer Diseases Mortality in China, Brazil and India during 1990-2019: An Age-Period-Cohort Analysis. *Healthcare (Basel)*. 2023 Apr 11; 11(8):1085. <https://doi.org/10.3390/healthcare11081085>.
20. Ali AM, Mohamed AN, Mohamed YG, Keleşoğlu Sİ. Clinical presentation and surgical management of perforated peptic ulcer in a tertiary hospital in Mogadishu, Somalia: a 5-year retrospective study. *World J Emerg Surg*. 2022 May 16; 17(1):23. <https://doi.org/10.1186/s13017-022-00428-w>.
21. Lin TY, Chuang YC, Kao FC, Ping-Yeh C, Tsai TT, Fu TS, et al. Early detection and intervention for acute perforated peptic ulcer after elective spine surgeries: a review of 13 cases from 24,026 patients. *BMC Musculoskelet Disord*. 2021 Jun 16; 22(1):548. Erratum in: *BMC Musculoskelet Disord*. 2023 Jan 19; 24(1):44. <https://doi.org/10.1186/s12891-022-06091-1>.
22. Xie X, Ren K, Zhou Z, Dang C, Zhang H. The global, regional and national burden of peptic ulcer disease from 1990 to 2019: a population-based study. *BMC gastroenterology*. 2022 Feb 10;22(1):58. <https://doi.org/10.1186/s12876-022-02130-2>
23. McEvoy L, Carr DF, Pirmohamed M. Pharmacogenomics of NSAID-Induced Upper Gastrointestinal Toxicity *Pharmacogenetics and Pharmacogenomics*. Volume 12 – 2021. <https://doi.org/10.3389/fphar.2021.684162>
24. Sivaram P, Sreekumar A. Preoperative factors influencing mortality and morbidity in peptic ulcer perforation. *Eur J Trauma Emerg Surg*. 2018; 44: 251–257. <https://doi.org/10.1007/s00068-017-0777-7>
25. Stern E, Sugumar K, Journey JD. Peptic Ulcer Perforated. [Updated 2023 Jun 12]. In: Stat Pearls [Internet]. Treasure Island (FL): Stat Pearls Publishing; 2025 Jan-.
26. Chung KT, Shelta VG. Perforated peptic ulcer - an update. *World J Gastrointest Surg*. 2017 Jan 27; 9(1):1-12. <https://doi.org/10.4240/wjgs.v9.i1.1>.
27. Wilhelmsen M, Møller MH, Rosenstock S. Surgical complications after open and laparoscopic surgery for perforated peptic ulcer in a nationwide cohort. *Br J Surg*. 2015 Mar; 102(4):382-7. <https://doi.org/10.1002/bjs.9753>.
28. Kurniawan E, Danardono E. Clinical presentation and outcome of perforated peptic ulcer patients at Dr. Soetomo Hospital Surabaya, Indonesia. *Bali Medical Journal* 2023; 12(3), 2578–2581. <https://doi.org/10.15562/bmj.v12i3.4745>
29. Liu J, Zhou S, Wang S, Xue X. Analysis of risk factors for duodenal leak after repair of a duodenal perforation. *BMC Surg*. 2023 May 10; 23(1):116. <https://doi.org/10.1186/s12893-023-02005-7>.
30. Sengupta TK, Prakash G, Ray S, Kar M. Surgical Management of Peptic Perforation in a Tertiary Care Center: A Retrospective Study. *Niger Med J*. 2020 Nov-Dec; 61(6):328-333. [https://doi.org/10.4103/nmj.NMJ\\_191\\_20](https://doi.org/10.4103/nmj.NMJ_191_20).
31. Shreya A, Sahla S, Gurushankari B, Shivakumar M, Rifai, Kate V, et al. Spectrum of perforated peptic ulcer disease in a tertiary care hospital in South India: predictors of morbidity and mortality. *ANZ J Surg*. 2024 Mar; 94(3):366-370. <https://doi.org/10.1111/ans.18831>.
32. Chen P, Gao J, Li J, Yu R, Wang L, Xue F, et al. Construction and efficacy evaluation of an early warning scoring system for septic shock in patients with digestive tract perforation: A retrospective cohort study. *Front Med (Lausanne)*. 2022 Sep 13; 9:976963. <https://doi.org/10.3389/fmed.2022.976963>.
33. Treuheit J, Krautz C, Weber GF, Grützmann R, Brunner M. Risk Factors for Postoperative Morbidity, Suture Insufficiency, Re-Surgery and Mortality in Patients with Gastroduodenal Perforation. *J Clin Med*. 2023 Sep 29; 12(19):6300. <https://doi.org/10.3390/jcm12196300>.
34. Pansa A, Kurihara H, Memon M; Updates in laparoscopic surgery for perforated peptic ulcer disease: state of the art and future perspectives, *Annals of Laparoscopic and Endoscopic Surgery* 2019,5(0). <https://doi.org/10.21037/ales.2019.11.03>.