Risk factors affecting morbidity and mortality in patients with perforated peptic ulcers in sub-Saharan Africa: A systematic review

E I U Niilonga;[1] **A M N Shatri,**[2] MSc (Applied Human Biology)

[1] *4th-year medical student, School of Medicine, Hage Geingob Campus, University of Namibia, Windhoek, Namibia*
[2] *Department of Human Biological and Translational Medical Sciences, School of Medicine, Hage Geingob Campus, University of Namibia, Windhoek, Namibia*

Corresponding author: *A M N Shatri (aiikasha@unam.na)*

Background. Peptic ulcer disease results from an imbalance between stomach acid pepsin and the mucosal defence barrier. It affects millions of people worldwide, with perforation being the second most common complication after bleeding. Despite the amount of data available globally, there are limited data on factors influencing mortality and morbidity from peptic ulcers in Africa.
Objectives. To evaluate factors that influence morbidity and mortality in patients with perforated peptic ulcers in sub-Saharan Africa (SSA).
Methods. A total of 25 cross-sectional studies conducted in SSA were used to compile this review. The review focused on aspects such as the epidemiology of, risk factors for and treatment of peptic ulcer disease from the SSA perspective. The total sample size of 1 377 patients was calculated from the total reviewed articles.
Results. The mortality for most countries was ≥8%, while the morbidity rate was ≤48%, with most cases reported in men. Major risk factors influencing morbidity and mortality in SSA were age >60 years, presence of shock at admission, delay in treatment >24 hours, and presence of coexisting diseases.
Conclusion. Surgery remains the standard treatment for perforated peptic ulcers in SSA, with the most common postoperative complications that influence morbidity and mortality being septic shock, wound infection and pulmonary infections. Additional studies should be done in other SSA countries to provide more data for comparative analysis.

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An ulcer refers to an open wound, with the two most common ulcers being gastric and duodenal.[1] Peptic ulcer disease results from an imbalance between stomach acid pepsin and the mucosal defence barrier. It affects ~4 million people worldwide annually, and its incidence has been estimated to be ~1.5 - 3%.[2,3]

Perforation is the second most common complication of peptic ulcer disease, after bleeding, and is characterised by a classic triad of sudden onset of abdominal pain, tachycardia and a rigid abdomen. *Helicobacter pylori*, one of the major risk factors for peptic ulcer perforation, is present in ~50% of the population worldwide, and it causes infection in ~70% of the population in developing countries.[4] Non-steroidal anti-inflammatory drugs (NSAIDs) are the second most common cause of peptic ulcer perforation, especially in the elderly. Other factors include smoking, alcohol consumption, and conditions such as Zollinger-Ellison syndrome.[5,6]

Studies have focused on addressing risk factors for morbidity and mortality in patients with perforated peptic ulcers, with contradictory results from Western and Asian countries.[7] Studies conducted in Africa are mainly cross-sectional and restricted to specific countries such as Somalia,[8] Ethiopia[9] and Liberia.[10] Over the years, scoring systems have been developed to help predict morbidity and mortality in patients with perforated peptic ulcers, such as the Boey score, Peptic Ulcer Perforation (PULP) score and American Society of Anesthesiology scoring system.[7,11] Scoring systems are not commonly used in sub-Saharan Africa (SSA) and were only found to have been used in studies in Cameroon,[12] where they used the Mannheim Peritonitis Index, and Côte d'Ivoire,[7] where they used the American Society of Anesthesiology scoring system.

Methods

Literature search

A total of 45 relevant research articles on perforated peptic ulcers in SSA were initially obtained from Google Scholar, PubMed and Medline using key words 'Perforated peptic ulcers', 'SSA' and 'Risk factors', and Boolean operators 'AND' and 'OR'. These were reviewed by the authors of the present study. Of 45 research articles, 10 were disregarded for this review because they were published prior to 2015, 5 showed only abstracts rather than complete papers, and 5 lacked pertinence to this article. As a result, only 25 articles were used in the preparation of this review. The overall sample size of the patients in all articles used in this review was 1 377. The articles used focused on the pathophysiology, treatment and epidemiology of perforated peptic ulcers in SSA. Inclusion factors were articles published between 2015 and 2022 and full-length cross-sectional studies.

Results and discussion

Epidemiology of peptic ulcers in SSA

A perforated peptic ulcer occurs when an untreated or poorly managed gastric or duodenal ulcer burns through the mucosal wall of the gastrointestinal tract. Morbidity was highest in Cameroon at 43.7%, and lowest in Burkina Faso at 6.6% (Table 1). Mortality was highest in Liberia at 35% and lowest in Ethiopia at 4.3%. A review by Rickard[13] reported that the overall case fatality rate for perforated peptic ulcers in SSA was 5 - 7%. Mortality rates in African countries were found to be lower than morbidity rates, with most studies recording within a range of 4 - 30% for morbidity.[7,14-16] Many SSA countries, such as Namibia, Madagascar, Seychelles, Gambia, Democratic Republic of the Congo, Malawi, Mozambique, Djibouti, Botswana and Angola, have no data recorded in the searched databases, while South Africa, Burundi, Ghana, Kenya, Zambia and Zimbabwe have data published before 2015, indicating a need to document recent cases in these countries.

Risk factors influencing morbidity and mortality in patients with perforated peptic ulcers in SSA

The literature on perforated peptic ulcers shows that morbidity and mortality increased when the patient had any of the following risk factors: presence of shock at the time of presentation, presence of underlying conditions, duration of perforation >24 hours before presentation, and age >60 years. Other risk factors such as gender, location of the ulcer, perforation diameter >1 cm and wound site infection were also recorded (Table 2).

Of the various studies that have been conducted, some have similar results to the literature and others do not. Most studies, however, have found that increasing age is associated with increased mortality, but that morbidity is more common in middle-aged patients, especially in developing countries such as Somalia, Nigeria and Ethiopia. Ali *et al.*[8] suggest that the high morbidity in middle-aged people is because they smoke more and drink more alcohol than other age groups, while an older age distribution is seen in developed countries because older people have more comorbidities than those who are younger, and are more likely to use NSAIDs.

The mean age of patients with perforated peptic ulcers in most studies was 31.2 - 54.2 years,[12,14,17,18] showing that more young people presented with perforated peptic ulcers, although it was mostly the elderly who died. Similarly, in a study by Ghosh *et al*.,[19] the incidence of perforated peptic ulcer was highest in the age group 15 - 30 years, and the mean patient age was 36.3 years. Several studies in SSA have shown that more men than women present with perforated peptic ulcers, and that men have higher morbidity and mortality.[3,12,14,20]

Reports from Ethiopia[20,21] and Nigeria[22] indicate that patient presentation 24 hours after perforation is often associated with a poor prognosis because the purulent intra-abdominal fluid that leaks from the perforation site may lead to shock, which will further increase morbidity and mortality rates. However, a study by Tas *et al.*[23] showed no correlation between time of presentation and morbidity, and their patients arrived at the hospital a mean (standard deviation) of 30.8 (31.4) hours after perforation (range 2 - 240 hours).

A probable reason for the reported delay in treatment in African patients is that they present to hospital late. Herbal medicine is often used as initial treatment, according to traditional beliefs,[7] and people only seek help at a hospital when their condition gets worse, or receive treatment from primary care units, which are likely to give analgesics only.[7]

While the presence of shock at the time of presentation has generally been reported to increase morbidity and mortality, in the study by Tas *et al.*[23] this was not the case, and they did not find an association between shock and morbidity. With regard to other factors such as advanced age and perforation diameter >1 cm, their findings did agree with the literature in that the older the patients were and the larger the perforation was, the greater was the risk of mortality.[23]

Treatment options for peptic ulcers in SSA (Table 3)

Peptic ulcer disease is common worldwide, and acute perforated peptic ulcer accounts for >70% of deaths.[24] Surgery remains the standard treatment for perforated peptic ulcers. A study by Ali *et al.*[8] in Somalia found that exploratory laparotomy and application of an omental patch (modified Graham patch repair) was an effective surgical approach. Although it is easy to perform, there is a high risk of recurrence of the ulcer if vagotomy is not included, in which case there is no effect on gastric acid secretion.

Recent studies have shown that postoperative morbidity in patients with perforated peptic ulcers, including pulmonary infections, wound infections and sepsis, ranges from 15% to 30%.[7,23,25] These figures are lower than those reported in older studies, which ranged from 21% to 42%.[23]

A recent advance in the treatment of peptic ulcers has been the introduction of histamine type 2 (H_2)-receptor antagonists, which have been shown to heal 77 - 92% of ulcers.[7] Although H_2-receptor antagonists

Table 1. Mortality and morbidity due to peptic ulcers in sub-Saharan Africa

Country	Year of publication	Morbidity, %	Mortality,%	Reference
Burkina Faso	2016	6.6	7.7	Coulbaly *et al.*[16]
Cameroon	2020	43.7	17.0	Bokalli *et al.*[12]
Côte d'Ivoire	2016	27.5	19.3	Gona *et al.*[7]
Ethiopia	2021	-	4.3	Tedesse *et al.*[9]
Liberia	2015	-	35.0	Moses *et al.*[10]
Nigeria	2017	-	17.3	Dongo *et al.*[14]
Rwanda	2020	-	28.0	Cyuzuzo *et al.*[3]
Somalia	2022	-	7.8	Ali *et al.*[8]

- = data were not recorded in the article.

have reduced the need for surgical treatment, treatment of peptic ulcer disease remains a challenge in Africa owing to cultural behaviours and the high costs of medication. Many patients therefore present in a critical condition as a result of complications,[7] which contributes to the high mortality and morbidity.

Conclusion

Literature from SSA indicated that the major risk factors influencing morbidity and mortality in patients with perforated peptic ulcers were age >60 years, presence of shock at admission, delay in treatment >24 hours, and presence of coexisting diseases. Surgery remains the

Table 2. Risk factors recorded as major contributors to morbidity and mortality in sub-Saharan African countries

Country	Common risk factors	Factors unique to country	Site of perforation	Reference
Burkina Faso	Gender: male > female	None	Gastric perforation	Coulbaly *et al.*[16]
Cameroon	Gender: male > female Smoking Alcohol use	Infection by *Helicobacter pylori* Use of NSAIDs	Gastric perforation	Bokalli *et al.*[12]
Côte d'Ivoire	Gender: male > female	Comorbidities: hypertension, diabetes and heart disease Delayed surgery up to 24 hours Postoperative factors: septic shock, hypovolaemia, wound sepsis and gastroduodenal fistula	Duodenal perforation	Gona *et al.*[7]
Ethiopia	Gender: male > female Smoking Alcohol use	Time of presentation >24 hours	Duodenal perforation	Tedesse *et al.*[9]
Liberia	Gender: male > female Smoking Alcohol use	Marital status: unmarried > married or divorced History of gastritis Previous use of antacids Blood group: Rh+ > than other blood groups	Duodenal perforation	Moses *et al.*[10]
Nigeria	Gender: male > female	History of peptic ulcer disease Use of anti-ulcer medication in the past 6 months Socioeconomic status: farmers > than any other profession	Gastric perforation	Dongo *et al.*[14]
Rwanda	Gender: male > female	Postoperative factors: sepsis and pneumonia	Gastric perforation	Cyuzuzo *et al.*[3]
Somalia	Gender: male > female Smoking	Age >40 years Use of NSAIDs Shock at time of presentation Duration of symptoms before presentation >24 hours	Gastric perforation	Ali *et al.*[8]

NSAIDs = non-steroidal anti-inflammatory drugs; Rh+ = rhesus positive.

Table 3. Treatment options used in different sub-Saharan African countries, based on recent studies

Country	Treatment options	Reference
Burkina Faso	Eradication therapy with or without antibiotics Omentoplasty	Coulbaly *et al.*[16]
Cameroon	Emergency laparotomy Omentoplasty	Bokalli *et al.*[12]
Côte d'Ivoire	Omentoplasty and one partial gastrectomy	Gona *et al.*[7]
Ethiopia	Eradication therapy with H_2-receptor antagonists Surgery: Graham patch	Tedesse *et al.*[9]
Liberia	Graham patch	Moses *et al.*[10]
Nigeria	Primary closure Omentoplasty Eradication therapy	Dongo *et al.*[14]
Rwanda	Graham patch	Cyuzuzo *et al.*[3]
Somalia	Graham patch Peritoneal lavage for sealed perforations Eradication therapy	Ali *et al.*[8]

H_2 = histamine type 2.

standard treatment, with the most common postoperative complications influencing morbidity and mortality being septic shock, wound infection and pulmonary infections. Other factors include smoking, male gender, and site and size of the perforation, as well as medical conditions such as Zollinger-Ellison syndrome. Although there are data on perforated ulcers from some African countries, more cross-sectional studies should be conducted to provide further information on risk factors, mortality and treatment options in a wider range of SSA countries.

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