PROFILES AND PREDICTIVE FACTORS FOR POOR OUTCOMES IN PATIENTS MANAGED SURGICALLY FOR PERFORATED PEPTIC ULCER DISEASE AT KENYATTA NATIONAL HOSPITAL.

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DECLARATION

I hereby declare that this dissertation is my original work and has not been presented to the best of my knowledge in any other institution for an academic award.

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DEPARTMENTAL APPROVAL

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LIST OF ABBREVIATIONS

KNH: Kenyatta National Hospital

PUD: Peptic Ulcer Disease

PPU: Perforated Peptic Ulcer

NSAIDS- Non-steroidal anti-inflammatory drugs

TNF- Tumour necrosis factor

PGE- Prostaglandin E

DU- Duodenal ulcer

GI- Gastrointestinal

SSI- Surgical site Infection

ARF-Acute Renal Failure

ECF- Enterocutaneous Fistula

SBP-Systolic Blood Pressure

WSES- World Society of Emergency Surgery

DEFINITION OF TERMS

Perforated Peptic ulcer: Defects in the gastric or duodenal mucosa that extend through the muscularis layer.

Gastrectomy: Resection of part of the stomach as part of treatment for gastric pathologies.

Peritonitis: Inflammation of the peritoneum, typically caused by bacterial infection either via the blood or after visceral perforation.

Ulcerogenic: Substances that predispose to development and progress of peptic ulcers.

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ABSTRACT

Background: Perforated peptic ulcer (PPU) is a complication of peptic ulcer disease (PUD) that bears a high rate of morbidity and mortality. Scanty data is available in our setup on PPU and the outcomes of surgical management of these patients have been shown to vary from region to region. This study is conducted to establish the patient profiles at presentation as well as operative factors vis a vis the surgical outcomes with an aim of identifying factors that significantly predict outcome in our set up.

Objective: To assess patient profiles and determine factors predictive of poor outcomes in patients managed surgically for perforated peptic ulcer disease in Kenyatta National Hospital (KNH).

Methods: This was a Retrospective Cross-sectional Study involving 88 records of PPU patients operated on at KNH from Jan 2014 to Dec 2020. Data was collected from medical records retrieved at the KNH records department using a pre-formed data extraction tool. Patient profile factors were evaluated as at presentation and then the peri-operative factors as recorded in the surgical notes. Outcomes analyzed in this study were the rate of post operative complications and mortality.

Results: There were more males (91.1%) managed surgically for PPU compared to females (8.1%). The mean age of the patients was 35.6years (SD14.92) with a peak incidence in the 3rd decade. Majority of the patients 66(75%) presented after 48 hours and 33(37.9%) had previous history of PUD. Most of the perforations were duodenal (68.2%) with the mean age of patients with duodenal and gastric ulcer perforations being 34.8 (SD14.8) years and 38.5 (SD15.5) years respectively. Among the 88 patients operated for PPU, 59.1% experienced post-operative complications while 10.2% (CI 4.8-18.5) died. Variables found significantly associated with complications by multivariate analysis were duration to surgery (0.027), cigarette smoking (<0.001), previous PUD history (<0.001) and hypoalbuminemia (<0.001). The ones predictive of mortality were duration to surgery (0.004), cigarette smoking (0.004), comorbid illness (0.005) and hypoalbuminemia (<0.001)

Conclusion: Perforated duodenal ulcer is the commonest location of PPU in our setup and it commonly involves young male patients without prior history of PUD.

CHAPTER ONE

1.0 INTRODUCTION

Acute peptic ulcer perforation is the commonest cause of morbidity and emergency admission in patients who are on management for peptic ulcer disease. Currently, it is estimated to account for about 70% of mortality in these patients (1). There has been a global reduction in the incidence of PUD over the recent years, that is attributed to the advances in diagnosis and treatment of the disease. The increasing availability of endoscopic facilities and expertise, H. Pylori eradication and the advent of Proton Pump inhibitors seem to have played a significant role (17)

Despite this reduction, perforations still pose a substantial health burden (7,13,14). This could be attributed to the increase in risk factors for PUD complications. These perforations occur either on the stomach or anterior surface of the duodenum (15). The patterns of presentation have been shown to vary depending on various factors including socio-demographic and environmental factors. Review of literature has demonstrated divergence in presentations and outcomes even within groups that would be considered homogeneous (3,5,25,28). This is a departure from the narrative of developing countries having a high incidence of young patients and smoking as a strong association (18) in contrast to developed countries' elderly patients with a predominance of ulcerogenic drug ingestion as an association (1).

Several factors have been associated with poor outcomes in patients presenting with perforations. They range from premorbid medical conditions (3) to delays in presentation to time between diagnosis and surgery. Other factors that have been studied include cigarette smoking, alcohol use, use of non-steroidal anti-inflammatory drugs (NSAIDS), history of previous peptic ulcer, age and the nature of ulceration. (3,12). Regionally, studies have shown that the use of recreational drugs such as miraa (khat), is associated with perforations (41).

Perioperatively, duration to surgery, size and location of perforation and the type of surgery have a bearing on the outcome of management in terms of complications and mortality. Post-operative reperforations(leaks) were reported in 16% of cases in a study done in a Tanzanian

tertiary hospital. The same study also demonstrated that delayed presentation and duration to surgery of >48 hours had a significant prediction for post-operative complications. (12).

Little work has been done on patient profiles and outcome predictors for those patients undergoing surgical management for perforations in our set up. Most of the studies carried out have focused on risk factors for Mortality and morbidity and have shown conflicting results due to varying methodology. Furthermore, epidemiological studies have shown a variance in these factors in different geographical areas. In this study we aim to describe these patients' profiles and the risk factors that contribute to adverse outcomes after surgical management.

1.1 Problem statement

Perforated peptic ulcer disease continues to contribute significantly to surgical morbidity and mortality in our region despite advancements in diagnosis and management. Studies demonstrate a variance in factors associated with poor outcomes from region to region. There is therefore a need to evaluate which factors contribute more significantly to adverse outcomes in our setup.

1.2 Objectives

1.2.1 Main objective

To determine the patient profiles and factors associated with poor outcomes in patients managed surgically for perforated peptic ulcer disease in Kenyatta National Hospital.

1.2.2 Specific objectives

1.To describe the demographic, clinical and peri-operative profiles of patients managed surgically for perforated PUD in KNH.

2.To determine the outcomes of patients managed surgically for perforated PUD in KNH.

3.To determine factors associated with poor outcomes in patients managed surgically for perforated PUD in KNH.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Background

Peptic ulcer disease is a world-wide health challenge, highlighted by its high rate of morbidity and mortality (1). In a systematic search, the estimated incidence of PUD was reported to be 0.10-0.19% with Spain posting the highest annual incidence at 141.8/100000 persons. In our region, duodenal ulcer is the most common lesion as demonstrated by Lule et al in an endoscopic observation study done in Kenyatta National Hospital (2)

The global incidence of peptic ulcer disease has shown a slight downward trend over the past few decades, this is due to the advances in the diagnostic and management modalities (7,14). Perforations, however remain a life-threatening complication and contribute substantially to the morbidity and mortality burden of the disease. This has been attributed to the increase in risk factors for PUD complications (13,14)

The profile of patients presenting with perforated PUD has shown a variance from region to region. Nasio et al demonstrated a predominance of male association for perforated PUD with an 8.3:1 male to female ratio with 57% of the patients aged 35years and below. (3) This is similar to the findings by Bekele et al in Ethiopia who observed that duodenal perforations commonly occurred in young patients, with the mean age of presentation at 33.4 years. In contrast, data from Nigeria reported perforated gastric ulcers as the commonest presentation with mean age of presentation being 49.9years (4,5)

The incidence and prevalence of PUD has been linked to rates of H. pylori infectivity with higher prevalence in countries where H. pylori is rampant. The rate of PUD in H. pylori positive individuals is around one percent, which is about six to ten-fold higher than in uninfected individuals. In these patients, the incidence of perforations increases with increasing age, with duodenal perforations occurring 2 decades earlier than gastric perforations, particularly in males. A study done at Mbagathi Hospital in Kenya found a H. pylori prevalence of 46.2% in patients with PUD (16).

There are various risk factors that have been demonstrated in literature to contribute to PUD complications which include perforations. Smoking of cigarettes has been established as an independent risk factor with incidence increasing progressively with increase in pack years. A population-based study showed a two-fold increase in the risk of PUD in smokers when compared to non-smokers. Smoking 15 cigarettes a day was found to triple the risk of perforation. (17,18)

Alcohol is associated with damage to the mucosal protective mechanisms and has been linked with increasing risk of bleeding and perforation in PUD. Heavy drinking (more than 42 drinks per week) triples this risk. (19) There is also evidence of genetic predisposition with variations in inflammatory mediators like Interleukins (IL-1b, IL-6, IL-8) and tumour necrosis factor alpha being associated with PUD (29). Genetic predisposition due to a heterogenicity of cytochrome P450 has been studied and there may be a link between this polymorphism and delays in NSAIDs metabolism. This results in prolongation of the drug effect thus enhancing their ulcerogenic effect [22].

Recreational drug use has also been demonstrated to contribute to poor outcomes in the management of PPU. Khat (*Catha edulis*), a stimulant plant whose leaves are chewed as a recreational drug across Eastern Africa and the Arabian Peninsula has been evaluated in a few studies for contribution to perforated peptic ulcers (PPU). One study in Ethiopia found 17.5% of patients with perforations had a history of khat chewing. (41)

Other factors that have been postulated include dietary factors linked to toxins associated with food storage (20). Psychological factors have been shown to have a link with studies demonstrating increase in perforations during periods of natural disasters or societal catastrophe (23).

2.2 Pathogenesis of Peptic ulcer disease and perforation

Peptic ulcer disease represents defects in the intramural aspect of the gastroduodenal wall that extend beyond the mucosa exposing the underlying layers. There are various mechanisms employed by the mucosa to prevent this damage. Protective mucus secretion by the epithelial lining in response to irritative assaults provides a physical barrier to damage of underlying layers by irritants. Besides, some cells secrete bicarbonate which acts a s a

buffering agent of acids around the mucosa. Prostaglandin E (PGE) has been postulated to increase production of both bicarbonate and mucosal layer regeneration hence useful in the protection against damage. (33, 35)

In the event of acid and pepsin breeching the epithelial cells, ion pumps in the basolateral membrane remove the extra hydrogen ions and are able to regulate the intracellular pH. Through reparation, healthy cells are able to translocate to the site of insult and aid in the regeneration of the damaged cells. Enhanced flow of blood within the mucosa also helps wash out acid that permeates through the breeched mucosa. Besides, the blood contains bicarbonate which buffers the acid on epithelial cells surface. (37)

Peptic ulcers result from the disruption of the normal mucosal protective mechanisms by superimposed insults such as H. pylori infection and the use of nonsteroidal ulcerogenic drugs like NSAIDs. These drugs act by inhibiting the of synthesis of prostaglandins which affects gastric acid secretion by the parietal cells of the stomach, the integrity of the mucosal layer, the quantity of generated bicarbonate and the mucosal blood flow rate. (34,36)

Gastric acid hypersecretion

Gastric ulcers involving the gastric body or distal antrum, and gastric ulcers associated with concurrent duodenal ulcers (DU) have a high-normal to increased acid secretion. In contrast, only a few of duodenal ulcer patients present with true acid hypersecretion. Normal to moderate levels of acid appear to be the characteristic finding in these patients regardless of their *H. pylori* infection status. (33)

Impaired duodenal bicarbonate secretion

Majority of DU patients have been found to have diminished levels of bicarbonate secretion in the duodenum. This combination of elevated gastric acid excretion and reduced local bicarbonate production results in a lower duodenal pH, which over time leads to gastric mucosa metaplasia (the presence of gastric epithelium in the first part of the duodenum) [21]. This has also been noted in patients with gastrinomas in whom excess acid secretion is linked to metaplasia of the duodenum mucosa.

The perforations can be located on the stomach or the anterior duodenal wall (4,13). In a study by Kakande (1991-2001) looking at 137 patients with peptic ulcer disease in a rural mission hospital in Kenya, the prevalence of duodenal ulcers was 87.3% with an overall mortality of 1.3% (24)

2.3 Diagnosis and Patterns of clinical presentation

Perforated peptic ulcers pose a diagnostic challenge in most patients as the presentation can vary from mild abdominal pain to marked peritonitis and shock. Some patients have presented with perforations without prior history of PUD. A study in MTRH found 14.3% of patients presenting with perforations had no prior symptoms (25). The finding of air under the diaphragm on erect plain radiograph is diagnostic in up to 75% of cases (26), it however is not specific as other causes of hollow visceral perforations can have a similar finding. Thus, a high index of suspicion and correlation with clinical profile is of the essence in making the diagnosis. CT scan is a preferred as it offers a higher diagnostic accuracy; as high as 98%. It also has the additional benefit of being able to exclude other differential diagnoses that would not warrant surgical intervention. This modality is however costly and not easily available especially in developing countries.

Upper G.I endoscopy has been used as a preferred diagnostic test in patients suspected to have complications of PUD. It has the benefit of directly visualizing the pathology and offers a chance at remedial measures in cases amenable to endoscopic intervention.

Routine laboratory tests are not helpful in diagnosis of perforation but can be used to rule out other differential diagnoses that don't require surgical intervention. These include serum amylase and lipase and acute reactant markers. Testing for H. pylori should be done in all PUD patients as positivity warrants eradication treatments.

2.4 Operative Management

Surgical management of patients presenting with perforated peptic ulcer disease has remained majorly unchanged for many years since John Mikulicz (1850 – 1905) who is credited as the first surgeon to close a perforated peptic ulcer (PPU) by simple repair. He is famously attributed to the quote, "Every doctor faced with perforated duodenal ulcer of the stomach or intestine, must consider opening the abdomen, sewing up the hole and averting

a possible inflammation by careful cleansing of the abdominal cavity" which still remains the main principle in PPU management to date. (6)

Many surgical techniques have been described for perforated PUD management, these include simple primary closure and the employment of a pedicled omental flap (patch) over the closure. (9,10) Recent studies have advocated use of non-operative methods as a stop gap measure before definitive surgical management (10). The downside of this approach in our set up has been high rates of mortality in cases of treatment failure and the lack of endoscopy and laparoscopy as adjunctive diagnostic and management facilities (10).

With advances described over the past 3 decades, the use of an omental patch with adjuvant H. pylori eradication is currently accepted as a simple, effective and safe choice in many centers. In a study done by Nasio et al, the main stay management of PUD in Kenya remains the omental patch repair with peritoneal lavage. Laparoscopic management has been tried in a few centers with varying success with most of the data being from single center audits (3). Studies have however not demonstrated differences in post-operative sepsis, re-operation rates and mortality in laparoscopic over open methods (27). The choice of technique is thus determined by the surgeons' competencies and institutional protocols.

Gastrectomy is the recommended procedure in patients with large distal gastric and malignant perforations. This has been demonstrated to enhance outcomes as patch repairs in these patients are associated with high rates of reperforations. However, Patients undergoing gastric resections (gastrectomy) still have poor outcomes compared to omental patch as demonstrated by Chung et al. The same study established that 10% of patients with perforated DU required gastric resection (9).

2.5 Outcomes

Despite advances in the diagnostic approaches and surgical techniques for the management of perforated peptic ulcers, morbidity and mortality still remain high. Post-operative complications have been associated to varying patient variables, including age, sex, shock status at presentation, presence of co-morbid conditions, time to surgery, site and size of perforation. Delays in diagnosis and institution of management has also been demonstrated to contribute to increased rates of mortality. (3).

Several Risk-stratification models have been studied for PPU, but most of them are only applicable to specific populations with distinct patient characteristics. Some of the tools that have been used include the Boey score, Acute physiology and Chronic Health Evaluation II (APACHE II), the American society of anaesthesiologists (ASA) score and the Hacettepe score. These tools employ different patient characteristics and attributes and as such the validity of each one of them varies from population to population. (39). The Boey score and ASA score have been utilized in varied population groups and are the commonly used scores for prediction of outcomes in PPU but both demonstrate variations in application accuracy. (40) According to the WSES guidelines of 2020, hypoalbuminemia has been shown to be the single most prognosticator of mortality in patients with PPU. (42,43).

Common post-operative complications that have been evaluated include Reperforation (repair leaks), intraabdominal sepsis and surgical site infections. Many reviews have observed that re-perforations significantly increased the morbidity and mortality rates in these patients in the post-operative period. In a study done in Tanzania, SSIs were the commonest post-operative complication (48%) with intra-abdominal sepsis being observed in 20% of the study subjects. (28). This is different from a study by Kuremu in MTRH which found pneumonia to be the most common complication following surgery for PPU. (25)

Risk factors for mortality have been evaluated in several studies and they have shown a variance by regions. In a study done in Tanzania, a significant association was observed between mortality and shock at presentation, age >40 years, premorbid illness, duration of disease of >24 hours and surgery delay of > 48 hours. Presence of post-operative complications was in itself a significant predictor of mortality [p value-0.011] (28)

In a study done by Nasio et al, on surgical outcomes in PPU patients in KNH, an overall mortality of 14.3% was reported which was higher than the 2.7-13% reported by Boey et al (3,38) The mortalities were attributed to long interval between perforation and surgical management. Past history of PUD, alcohol use and cigarette smoking were not statistically significant associations to mortality.

2.6 Study justification

Despite improvements in the surgical management of perforated PUD in the last three decades, little data exists in our setup looking at the outcomes and factors that are associated with the high morbidity and mortality rates that have been observed in the region. This study seeks to address this gap by demonstrating these patients' demographic, clinical and operative factors and assessing their association to surgical outcomes in an effort to build local data with the aim of improving morbidity and mortality from the disease.

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study design

The study design was a Retrospective Cross-Sectional Study analyzing records for patients operated on for perforated PUD between January 2014 and December 2020.

3.2 Study site

The study was conducted at the Kenyatta National Hospital Health Information and Records Department.

3.3 Study population

The target population for this study comprised all patients surgically managed for perforated PUD from January 2014 to December 2020 in KNH.

3.4 Inclusion Criteria

All patients surgically managed for perforated PUD at KNH during the study period.

3.5 Exclusion criteria

1. Patients operated on in peripheral facilities before referral to KNH with post- operative complications.
2. Perforations due to any histologically confirmed gastrointestinal malignancies.

3.6 Sample size

This was a Census study and all the patients in the study population who met the inclusion criteria were recruited.

3.7 Materials

A pre-designed data extraction tool (Appendix 1) was used to collection data from the patients records at the health information and records department. The Boey score (Appendix 2) was included in the extraction tool and was used as a validated predictor of outcome against which the dependent variables were measured. Data was abstracted retrospectively from the patient files at the KNH Health Information registry.

3.8 Data collection and storage

This was done by the principal investigator and two research assistants who were medical officers at KNH. The officers were trained on data collection methodology and utilization of the study data collection tool.

Both Electronic and manual document searches were employed in patient file retrieval. ICD codes for perforated PUD, perforated duodenal ulcers and perforated gastric ulcers were used to electronically search for files by file number in the KNH patients' records database. These statistics were then be used to manually retrieve the physical patient files from the registry.

A predesigned data extraction tool was used to collect data from patient records and each participant will be designated by a study specific serial number.

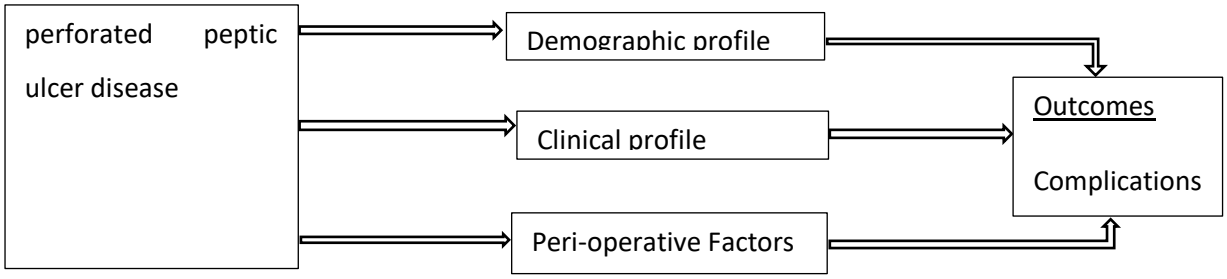
Data collected was tabulated and entered in tally sheets and collated using spread sheets in Microsoft excel. Electronic copies of spread sheets, data analysis sheets were stored in a password protected external hard drive accessible only to the investigator and supervisors.

3.9 Data Variables

Independent variables were categorized into demographic profile, clinical profile and operative factors with several factors evaluated in each group (as shown in the table below). Outcomes of interest in this study were post-operative complications and Mortality.

Type of Variable	**Characteristic/Objective**	**Variables**
Independent	Demographic profile	Age, gender, occupation
	Clinical profile	Presenting symptoms, Duration of symptoms, associated co-morbid illnesses, previous PUD history, History of NSAID use, smoking, alcohol use.
	Peri-operative factors	Duration to surgery, location and size of perforation, type of surgical procedure.
Dependent	Outcomes	Post-operative complications, mortality.

3.10 Conceptual framework



3.11 Data analysis

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 24.0 for windows. Continuous variables were analyzed and presented as means, medians, standard deviations and ranges. Categorical data was presented as frequencies and proportions.

Continuous variables were categorized and bivariate logistic regression used to evaluate the level of significance of association between independent variables and the outcomes.

Variables found to be significant advanced to Multivariate logistic regression analysis to determine independent variables predictive of outcome. Results of regression analysis were presented in odds ratios with a 95% confidence interval. P value of <0.05 were considered statistically significant for both models of logistic regression analysis.

3.12 Ethical considerations

The ethical approval to carry out this study was obtained from the KNH-UON ethics and research committee as per the letter referenced KNH-ERC/A/200 dated 11th June 2021.The permission to collect data was the sought from the KNH research office.

All patients' information was handled with confidentiality with participants being assigned unique serial numbers to conceal identity.

The findings of the study shall be disseminated to the KNH and UoN and be presented for publication in reputable medical journals for the benefit of the medical profession and public.

3.13 Quality assurance

The research assistants were trained in handling of the data to improve quality of and minimize standard errors. Cleaning and sorting out of data fields was done before data

analysis and electronically checked for duplications. Statistical summaries were used to check for any discrepancies and the procedures documented.

CHAPTER 4

4.0 RESULTS

4.1 Statistics

A total of 104 patient records were retrieved from the KNH records and information file archives. Out of these, 88 were eligible for the study with 16 files excluded from the study due to incomplete data and failure to meet the inclusion criteria.

4.2 Socio-demographic profile

Out of the 88 patients operated on for Perforated peptic ulcers during the period of the study, eighty-one (92.0%) were males while seven (8.0%) were female with a male to female ratio of 11.3: 1.

The overall range of age for the patients presenting and operated on for perforated PUD was 14-83 years with a mean age of 35.6 (SD 14.92) and a median age of 33 years as indicated in figure 1 below.

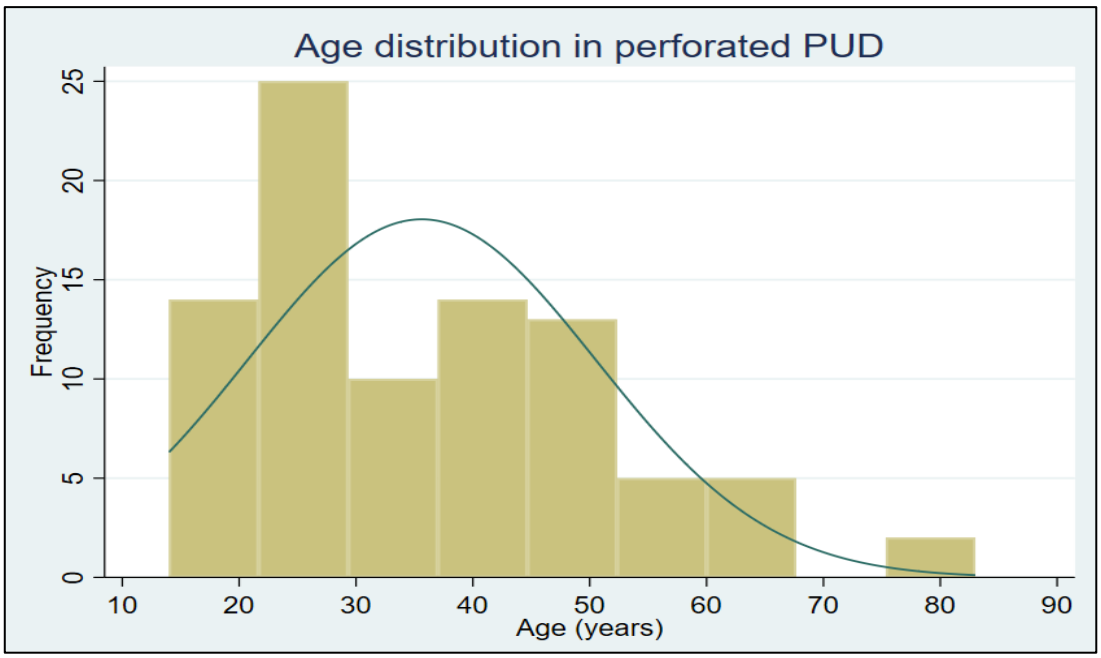


Figure 1: Age distribution of patients operated on for perforated PUD

These patients were categorized in groups of 10 years intervals. The peak incidence of the patients in this study was in the third decade (20-29 years) as presented in table 1; majority of the patients, 45 (51.1%) were younger than 40 years.

Table 1: The age incidence of perforated PUD

Decade	Age group	Frequency	Percent
2	10 – 19	6	6.8
3	20 – 29	33	37.5
4	20 – 39	16	18.2
5	40 – 49	18	20.5
6	50 – 59	8	9.1
7	60 – 69	5	5.7
8	70 – 79	1	1.1
9	80 – 89	1	1.1

4.3 Clinical Profile

The duration of symptoms at presentation ranged from 1-14 days with a mean of 4.4 (SD 2.9) days. The median duration was 4 days.

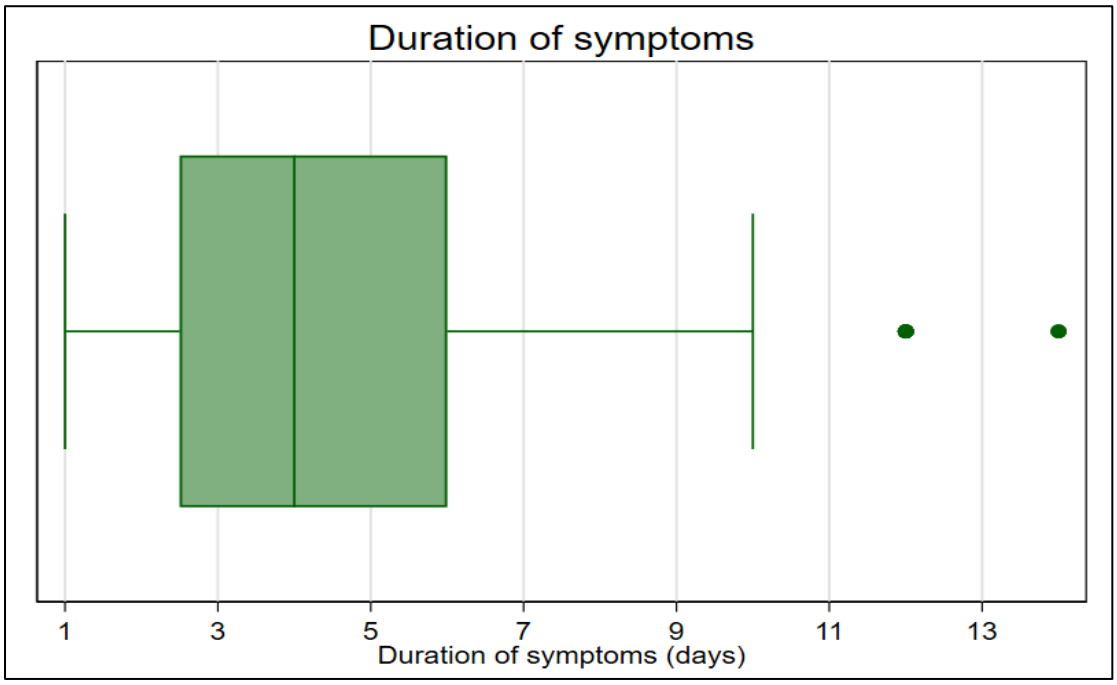


Figure 2: Box plot showing duration of symptoms (days)

Twenty-two patients (25%) presented within 48hours of onset of symptoms compared to 66(75%) who presented after 48 hours. The commonest presenting symptoms were

abdominal pain 84(95.5%), Vomiting 53(60.3%) and abdominal distension 29(33.0%) as shown in figure 3 below.

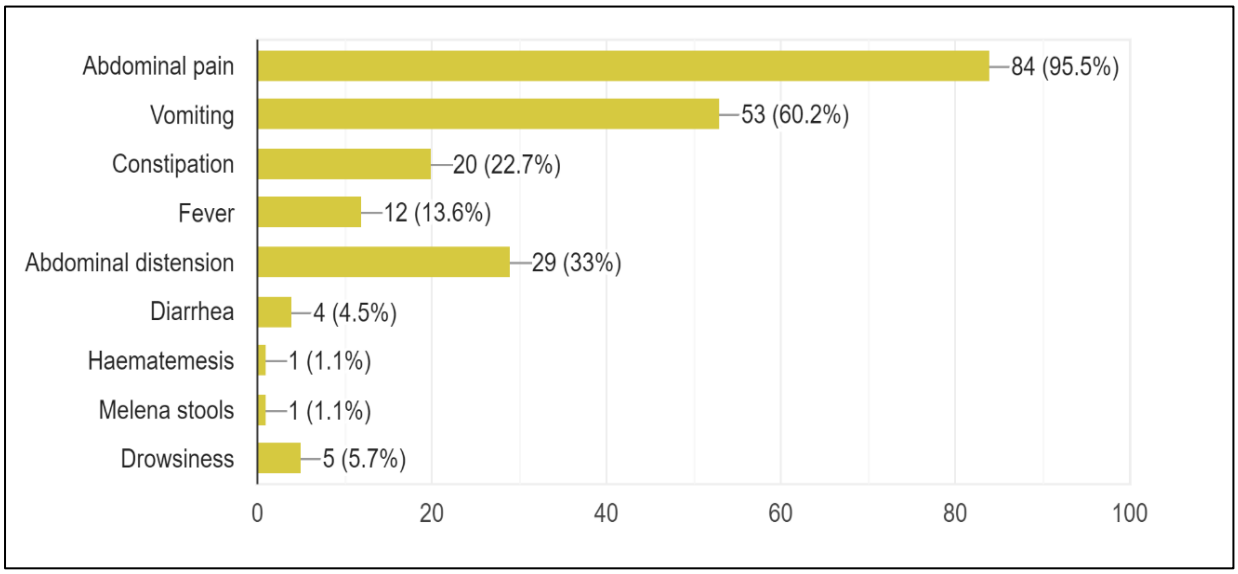


Figure 3: Presenting complaints

Several variables were assessed for prediction of outcomes. Fifty-four (62.1%) of the patients reported no prior history of PUD compared to thirty-three (37.9%) who had prior history. All those who had history of PUD were not on regular anti- ulcer treatment. Ingestion of ulcerogenic drugs was recorded in only 10 (12.7%) of the participants, with all being on an NSAID for management of some form of pain.

Other risk factors that were evaluated included Alcohol consumption and cigarette smoking. These were found in 45 (51.7%) and 37 (43.0%) of the patients respectively. Of note was that most of the patients who consumed alcohol also had a history of cigarette smoking. Co-morbid illnesses were reported in 7 (8%) of the participants, with hypertension reported in 3 patients and CCF, rheumatoid arthritis, Bladder outlet obstruction and femur fracture each in one patient.

Recreational drug use was reported in 11 patients with 9 out of these presenting with history of khat (miraa) chewing and 2 marijuana smoking.

Low albumin levels were demonstrated in 41(60.3%) of the 68 patients who had their levels assessed at presentation which was a representation of 77.2% of the total number of

participants enrolled in the study. We also looked at the haemoglobin levels at presentation and 7 (7.9%) of the sample size had haemoglobin levels below 10g/dl.

4.4 Peri-Operative profile

The time from presentation to surgery ranged from 4- 264 hours with a median of 17.4 hours. Intraoperatively, most of the perforations were located in the duodenum 58 (68.2%) whereas the remaining 27(31.8%) were gastric in location. The site was not indicated in three patients.

The mean age of patients with gastric ulcers was 38.5(SD 15.5) which was higher than those with duodenal ulcers 34.8(SD 14.8) as shown in table 2 below. This difference was statistically insignificant.

Table 2: Distribution of age by location of perforation

Type of ulcer	Frequency	Mean age	SD	Range	median
Duodenal	58	34.8	14.8	14 – 79	30.5
Gastric	27	38.5	15.5	16 – 83	36

Intra- operatively, majority of the perforations were found to be less than 2centimetres in size 67 (79.13%) while 8(9.09%) were more than 2centimetres. Three patients (3.4%) had self-sealed perforations at laparotomy.

4.5 Surgical management

Modified Graham's omental patch was the repair method of choice in majority of the patients, being employed in 76 (86.4%) of the perforations while 7(8.0%) were repaired with simple closure. One patient had a falciform ligament patch closure and another one had pyloric exclusion with a gastro-jejunostomy by-pass due to large size of ulcers. Of the omental patch closures, 5 were done as revision surgeries after initial patch closure failure. Two patients had partial gastrectomy and gastro-jejunostomy by pass as part of revision surgery while one had pyloric exclusion with the gastro-jejunostomy by pass.

4.6 Outcomes of surgery

Out of the study sample, 52 (59.1% [CI 48.1 – 69.5]) patients had post- operative complications while 36 (40.9%) did not have complications.

The Mean age of patients who developed complications post operatively was found to be 37.6 (SD 16.6) years while those who didn't was 32.8 (SD 11.6). The difference in these mean ages was not statistically significant (p=0.137).

Mortality was reported in 9 patients (10.2% [CI 4.8-18.5]) with 79 (89.8%) surviving.

Table 3: Incidence of complications by age

Complications	Observations	Mean	SD	P value (t test)
No	36	32.8	11.6	0.137
Yes	52	37.6	16.6	

The post-operative complications that were recorded are as in figure 7 below, with acute renal compromise being the commonest complication 29(33%) followed by electrolyte derangements 22(25%) and surgical site infection 17(19.3%). Some patients experienced more than one complication.

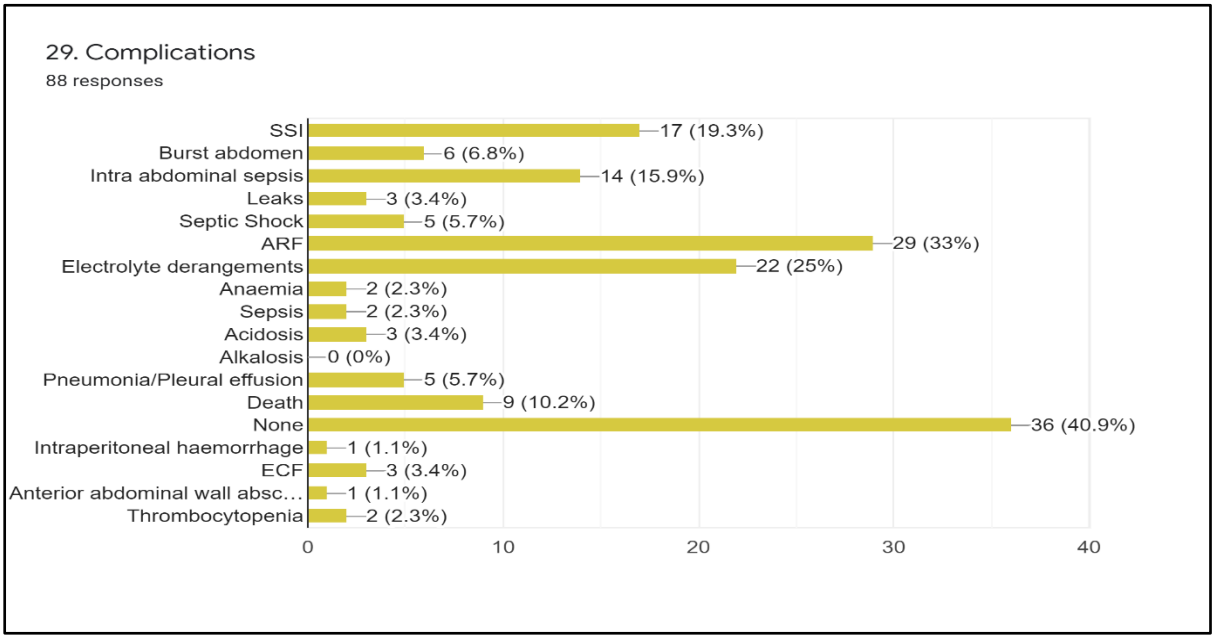


Figure 4: Post-operative complications

Complication rates and mortality rates for Boey score were as indicated table 4 below. In this study we found that as the Boey score increased, the risk of morbidity and mortality increased significantly. Values were analyzed against a validated Boey score as indicated in Appendix 2.

Table 4: Boey scores vs complications and mortality

Risk score	Mortality rate				Complication rate			
	Alive	Died	Mortality rate %	P value against validated scores	Yes	No	Complication rate (%)	P value against validated scores
0	6	0	0	-	1	5	16.7	-
1	58	3	4.9	0.372	33	28	54.1	0.267
2	15	5	25	0.447	17	3	85	0.302
3	0	1	100	-	3	0	100	0.344

Table 5: Predictors of complications according to univariate logistic regression analysis

Independent variable	Categories	N (%)	Complications N (%)		Univariate analysis	
			Yes	No	Crude OR 95% CI	p- Value
Age	<35 >35	48 (54.6) 40 (45.5)	27 (30.7) 25 (28.4)	21 (23.9) 15 (17.1)		0.553
Sex	Male Male	81 (91.9) 7 (8.1)	47 (54.7) 4 (4.7)	34 (37.2) 3 (3.5)		0.601
Comorbid illness	Yes No	7 (8.1) 80 (92)	5 (5.8) 46 (52.9)	2 (2.3) 34 (39.1)		0.385
NSAID use	Yes No	10 (12.7) 69 (87.3)	4 (5.1) 44 (55.7)	6 (7.6) 25 (31.7)		0.138
Alcohol use	Yes No	45 (51.7) 42 (48.3)	29 (33.3) 22 (25.3)	16 (18.4) 20 (23.0)		0.283

Cigarette smoking	**Yes** **No**	**37 (43.0)** **49 (57.0)**	**27 (31.4)** **24 (27.9)**	**10 (11.6)** **25 (29.1)**	**2.8 (1.0 – 7.9)**	**0.025**
Recreational drug use	Yes No	11 (12.5) 77 (87.5)	7 (8.0) 45 (51.1)	4 (4.6) 32 (36.4)		0.506
Albumin level	**Low** **Normal**	**41 (60.3)** **27 (39.7)**	**30 (44.1)** **13 (19.1)**	**11 (16.2)** **14 (20.6)**	**2.9 (1.1 – 8.2)**	**0.036**
Previous PUD	**Yes** **No**	**33 (37.9)** **54 (62.1)**	**27 (31.0)** **24 (27.6)**	**27 (31.0)** **9 (10.3)**	**2.7 (1.04 – 6.8)**	**0.037**
Location of ulcer	Duodenal Gastric	58 (68.2) 27 (31.8)	33 (38.8) 16 (18.8)	25 (29.4) 11 (12.9)		0.514
Size of ulcer	<2 cm >2cm	67 (89.3) 8 (10.7)	38 (50.7) 6 (8.0)	29 (38.7) 2 (2.7)		0.275
Duration to surgery	<48 hours >48 hours	78 (90.7) 8 (9.3)	46 53.5) 6 (7.0)	32 (37.2) 2 (2.3)		0.235

Factors significant in the bivariate analysis were advanced to multivariate model using the logistic regression. In the model, the strongest risk factors predicting occurrence of complications were cigarette smoking, history of previous PUD, and albumin levels

Table 6: Predictors of complications according to multivariate logistic regression analysis

Risk factor	Adjusted odds ratio	95% CI	P value
Cigarette smoking	2363.4	533.3 – 10474.3	<0.001
Previous PUD	593.4	101.9 – 3453.5	<0.001
Albumin level	3854.5	516.5 – 28764.0	<0.001

Table 7: Predictors of mortality according to univariate logistic regression analysis

Independent variable	Categories	N (%)	Mortality N (%)		Univariate analysis	
			Yes	No	Crude OR 95% CI	p-Value
Age	<35 >35	48 (54.6) 40 (45.4)	3 (3.41) 6 (6.8)	45 (51.1) 34 (38.6)		0.160
Sex	Male Female	79 (91.9) 7 (8.1)	8 (9.3) 1 (1.2)	71 (82.6) 6 (6.9)		0.552
Comorbid illness	**Yes No**	**7 (8.1) 80 (92.0)**	**4 (4.6) 5 (5.8)**	**3 (3.5) 75 (86.2)**	**20.0 (3.5 – 115.0)**	**0.002**
NSAID use	Yes No	10 (12.7) 69 (87.3)	1 (1.3) 8 (10.1)	9 (11.4) 61 (77.2)		0.682
Alcohol use	Yes No	45 (51.7) 42 (48.3)	5 (5.8) 4 (4.6)	40 (45.9) 38 (43.7)		0.544
Cigarette smoking	**Yes No**	**37 (43.0) 49 (57.0)**	**7 (8.1) 2 (2.3)**	**30 (34.9) 47 (54.7)**	**5.4 (1.1 – 28.2)**	**0.031**
Recreational drug use	Yes No	11 (12.5) 77 (87.5)	1 (1.1) 8 (9.1)	10 (11.4) 69 (78.4)		0.687
Albumin level	**Low Normal**	**41 (60.3) 27 (39.7)**	**7 (10.3) 0 (0.0)**	**34 (50.0) 27 (39.7)**	**_**	**0.023**
Previous PUD	Yes No	33 (37.9) 54 (62.1)	4 (4.6) 5 (5.8)	29 (33.3) 49 (56.3)		0.466
Site of ulcer	Duodenal Gastric	58 (68.2) 27 (31.8)	5 (5.9) 4 (4.7)	53 (62.4) 23 (27.1)		0.305
Size of ulcer	<2 cm >2cm	67 (89.3) 8 (10.7)	8 (10.7) 0 (0)	59 (78.7) 8 (10.7)		0.387
Presence of complication	Yes No	**52 (59.1) 36 (40.9)**	**9 (10.2) 0 (0.0)**	**43 (48.9) 36 (40.9)**	**_**	**0.006**
Anaemia	<10g/dl >10g/dl	7 (7.9) 81 (92.1)	2 (2.2) 7 (8.0)	5 (5.7) 74 (84.1)		0.149
Shock at admission	SBP > 100 SBP<100	65 (73.9) 23 (26.1)	6 (6.8) 3 (3.4)	59 (67.1) 20 (22.7)		0.433
Duration to surgery	<48 hours >48 hours	78 (90.7) 8 (9.3)	8 (9.3) 1 (1.2)	70 (8.4) 7 (8.1)		0.843

Factors significant in the bivariate analysis were advanced to multivariate model using the logistic regression to assess the risk of mortality. In the model, the strongest risk factors predicting mortality were low albumin levels, cigarette smoking, comorbid illnesses and presence of complications.

Table 8: Predictors of mortality according to multivariate logistic regression analysis

Risk factor	**Adjusted odds ratio**	**95% CI**	**P value**
Cigarette smoking	53.3	8.8 – 323.6	0.004
Comorbid illness	1436719	73.5 – 2.81^10	0.005
Albumin level	343.7	19.3 – 6135.4	<0.001
Complications	17.9	2.2 – 145.7	0.007

CHAPTER 5

5.0 DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Discussion

In this study a total of 88 patients were operated on in KNH for perforated PUD over a period of 5 years. This translates to an average of 17.6 cases annually. This finding is in comparable to a study done in Tanzania (12) that found an average of 17 patients. Similarly, a study done in Liberia recruited 20 patients over a period of one year (28). Another study done in KNH found an annual average of 25 patients underwent surgery for perforated PUD (3). These figures may be an under representation as several cases were excluded from these studies for failure to meet the inclusion criteria and document retrieval challenges.

We noted that Perforated PUD predominantly affected young males with a male: female ration of 11.3:1. This is slightly higher than figures in previous literature across the continent with 3.5:1 in Nigeria and 1.3:1 in Tanzania (5,12). It however comes in the range of figures found in a study by Nasio et all in KNH that recorded a ratio of 8.3:1. (3). This contrasts the western world depiction of Perforated PUD as a disease of the elderly female (1). The male predominance in this study could be attributed to excessive alcohol consumption and cigarette smoking which is more common among men in our set up as demonstrated by Risa T. et al (45). Alcohol is a noxious agent that is associated with damage to mucosal protective mechanisms and cigarette smoking impedes regeneration by affecting mucosal blood flow and angiogenesis (18,19).

The use of recreational drugs has been reported in emerging literature as a contributor to perforations in PUD. Khat has been studied in a few horn of Africa countries and found to be a significant risk factor for perforation (41). In this study 10.2% of the patients reported history of chewing Khat.

The mean age of presentation of patients with perforated PUD was found to be 35.6 years with a peak incidence in the third decade. PPU were found to afflict the young patients equally with no significant difference in mean age of presentation for duodenal and gastric ulcers (34.8years and 38.5 years respectively). This is unlike findings by Bekele et al in Ethiopia who reported that duodenal perforations were more common than gastric ones

(4). In Nigeria Dongo et al found that PPU were more common in gastric ulcers with a mean age of presentation of 49.9 years (5).

More than 95% of patients had the classical presentation of acute abdominal pain. This may be due to the average young patients in this study as opposed to elderly patients who are likely to present with silent perforations. The duration of symptoms was descried as the time from onset of acute symptoms of abdominal pain to presentation. We found 76.1 % of the patients presented after 48 hours of onset of symptoms. This is in agreement with studies in developing countries that report delayed presentation in patients managed for perforated PUD (3,4,5) This can be attributed to the socio-economic status of most of the patients and the lack of access to health care facilities. Healthcare itself is expensive and this may inform the fact that patients only seek help when the pain becomes unbearable after trial of homemade and over-the-counter remedies.

Ingestion of ulcerogenic drugs is a prominent risk factor for perforated peptic ulcers in the developed world (36). In this study, this only 10 (12.7%) patients out of the sample size reported history of chronic ulcerogenic drugs. The offending drugs were mostly NSAIDS taken for pain management of chronic pain. This low percentage could be attributed to the availability of alternative classes of analgesics. Our findings were similar to study by Chalya et al that found an incidence of 10.7% NSAID use among patients with perforated DU. The reason for these low figures compared to western data may be due to the fact that our patients are predominantly young and may not have significant chronic pain conditions like the elderly patients seen in the west.

In agreement with other studies (3, 12, 25) majority of the patients did not have a history of prior PUD, and for the 37.9% who did, it was established that they were not on regular anti-ulcer medication. This confirms the observation in many other studies that found out that the diagnosis of PUD in most developing countries is first made when the patients present with a perforation. This underscores the fact that the patients without prior history of PUD or the ones with asymptomatic disease are at a higher risk of perforation as they are unlikely to have taken any preventive measures or have been on proactive management.

The prevalence of hypo-albuminemia in this study was 60.3%. This is in agreement with a few studies that have found hypoalbuminemia as a predictor of outcome in patients with

perforated PUD (43). The WSES guidelines 2020 quote hypoalbuminemia as the single most prognosticator of mortality in patients with perforated PUD (42). Hypo albuminemia is a negative marker of infection and nutritional status which is a reflection of reduced immunity hence these patients may be more susceptible to perforations.

Duodenal ulcers perforations were the commonest with a duodenal to gastric perforation ratio of 2.1:1. This is in contrast to previous data that has reported low cases of gastric perforations in our set up. A study done in KNH (3) found duodenal to gastric perforation ratio of 13: 1 and one by Tenge et al in Eldoret reported a ratio of 11.5:1 (25). We found no obvious reason to explain this changing epidemiological profile but we note the similarity in pathogenesis of PPU and the role of H. pylori infestation which is more common in young patients (16,33).

The operation of choice was a modified Graham's omental patch. This is consistent with data from other studies across the globe which have concluded the patch repair as simple and effective (3,6,9,10,13). Simple closure was employed in 7.9% of the cases. Pyloric exclusion or gastrectomy with bypass roux-n-y in was used in 4.5% of cases but was used for large ulcers >2cm or in revision repairs after failure of the primary repair. Graham's patch has been recorded as an effective and safe method of closure of the perforations, though it has been associated with ulcer recurrence rate of up to 40% in some series. Better results are achieved with concomitant H. pylori eradication (44). This study reported a 9.6% failure/leaks after the primary repair with omental patch.

In this study the outcomes were measured by the rate of post operative complications and the incidence of mortality following surgical management of perforated PUD. The rate of post-operative complication was 59.1% with the incidence of mortality at 10.2%. The Commonest complications observed in this study was acute renal failure 29(33%) followed by deranged electrolytes 22(25%) and surgical site infections 17(15.9%) respectively. This could be attributed to sepsis as majority of the patients had delayed presentation. The complication rates and mortality rates for Boey scores in this study was consistent with other studies where the rates increased with increase in score (38,39,40).

Determining the best predictors of complications was evaluated by the logistic regression models after adjustment for confounding factors. Cigarette smoking and hypoalbuminemia

levels were the most important risk factor for post operative complications and mortality. Previous studies have shown similar associations (3,5,18). The low albumin level was found to be a significant predictor of post- operative complication as well as mortality ($p<0.001$) and this is consistent with literature and the WSES guidelines that cite it as an independent predictor of poor outcomes in patients with PPU (42,43). Previous history of PUD was a risk factor for post operative complications but did not have a significant association with mortality. The effect of this variable on outcomes in perforated PUD is still in debate.

As reported in other studies (12), comorbid illnesses and the presence of post- operative complications were significantly associated with mortality in this study (p 0.005; 0.007). Hypertension and Congestive cardiac failure were the most common comorbid conditions recorded in this population.

5.2 Conclusion

Perforated duodenal ulcers are the commonest presentation of PPU in our setup with majority of the patients presenting in the third decade of life without previous history of PUD. Gastric ulcer perforations are however increasingly becoming a common presentation in this population.

Majority of the patients have delayed presentation, with majority showing hypo-albuminemia at presentation. This was found to be a significant predictor of post- operative complications and mortality.

The strongest predictors of post operative outcomes were duration to surgery, cigarette smoking, low albumin levels, previous PUD, presence of comorbid illnesses and the presence of complications.

5.3Recommendations

1.The findings in this study can be used to inform policy on management of PUD. Sensitization and screening of the public for this condition should be enhanced so that preventive measures are instituted early to avert complications. Public health strategies can also be extended to measures to mitigate malnutrition as low albumin levels has been shown to be a significant risk for PPU.

2.Further research possibly in the form of a prospective or a multi-Centre study that recruits a larger sample size would be helpful in determination of these profiles and associations in the country.

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APPENDICES

Appendix 1: Data extraction tool

Serial no……..

A. BIODATA

Age (In Years)	……	
Gender	Male □	Female □

B. CLINICAL PROFILE

Presenting complaints	□Abdominal pain	□Vomiting
	□Constipation	□Fever
	□Abdominal distension	□Dyspepsia
	□Other (Specify)……..	
Duration of symptoms	…….	
Vital signs at presentation	BP……/……. Pulse……	Respiratory rate……
Previous history of PUD	Yes □	No□
Co-morbid illness	Yes□	No□

If yes, specify ……..

History of cigarette smoking	Yes □	No □
History of alcohol use	Yes□	No□
History of other recreational drugs use	Yes□	No□

If yes, specify…….

History of ulcerogenic drug use	Yes□	No□
Laboratory investigations	Hb level ……g/dl	Albumin……. g/l

C. PERI- OPERATIVE FACTORS

Time to surgery (Time from presentation to operation) ……..

Location of perforation	□Gastric	□Duodenum
Size of perforation (cm)	…….	
Type of surgery performed	□ modified omental patch	
	□Omental patch with pyloric exclusion	
	□Gastrectomy	

□Others (specify) ……..

D. OUTCOMES

Post-operative complications	□Superficial and deep SSI	□Burst abdomen
	□Intra- abdominal sepsis	□Septic shock
	□Leaks	□ECF
	□Pneumonia/ Pleural effusion	□ARF
	□Electrolyte derangements	□Death
	□Others (Specify)……	
Mortality	Yes □	No □

E. BOEY SCORE

Risk factors	**Score**
Duration of initial symptoms to admission >24hours	
Pre-operative SBP <100mmHg	
Any one or more systemic illness	
Total	

NB. -A score of 1 is given for presence of each of the risk factors and 0 for absence

Appendix 2: Validated Boey score

Risk score	Mortality (OR)	Morbidity (OR)
1	8% (2.4)	47% (2.9)
2	33% (3.5)	75% (4.3)
3	38% (7.7)	77% (4.9)

Boey score factors.
Concomitant severe medical illness.
Preoperative shock.
Duration of perforation > 24 hours.
Score: 0–3 (Each factor scores 1 point if positive).
Adapted from Lohsiriwat V, Prapasrivorakul S, Lohsiriwat D. Perforated peptic ulcer: clinical presentation, surgical outcomes, and the accuracy of the Boey scoring system in predicting postoperative morbidity and mortality. World J Surg. 2009 Jan;33(1):80–65.