

**A STUDY OF FACTORS ASSOCIATED WITH MORTALITY IN
PATIENTS MANAGED FOR PERFORATED PEPTIC ULCERS
AT UNIVERSITY TEACHING HOSPITAL, LUSAKA, ZAMBIA**

**DR. EDWARD NKHULA NYIMBILI
(BSC.HB, MBChB)**

**A dissertation submitted to the University of Zambia in partial
fulfillment of the requirements for the award of the Master of
Medicine Degree in General Surgery**

**University Of Zambia
School Of Medicine
Lusaka
2019**

COPYRIGHT

All rights reserved. No part of this dissertation may be reproduced, stored in a retrieval system or transmitted in any form by other means – electronic, mechanical, photocopying or recording without prior consent from the author.

Dr. Edward Nkhula Nyimbili.

DEDICATION

To my loving wife, Hope Phiri, and our children Khumbo and Chigomezzyo, thank you for your support and encouragement and your understanding when I was spending time away from you during preparation of this work. This would not have been possible without you by my side, you are my inspiration. To the memory of my mother and father, I know this would have made you proud.

DECLARATION

I Dr. Edward Nkhula Nyimbili, do hereby declare that this dissertation herein presented for the Degree of Master of Medicine General Surgery represents my own work. It has not been previously submitted either in whole or in part for any other Degree at this or any other university, nor is it currently being submitted for any other Degree.

Signed:

Approved by:

.....

Student: **Dr. Nyimbili Edward Nkhula – BSc. (H.B.), MBChB**

Approved by:

.....

Supervisor: **Dr. Zulu Robert – BSc. (H.B.), MBChB, MMed. (Gen. Surgery)**

APPROVAL

This dissertation of Dr. Edward Nkhula Nyimbili is approved as fulfilling part of the requirements for the award of the degree of Master of Medicine in General Surgery by the University of Zambia.

Examiner 1:.....

Signature

Date:.....

Examiner 2:.....

Signature:.....

Date:.....

Examiner 3:.....

Signature:.....

Date:.....

Chairperson,

Board of Examiners:.....

Signature:.....

Date:.....

Supervisor:.....

Signature:.....

Date:.....

ABSTRACT

Perforated Peptic ulcers (PPU) is one of the common finding in patients undergoing emergency laparotomy for peritonitis at UTH, Adult Hospital, department of surgery, representing about 26.45% of these cases in a calendar year. A high risk of mortality and morbidity is encountered in patients treated with surgery for PPU. Patient stratification and appropriate management according to patients risk of mortality, has been recommended as a way of trying to improve outcomes in patients with PPU. The aim of the study was to investigate the factors associated with mortality in patients that present with PPU managed surgically at UTH. This was a prospective cohort study, conducted at UTH-Adult Hospital, Department of surgery targeting patients with PPU that had undergone emergency laparotomy. They were enrolled using interview administered questionnaire and followed up for 30-days post-operation. The primary outcome was 30 day post-operation mortality. The study enrolled 38 participants of which 35 participants met the inclusion criteria, 88.57% (n=31) male and 11.43% (n=4) female. The age ranged from 14 years to 84 years with the mode age ranges 20 years – 30 years and 40 years – 50 years. Most patients presented with two (2) or more complaints. Abdominal pain was common presenting complaint in all the patients and other complaints included, nausea and vomiting, abdominal distension and constipation. 82.86% (n=29) of the participants presented after 24 hours of onset of symptoms, 17.14% (n=6) were HIV positive and 42.86% (n=15) were in shock on presentation. More than half of the participants were assessed as ASA score III or greater. On admission 40.00 % (n=14) had elevated serum creatinine and 37.1 % (n=13) had low serum albumin. 91.43% (n=32) of PPU were gastric perforations and 8.57 % (n=3) duodenal perforations and the mode and median range of size of perforation was 5mm – 10mm. Length of hospital stay ranged from one(1) day to 13 days with a mean of 7.29 days. 30-day post-operation mortality was 34.29% and 40% of the participants developed a post operation complication. Univariate binary regression analysis found Age, ASA score, Serum creatinine, and Size of perforation to be significantly associated with mortality (p-value <0.05, C.I. 95%). Univariate linear regression analysis found HIV positive Status, and CD4 cell count level to be significantly associated with mortality(p-value <0.05; 95% C.I.). Multivariate binary regression analysis found no significant association with mortality of the above variables (p-value <0.05; C.I. 95%). PPU is a common finding among patients with peritonitis undergoing emergency surgery at UTH and is associated with high mortality. Univariate statistical analysis found Age, ASA score, Serum creatinine, Size of peptic ulcer perforation, HIV Status and CD4 cell count level to be associated with mortality. However, no factor was found to be significantly associated with mortality on multivariate regression analysis.

KEY WORDS: *PPU, 30-Day post-operation Mortality, Laparotomy*

ACKNOWLEDGEMENTS

I would like to sincerely thank my supervisor, Dr. Robert Zulu, for all the encouragement and support during the whole study period. I am in your debt. My consultant, Dr. Mwila Lupasha for constantly asking about the progress of the study, this kept me focused on what needed to be done. I would like to thank Dr. Chadwick L. Ngwisha and Dr. Soka Nyirenda for their input in the early stages of my research proposal formulation, your input is invaluable. Lastly but not the least, Dr. Edgar P. Shilika and all the registrars in the Department of pathology for helping expedite the pathology result for my study participant, am grateful.

TABLE OF CONTENTS

COPYRIGHT	i
DEDICATION.....	ii
DECLARATION.....	iii
APPROVAL	iv
ABSTRACT.....	v
ACKNOWLEDGEMENTS	vi
LIST OF TABLES	x
LIST OF FIGURES	xi
LIST OF APPENDICES	xi
ABBREVIATIONS	xii
CHAPTER ONE: INTRODUCTION.....	1
1.1 Background	1
1.2 Introduction	2
1.3 Statement of the Problem	2
1.4 Study Justification	3
1.5 Research Question.....	3
1.6 Objectives.....	4
1.61 Main Objective.....	4
1.62 Specific Objectives.....	4
CHAPTER TWO: LITERATURE REVIEW.....	5
2.1 Perforated Peptic Ulcer and Surgery.....	5
2.2 Factors associated with mortality globally.....	6
2.3 Factors associated with mortality Sub-Sahara Africa	7
2.4 Clinical Scores Predicting Mortality.....	8
CHAPTER 3: STUDY METHODOLOGY	9
3.1 Study design and duration.....	9
3.2 Target Population	9
3.3 Study Site Area.....	9
3.4 Inclusion Criteria.....	9
3.4 Exclusion Criteria.....	9
3.5 Definition used in the Study.....	9
3.6 Sample Size	10
3.7 Sampling Method	10
3.8 Data Collection.....	10
3.9 Data Analysis Plan	10

3.10 Variables.....	11
3.10.1 Independent (predictor) Variables	11
3.10.2 Dependent (outcome) Variables	11
3.11 Ethical Considerations.....	11
3.12 Study Limitation.....	12
CHAPTER FOUR: RESULTS	13
4.1 Demographic Characteristic of Participants.....	13
4.1.1 Sex of the participants	13
4.1.2 Age distribution.	14
4.1.3 Residential Address	15
4.1.4 Level of Education.....	15
4.1.5 Logistic binary regression for age with 30-day post operation mortality.....	16
4.2 Clinical Presentation	16
4.2.1 Presenting Complaints.....	16
4.2.2 Duration of Symptoms.....	17
4.2.2.1 Logistic binary regression for duration of symptoms.....	17
4.2.3 Retroviral Disease Status.....	18
4.2.3.1 Univariate Linear Regression for HIV positive status.....	18
4.2.4 AIDS defining diseases.	19
4.2.5 Shock at presentation.....	19
4.2.5.1 Univariate binary logistic regression analysis of shock on Admission.	20
4.2.6 ASA Score Distribution.....	20
4.2.6.1 Univariate binary logistic regression analysis of ASA Score.....	21
4.2.7 Serum Creatinine on Presentation	21
4.2.7.1 Univariate logistic regression analysis of Creatinine level on Admission.	22
4.2.8 Serum Albumen on admission.....	22
4.2.8.1 Univariate binary logistic regression analysis of Serum Albumen	23
4.2.9 CD4 cell count	23
4.2.9.1 Univariate linear regression analysis of CD4 cell count.	24
4.3 Operation Findings and Post-operation Outcome	25
4.3.1 Site of Perforated peptic ulcer	25
4.3.1.1 Univariate Logistic regression analysis of Site of perforation	26

4.3.2 Estimated Size of PPU.....	26
4.3.2.1 Univariate binary logistic analysis of estimated size of perforation	27
4.3.3 Type of Operation Done	27
4.3.3.1 Univariate binary logistic regression analysis of type of operation done.....	27
4.3.4 Post-Operative Care.....	28
4.3.4 Post-Operative Complication	30
4.3.5 30 day post-operation mortality.....	31
4.3.6 Duration Post operatively to Mortality.....	32
4.3.7 Multivariate Linear Regression Analysis of variables	32
CHAPTER FIVE: DISCUSSION.....	34
5.1 Discussion	34
5.2 Study Limitation.....	12
CHAPTER SIX: CONCLUSION.....	40
6.1 Conclusion.....	40
6.2 Recommendations	40
REFERENCES.....	41

LIST OF TABLES

Table 1. Residential Address of Participants	15
Table 2. Participants Education Level	15
Table 3. Univariate binary logistic regression analysis of age	16
Table 4. Duration of symptoms on presentation	17
Table 5. Univariate binary logistic regression analysis of duration of symptoms	17
Table 6. HIV status of patients	18
Table 7. Univariate linear regression analysis of HIV status	18
Table 8. AIDS defining condition	19
Table 9. Univariate binary logistic regression analysis of Shock	20
Table 10. Univariate binary logistic regression analysis of ASA score.....	21
Table 11. Serum creatinine on admission	21
Table 12. Univariate binary logistic regression analysis of serum creatinine	22
Table 13. Univariate binary logistic regression analysis of serum albumen	23
Table 14. CD4 cell count of HIV reactive patients	23
Table 15. Univariate linear regression analysis of CD4 cell count	24
Table 16. Univariate binary logistic regression analysis of site of perforation	26
Table 17. Univariate binary logistic regression analysis of size of perforation	27
Table 18. Type of operation	27
Table 19. Univariate binary logistic regression analysis of type of operation	28
Table 20. Duration to death	32
Table 21. Multivariate Regression Analysis of significant Variables	33

LIST OF FIGURES

Figure 1. Pie Chart Showing sex distribution	13
Figure 2. Age distribution ranges	14
Figure 3. Pie Chart of presenting complaints	16
Figure 4. Shock on presentation	19
Figure 5. ASA score Distribution.....	20
Figure 6. Serum albumen on admission	22
Figure 7. Frequency of site of perforation	25
Figure 8. Estimated size of peptic ulcer perforation	26
Figure 9. Patient post-operation ward of admission	28
Figure10. Post-operation length of hospital stay	29
Figure 11. Post-operation complication	30
Figure 12. Post-operation mortality	31

LIST OF APPENDICES

APPENDIX A: Participants Information Sheet	44
APPENDIX B: Consent Form.....	47
APPENDIX C: Data Collection Tool.....	48

ABBREVIATIONS

ASA	American Society of Anaesthesiologists
AIDS	Acquired Immunodeficiency Syndrome
AUC	Area Under the Curve
HIV	Human immunodeficiency virus
BP	Blood pressure
bpm	beats per minute
HDU	High Dependency Unit
ICU	Intensive Care Unit
PI	Principle Investigator
PPU	Perforated Peptic Ulcer
PUD	Peptic Ulcer Disease
PULP	Peptic Ulcer Perforation Score
mmHg	millimeters of Mercury
MPI	Mannheim Peritonitis Index
NSAID	Non-Steroidal Anti-Inflammatory Drug
ROC	Receiver Observer Curve
SPSS	Statistical Package for Social Science
UTH	University Teaching Hospital

CHAPTER ONE: INTRODUCTION

1.1 Background

The University Teaching Hospitals (UTH), are the highest referral hospitals in Zambia. It is comprised of Adult Hospital, Mother and New born Hospital, Children's Hospital, Eye Hospital and Cancer Diseases Hospital. It is located in Lusaka, the capital city approximately 4km east of the city Centre. The Adult Hospital is a third level hospital, but provides 1st, 2nd and 3rd level health services for the city of Lusaka. The department of surgery is situated in the Adult Hospital and has a bed capacity of 371 and provides General Surgery and other specialist surgical services: Orthopaedic, Urology, Neurosurgery, ENT (ear nose and throat), Maxillofacial, Plastic, Cardiac and Anaesthesia. UTH has a Main Intensive Care Unit (MICU) with a bed capacity of 10, that is shared by all its departments.

PPU is one of the common findings in patients undergoing emergency exploratory laparotomy at University teaching hospital (UTH). In unpublished surgical audit data, between April 2014 to April 2015 at UTH, a total of 189 exploratory laparotomies were performed for peritonitis. In 50 of the cases, the cause of the peritonitis was found to be due to perforated gastric ulcers, representing 26.45% of the all cases of peritonitis operated on in that calendar year. The peak age for PPU in patients seen at UTH is 16 to 45 with a male preponderance of 85.7%. (Sondashi, 2010). The post-operative hospital stay is 10days or more in 51.4 % of PPU cases and the mortality rate stands at 37% (Sondashi, 2010).

To facilitate appropriate level of care of PPU patients and to improve the outcomes, it is important to stratify patients into different risk categories based on the likelihood of morbidity and mortality, so that high-risk patients can receive more appropriate treatment and intensive care (Munir, 2014). Currently we do not know the determinants of morbidity and mortality at UTH to use to stratify risk morbidity and mortality and there is no clinical tool that is being used to stratify risk of mortality and morbidity for patients with PPU undergoing emergency surgery at UTH.

1.2 Introduction

Peptic ulcer disease is defined as the breakdown of the defensive epithelial mucosal barrier of the stomach and/or duodenum characterized by inflammation and ulcer formation (Proctor, 2014). Each year peptic ulcer disease (PUD) affects 4 million people around the world (Thorsen, 2013). Globally, the incidence of peptic ulcer disease has fallen in recent years (Chalya, 2011). There is a paucity of information with regard to epidemiology of PUD in Sub-Sahara Africa. However, PUD was a common finding at endoscopy at UTH, comprising 18.2% of all endoscopies done (Kelly, 2008).

Several risk factors are implicated in the development and progression of peptic ulceration. However, *H. pylori* infection and non-steroidal anti-inflammatory drugs (NSAIDs) play the biggest role (Proctor, 2014). Complications are encountered in 10%-20% of patients with PUD and 2%-14% of the ulcers will perforate (Thorsen, 2013; Ramakrishnan, 2007). It has also been noted that perforation is the second most frequent complication after bleeding. While the clinical picture of patients with perforated peptic ulcer (PPU) sometimes can be blurred by vague symptoms, most PPU patients present with overt symptoms and signs of peritonitis and eventually sepsis.

The pattern of perforated PUD has been reported to vary from one geographical area to another depending on the prevailing socio-demographic and environmental factors (Chalya, 2011). In the developing world, the patient population is young with male predominance, patients present late, and there is a strong association with drinking and smoking. (Ugochukwu, 2013). In the West the patients tend to be elderly and there is a high incidence of ulcerogenic drug ingestion (Chalya, 2011). A high risk for morbidity (20-50%) and mortality (3-40%) is encountered in surgically treated PPU patients (Thorsen, 2013). Certain factors have been noted to increase the risk of morbidity and mortality following surgical management of PPU, these include, age, time taken from perforation to operation, and presence of shock at presentation.

1.3 Statement of the Problem

Perforated peptic ulcer disease is a major cause of peritonitis in patients presenting for emergency Surgery at UTH in Zambia and other African countries. In calendar year April 2014 to April 2015, PPU accounted for 26.4% of all case of peritonitis managed surgically at UTH, Adult Hospital. In

a study in Uganda, PPU represented 50% of causes of peritonitis (Ojuka, 2014). PPU affects mostly young population at UTH, just like other Sub-Saharan African countries. However, the mortality associated with PPU at UTH was found to be 37%, this is high, even when compared to other African studies. Despite PPU being a common cause of peritonitis and over one third of patient managed surgically for PPU dying after surgery, we do not know the factors associated mortality in patient with PPU at UTH.

It is known that young healthy patients who present early have excellent prognosis after surgery for PPU, while older patients with co-morbidity with neglected perforation have poor prognosis. The situation at UTH is not in keeping with this, despite a young population, mortality and morbidity associated with PPU is high. There is clear need identify risk factor associated with of mortality in patients with PPU at UTH and of great interest are modifiable factors with the potential to improve outcome.

It is clear from literature that, perforated peptic ulcer patients show differences in age, sex and presentation patterns that it is difficult to simply adopt the identified factors known that predict poor outcome elsewhere to our patient (Soreide, 2015).

1.4 Study Justification

PPU is associated with high morbidity in our population despite it affecting predominately the young. This study aims to identify factors predictive of mortality in the patient presenting with PPU at UTH. This will allow us to determine whether any of these factor are modifiable, hence influence change in the care for patient with PPU with the goal to reduce morbidity and mortality associated with the condition. Identification of factors associated with mortality and morbidity will allow stratification of risk of morbidity and mortality in patient presenting with PPU. This will enable us to identify patients at great risk of morbidity and mortality and help provide appropriate level of care for them, such as the need of ICU/HDU care.

1.5 Research Question

What factors are associated with mortality in patients with perforated peptic ulcer disease managed surgically at the University Teaching Hospital?

1.6 Objectives

1.6.1 Main Objective

To investigate the factors associated with mortality in patients that present with PPU managed surgically at UTH.

1.6.2 Specific Objectives

1. To determine the social demographic characteristics of the patient presenting with PPU.
2. To establish the relation of clinical presentation of patients with PPU to mortality.
3. To determine the relationships between Size and Site of perforation to mortality.
4. To estimate the frequency of surgical site infection following PPU surgery.

CHAPTER TWO: LITRETURE REVIEW

2.1 Perforated Peptic Ulcer and Surgery

Elective peptic ulcer surgery has been virtually abandoned. (Chalya, 2011) Currently, surgery for peptic ulcer disease is largely restricted to the treatment of complications, particularly bleeding, perforation, and obstruction, while relying on *H. pylori* eradication to prevent ulcer recurrence. (Ugochukwu, 2013)

At laparotomy for PPU, simple closure of the perforation with omental patch followed with *H. pylori* eradication therapy has been shown to be a safe method. (Chalya, 2011) It has been shown that there is no significant difference in morbidity and mortality when simple closure is performed by a Surgical Registrar or consultant. (Leeman, 2013)

Mortality and morbidity following perforated peptic ulcer (PPU) is substantial, and mortality proportions of 25–30% have been reported in population-based studies. (Moller, 2011)

The risk of mortality (6-30%) and morbidity (21-43%) at PPU unfortunately have not changed during the last decades. (Menekse, 2015)

In a study done at UTH, mortality was found to 37% (Sondashi, 2010), this mortality is high compared to studies done in Nigeria, Tanzania where mortality was found at 21% and 10.7% respectively. (Sondashi, 2010; Ugochukwu, 2013;Chalya, 2011)

It has been demonstrated that if the high risk patients got extra perioperative care, the hospital mortality rate could be reduced from the standard care patients (17% and 27%, respectively, $p = 0.005$). (Soreide, 2013)

In a review of surgical audit data in Scotland, it was found that increased use of HDU/ICU for operated cases of PPU was a significant factor to reduction in the death rate in PPU patients. (Aga, 2012)

A simple and easy applicable system in predicting risk mortality for PPU patients may lead to reduction in mortality rates, as patient at high risk of mortality can be easily discriminated and enhanced care provided. (Menekse, 2015)

2.2 Factors associated with mortality globally

Concerning factors determinant of morbidity in PPU, a study in Portugal, found the variables; age, pulse and blood pressure at admission, associated illnesses, perforation evolution, and type of surgery performed to statistically significant lead to morbidity. (Noguiera, 2003)

In a Finnish study, morbidity was predicted by sex, age group, duration of symptoms, associated medical illness, two or more associated medical illnesses, preoperative shock, and the amount of abdominal fluid, the type of abdominal fluid, organisms grown on culture, the use of non-steroidal anti-inflammatory drugs, and the albumin concentration as significant. (Makela, 2002)

Investigation from a study in Korea deduced that, a high ASA score, the presence of preoperative shock, an open surgery, and a long operation time were statistically significant as independent predictors of morbidity. (Kim, 2012) However, the same study disputed hypertension, diabetes mellitus, pulmonary disease, age and sex as significant factors in predicting morbidity. (Kim, 2012)

In Hong Kong China, they discovered from their study that the Boey score and ulcer size to be non-significant factors in predicting morbidity in perforated peptic ulcer disease. (Lee, 2001)

Regarding determinates of mortality in PPU, a study in India identified age, duration of symptoms, preoperative blood sugar levels, blood urea, serum creatinine levels, Mannheim peritonitis Score (MPI), and the delay in instituting surgical intervention as the predictors of mortality. (Singh, 2011)

In Turkey they showed that older age, ASA status, delayed admission to hospital, presence of shock, and the type of operation were independent predictors of mortality. (Kocer, 2007)

In Finland the results of the univariate analysis suggested that five factors could contribute to mortality, but only the duration of symptoms for more than 24 hours and the amount of abdominal fluid were deduced to be independent factors. (Makela, 2002)

In another Finnish study they demonstrated that, the severity of sepsis, chronic kidney insufficiency and preexisting cardiovascular disease were independent predictors of 30-day mortality or ICU admission. (Tolonen, 2016)

Lee, et.al. (2001) in Hong Kong China study concludes that, the Boey score and ulcer size independently predicted mortality and morbidity of patients with perforated peptic ulcer but multivariate analysis showed that only the Boey score and not ulcer size predicted mortality.

A study in the USA, Texas, found that univariate analysis showed that patients with; Increasing ASA score, known H. pylori status, no prior history of PUD before operation were at increased risk of mortality. (Sarosi, 2005)

A study in Denmark found that, every hour of delay from admission to surgery was associated with an adjusted 2.4 per cent decreased probability of survival compared with the previous hour. (Buck, 2013)

2.3 Factors associated with mortality Sub-Sahara Africa

In the sub-Sahara Africa, when it comes to factors predictive of mortality and morbidity, in Liberia they adduce that; Long symptom duration and age > 30years of age were significantly associated with high in-hospital mortality on univariate and multivariate testing compared to short duration of symptom and young age. (Moses, 2014)

A Tanzanian study, discovered the following as being statistically significant predictors of complication and mortality in patient; age ≥ 40 years of age, presence of premorbid illness, HIV seropositive status, a CD4count < 200cells/ml., shock on admission, surgical treatment done >48hrs after onset of symptoms and site of perforation being gastric. (Chalya, 2011)

In Nigeria, they found high mortality in patients who were ≥ 40 years of age, delayed Presentation (>24 h), shock (systolic BP < 90mmHg) on admission. (Ugochukwu, 2013)

2.4 Clinical Scores Predicting Mortality

The PULP score was developed from nationwide cohort study of 2668 patients surgically treated for PPU from February 2003 through August 2009, in Denmark. The new clinical prediction rule – the PULP score – ranges from 0 to 18 points. (Moller, 2011)

Based on the optimal cut-off value of the PULP score, patients could be divided into low-risk patients, with less than 25% risk of mortality (a score of <7 points), and high-risk patients, with more than 25% risk of mortality (a score of ≥ 7 points). (Moller, 2011)

The nationwide PULP study is the largest recent study evaluating outcome prediction for PPU patients. Hence the external validity may be stronger, at least for comparable, western populations with demography similar to Denmark. (Thorsen, 2013)

Despite the demographic, clinical and outcome differences between a study in Singapore and PULP study, PULP score provided similar AUC (0.75 vs. 0.83). (Anbalaka, 2015)

Another study in Thailand demonstrated that PULP score had highest AUC compared to Boey Score, ASA classification and MPI. (Nichakankitti, 2016)

The Singapore study had a mean age of 54.7years (age range 17-109years) and while Thailand study mean age was 40.5years (age range 18-89years) which is closer to the UTH demographic, mean age 39.9years (age range 16-82years). (Anbalaka, 2015; Nichakankitti, 2016; Sondashi, 2010)

In comparison to the latest Score developed to predict PPU mortality, Predicting of Mortality in Perforated Peptic Ulcer (POMPP), the mortality predictive power of PULP scoring system was found to be a little better. (Menekse, 2015).

CHAPTER 3: STUDY METHODOLOGY

3.1 Study design and duration

Prospective Cohort Study. The study was conducted for a period of 1 year.

3.2 Target Population

The study enrolled eligible participants with PPU seen at the UTH- Adult Hospital that had undergone emergency Laparotomy.

3.3 Study Site Area

The study was conducted at the University Teaching Hospital UTH, Adult Hospital, located in Lusaka, Zambia.

3.4 Inclusion Criteria

PPU Patient who had undergone emergency laparotomy and met the case definition were.

3.4 Exclusion Criteria

Perforation that resulted from malignancy.

3.5 Definition used in the Study

PPU was defined as any non-malignant ulcer perforation involving the stomach and duodenum by histology.

Post-Operation Mortality was defined as any death that occur 30 days from the day of operation or a death occurring after 30 days post operatively during the same admission following the operation.

Shock was defined as Systolic pressure less 100mmHg with a Pulse of greater than 100 beats per minute.

AIDS was defined as per World Health Organisation definitions.

Time of perforation was assumed to be at time of onset of abdominal symptoms.

3.6 Sample Size

Sample size was calculated using open Epi version 3, open source calculator sample size for cohort studies. Fleiss formula 3.18 was used. Exposed with outcome was 37%, the mortality rate at UTH in patients with PPU after laparotomy (Sondashi, 2010).

Sample size was calculated to be 38 at 90 % confidence level with a power of 80 %.

3.7 Sampling Method

Simple consecutive sampling of all patients that met the inclusion criteria was done.

3.8 Data Collection

Patients that had undergone Emergency laparotomy for perforated peptic ulcers were enrolled and followed up for 30 days from the day of operation. Recruitment was done after participants have undergone emergency laparotomy. Participants were recruited from all General Surgery Firms. Follow up was done on day 5, day 10 and day 30 post operatively and on their first clinic visit post operatively. Follow up was done in the surgical wards and clinic by the respective Firms and the PI was there to observe and collect data. The operations were performed by registrar or any senior member of the General Surgery Firms.

Participation in the study was at the participants' free will and refusal to take part in the study did not in any way interfere with their treatment/care. Where there was need to do an HIV test, consent was sort and confidentiality kept for all the information collected. Data collections was done using an interview administered questionnaire and was checked to be complete before being entered. Consent to obtain Phone numbers of next of kin was obtained for follow up purpose of participants that may be lost to follow up or cannot be reached after discharge from hospital. This was for the sole purpose of ascertaining whether participants reached the completion point of the study.

3.9 Data Analysis Plan

Every time data collected was checked to be complete and accurate before being entered using EPI data 2.1b software. Data was backed on hard copies and soft copies. All data collected was kept strictly confidential.

Data was analysed using SPSS version 16. Univariate and Multivariate regression analysis where done to identify variables associated mortality. Odds ratio and p-values for the identified variable

associated with mortality were calculated at 95% confidence interval. A statistician was consulted to help with data analysis.

3.10 Variables

3.10.1 Independent (predictor) Variables

- i. Age
- ii. Shock on Admission
- iii. Time from perforation to Surgical intervention
- iv. Co-morbid conditions; Malignancy, AIDS, Liver Failure, CKD
- v. Serum Creatinine
- vi. Serum Albumin
- vii. CD4 count if HIV positive
- viii. Site of perforation
- ix. Size of perforation
- x. Type of operation Performed
- xi. ASA score

3.10.2 Dependent (outcome) Variables

Primary outcome

- 30 day post-operative mortality

Secondary Outcomes

- i. Length of Hospital stay
- ii. Post-operative complication

3.11 Ethical Considerations

Ethical approval was sought from ERES CONVERGE before the research was conducted. Permission from the UTH-Adult Hospital management was obtained to conduct the study in the institution. All patients taking part had signed an informed consent form. Participation was at the participants' free will and refusal to take part in the study did not in any way affect the participants' standard and level of care. It was explained to all the participants that information collected and details will be kept strictly confidential and the information was to be used solely for purpose of the study.

Once enrolled, participants were given an identity number and for the purpose of the study, they were only referred to using this number henceforth. Personal information about the participants will not be release to anyone and will not be used in any publication. Participants requiring HIV testing, national guidelines were followed.

3.12 Study Limitation

Patient were managed by different firms and since there is no standard protocol on the management of PPU at UTH, there could have be some difference in the way patients were managed among the different firms that could have affected patients outcomes.

CHAPTER FOUR: RESULTS

This study enrolled 38 participants, but the data analysis is for 35 participants that met the inclusion criteria set out in the methodology chapter. Two of the participant where lost to follow up despite the PI best effort to follow them up and their next of kin and one participant had a histology showing dysplasia and repeat biopsy was requested and the repeat biopsy had not been done at the time of data analysis. These participants were excluded due to incomplete data.

4.1 Demographic Characteristic of Participants

4.1.1 Sex of the participants

The sex distribution in percentages of participants is shown in Figure 1, male 88.57% (n=31) and female 11.43% (n=4).

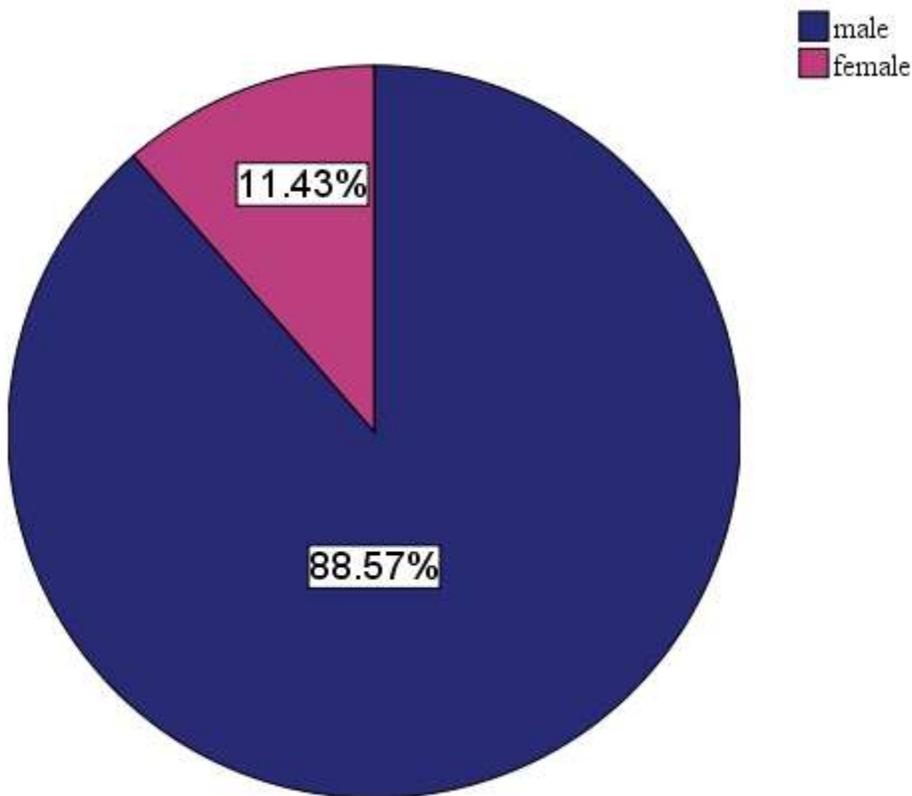


Figure 1. pie chart showing sex distribution: male 88.6%, female 11.4%.

4.1.2 Age distribution.

The age distribution of the participants ranged from 14 years to 84 years old but majority of the participants were age between 20 years and 50 years old as shown in Figure 2.

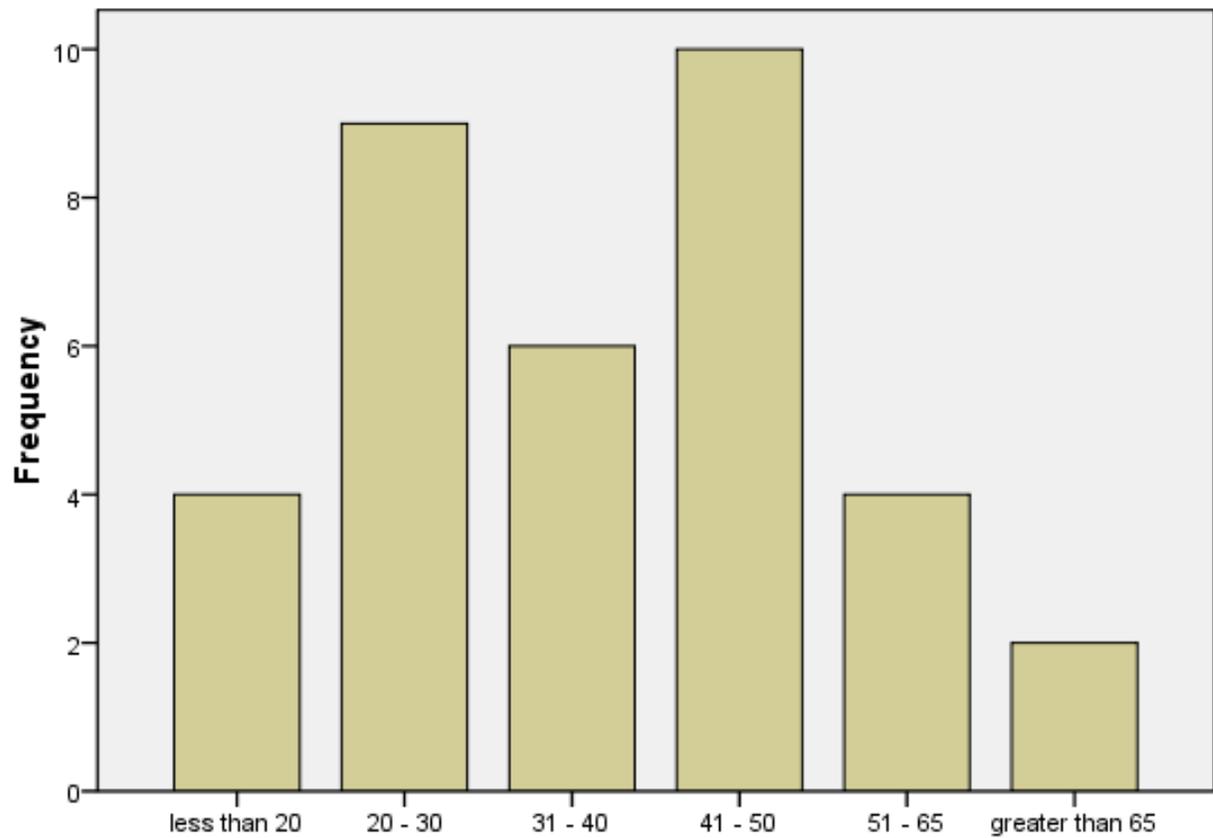


Figure 2. showing the age distribution in age ranges

4.1.3 Residential Address

More than half of the patients resided in high density residential areas, 54.3% (n=19), followed by medium density 22.9% (n=8) and rural 17.1% (n=6) residential areas respectively. This is shown in Table 1.

Table 1. Residential Address of the Patients

Residential Class	Frequency	Percent	Valid Percent	Cumulative Percent
low density	2	5.7	5.7	5.7
medium density	8	22.9	22.9	28.6
high density	19	54.3	54.3	82.9
rural	6	17.1	17.1	100.0
Total	35	100.0	100.0	

4.1.4 Level of Education

Close to half of the patient 48.6% (n=17) had secondary level of education, followed by primary level 34.3% (n=12). However, a meager 5.7% had tertiary level education as demonstrated in Table 2.

Table 2. Patients' Education Level

Level of Education	Frequency	Percent	Valid Percent	Cumulative Percent
None	4	11.4	11.4	11.4
Primary	12	34.3	34.3	45.7
Secondary	17	48.6	48.6	94.3
Tertiary	2	5.7	5.7	100.0
Total	35	100.0	100.0	

4.1.5 Logistic binary regression for age with 30-day post operation mortality

The analysis found a statistically significant relation between age and 30-day post-operation mortality (p-value 0.023; odds ratio 2.06) as illustrated in Table 3.

Table 3. Univariate binary logistic regression analysis of Age and 30-day Mortality.

	B	S.E.	Wald	df	Sig. (P value)	Exp(B) (odds ratio)	95.0% C.I. for EXP(B)	
							Lower	Upper
Step 1 ^a Age	.722	.318	5.148	1	.023	2.059	1.103	3.843
Constant	-3.100	1.196	6.722	1	.010	.045		

a. Variable(s) entered on step 1: Age.

4.2 Clinical Presentation

4.2.1 Presenting Complaints

Commonly, patients presented with two or more symptoms as shown in the Figure 3.

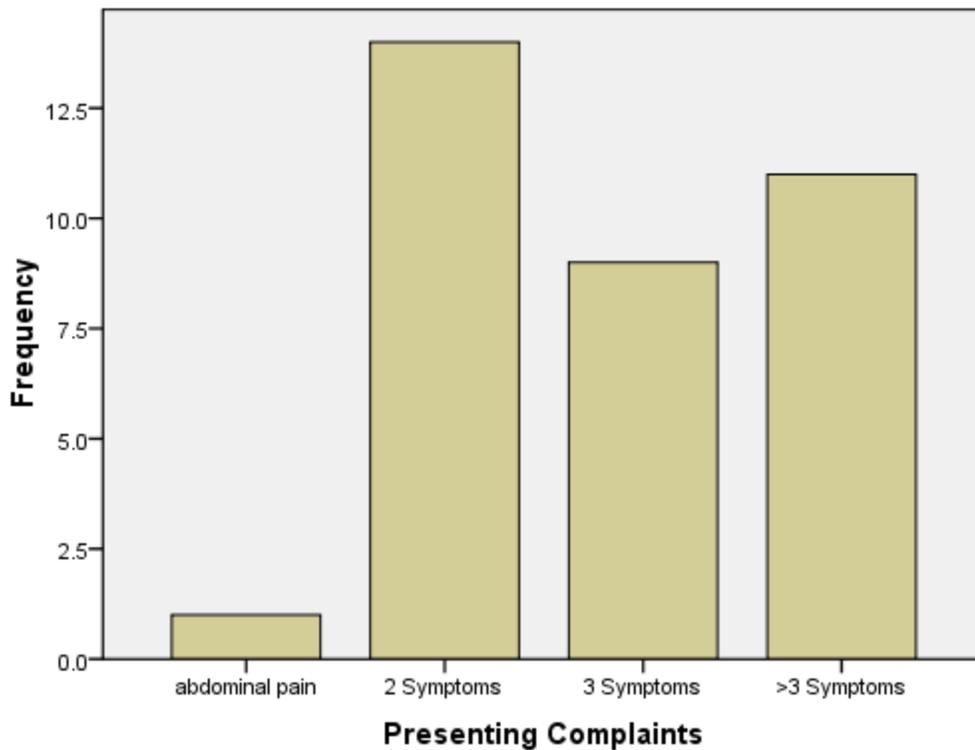


Figure 3. Number of presenting complaints at presentation, where a patient presented with one complaint only that complaint and its frequency is shown.

4.2.2 Duration of Symptoms

Patients presented mostly after 24 hours from the onset of symptoms and only 17% (n=6) presented within 24 hours of onset of systems as the Table 4, demonstrates.

Table. 4 Duration of Symptoms on Presentation

Duration of Symptoms	Frequency	Percent	Valid Percent	Cumulative Percent
less than 24hrs	6	17.1	17.1	17.1
24 - 48hrs	12	34.3	34.3	51.4
48 - 72hrs	8	22.9	22.9	74.3
more than 72hrs	8	22.9	22.9	97.1
5	1	2.9	2.9	100.0
Total	35	100.0	100.0	

4.2.2.1 Logistic binary regression for duration of symptoms.

The analysis did not yield a statistically significant association between duration of symptoms at presentation and 30 day post-operation mortality (p-value 0.23; odds ratio 1.50) as illustrated in the Table 5.

Table 5. Univariate logistic Regression analysis of Duration of symptoms and 30-day Mortality.

	B	S.E.	Wald	df	Sig. (p value)	Exp(B) (odds ratio)	95.0% C.I. for EXP(B)	
							Lower	Upper
Step 1 ^a Duration of symptoms	.406	.336	1.462	1	.227	1.500	.777	2.896
Constant	-1.735	.990	3.075	1	.079	.176		

a. Variable(s) entered on step 1: duration of symptoms.

4.2.3 Retroviral Disease Status

The incidence of HIV positive patient in this cohort was 17.1 % (n=6) as the Table 6, illustrates.

Table 6. HIV Status of Patients.

HIV Status	Frequency	Percent	Valid Percent	Cumulative Percent
Non-reactive	29	82.9	82.9	82.9
Reactive	6	17.1	17.1	100.0
Total	35	100.0	100.0	

4.2.3.1 Univariate Linear Regression for HIV positive status

HIV positive status was significantly associated with 30 day post-operation mortality among the patients (p-value 0.000), as in Table 7. In this study, all the patient that were HIV reactive die within 30 days post-operative period, so binary analysis could not be used to find association between HIV status and 30-day mortality, because there was only one outcome for the dependent variable, hence the use of univariate linear regression analysis.

Table 7. Univariate Logistic Regression Analysis of HIV Status and 30-day Mortality

Model		Unstandardized Coefficients		Standardized Coefficients	Sig. (P value)	95% Confidence Interval for B		
		B	Std. Error	Beta		t	Lower Bound	Upper Bound
1	(Constant)	.762	.126		6.071	.000	.507	1.017
	HIV Status	.424	.080	.677	5.289	.000	.261	.586

a. Dependent Variable: Mortality within 30days Post-operative

4.2.4 AIDS defining diseases.

Among the patient who were positive for HIV, only one had a clinical AIDS defining disease condition meeting the WHO criteria as in Table 8.

Table 8. AIDS defining Disease

AIDS Defining Disease	Frequency	Percent	Valid Percent	Cumulative Percent
yes	1	2.9	2.9	2.9
no	34	97.1	97.1	100.0
Total	35	100.0	100.0	

Univariate not done for AIDS defining diseases due to insufficient sample for the variable.

4.2.5 Shock at presentation

Figure 4, shows that 42.9% (n=15) of the patient in the study were in Shock (Systolic BP < 100 mmHg, Pulse above 100 bpm) at presentation.

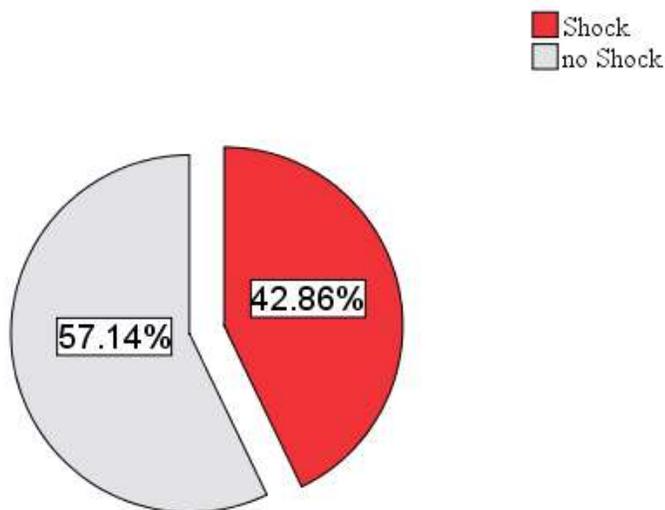


Figure 4. Pie Chart of patient in Shock on Presentation

4.2.5.1 Univariate binary logistic regression analysis of shock on Admission.

There was no statistically significant association between shock on presentation and 30 day post-operation mortality as illustrate in Table 9, (p-value 0.19; odds ratio 2.63 at 95% C.I.).

Table 9. Univariate Logistic Regression Analysis of Shock on presentation and 30-day Mortality

	B	S.E.	Wald	df	Sig. (p value)	Exp(B) (odds ratio)	95.0% C.I.for EXP(B)	
							Lower	Upper
Step 1 ^a Shock on presentation(1)	.965	.731	1.742	1	.187	2.625	.626	11.002
Constant	-1.099	.516	4.526	1	.033	.333		

a. Variable(s) entered on step 1: shock on presentation

4.2.6 ASA Score Distribution

Assessment of the ASA score of the patients on presentation revealed that most patients were classified as ASA 3, 45.7% (n=16), followed by ASA 2, 37.1% (n=13) as shown in Figure 5.

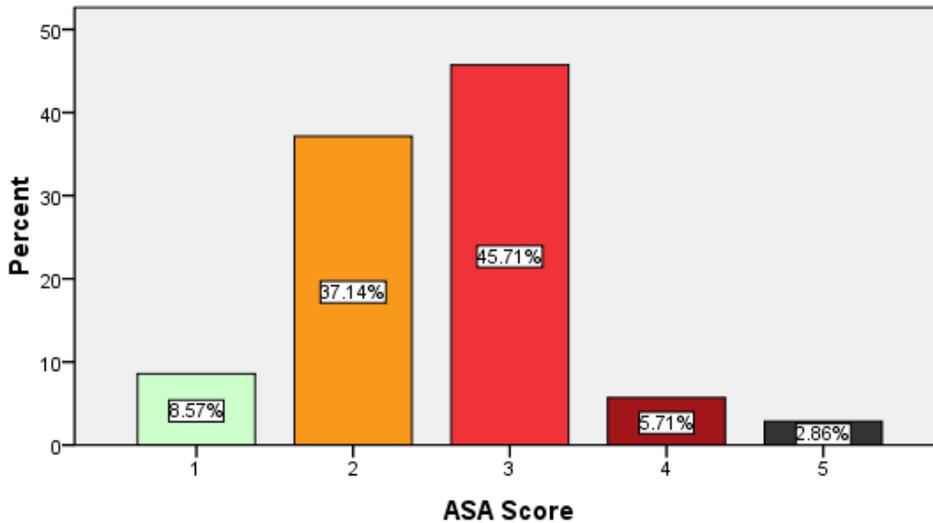


Figure 5. Patient ASA Score Distribution

4.2.6.1 Univariate binary logistic regression analysis of ASA Score.

The ASA Score before operation was found to be significantly associated with 30 day post-operation mortality among the patients in this study (p-value 0.048; odds ratio 2.96) as Table 10, indicates.

Table 10. Univariate logistic regression Analysis of ASA and 30-day Mortality

	B	S.E.	Wald	df	Sig. (p value)	Exp(B) (odds ratio)	95.0% C.I.for EXP(B)	
							Lower	Upper
Step 1 ^a ASA score	1.084	.547	3.926	1	.048	2.956	1.012	8.634
Constant	-3.535	1.538	5.285	1	.022	.029		

a. Variable(s) entered on step 1: ASA score.

4.2.7 Serum Creatinine on Presentation

On admission, 40% (n=14) had an elevated serum creatinine as shown in Table 11,

Table 11. Serum Creatinine on Admission

Creatinine level	Frequency	Percent	Valid Percent	Cumulative Percent
normal	20	57.1	57.1	57.1
elevated	14	40.0	40.0	97.1
low	1	2.9	2.9	100.0
Total	35	100.0	100.0	

4.2.7.1 Univariate logistic regression analysis of Creatinine level on Admission.

Patients' Serum creatinine level on presentation was significantly associated with 30 day post-operation mortality (p value 0.033; odds ratio 4.63) as Table 12 shows.

Table 12. Univariate logistic regression analysis of Serum Creatinine and 30-day Mortality.

	B	S.E.	Wald	df	Sig. (p value)	Exp(B) (odds ratio)	95.0% C.I.for EXP(B)	
							Lower	Upper
Step 1 ^a Serum creatinine	1.532	.719	4.539	1	.033	4.629	1.131	18.956
Constant	-2.971	1.186	6.272	1	.012	.051		

a. Variable(s) entered on step 1: serum creatinine.

4.2.8 Serum Albumen on admission

The bar chart, Figure 6, shows the serum level of the patient on admission, 37.1% (n=13) had a low serum albumen on admission and 5.7% (n=2) had an elevated serum albumen.

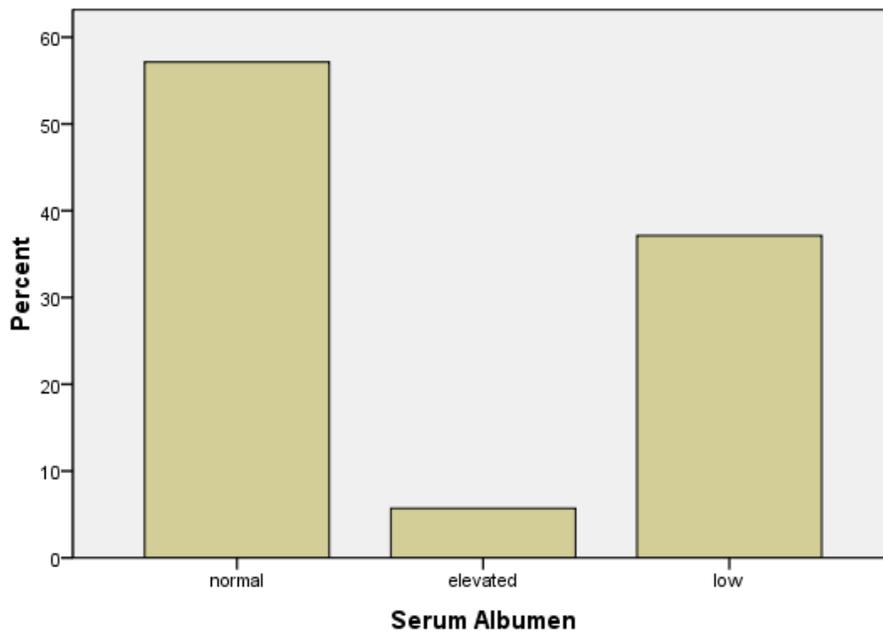


Figure. 6 Shows Distribution of Serum Albumen on presentation

4.2.8.1 Univariate binary logistic regression analysis of Serum Albumen

Serum albumen level at presentation did not have significant association with 30 day post-operation mortality (p-value 0.21; odds ratio 1.61) as indicated in Table 13.

Table 13. Univariate Logistic binary regression analysis of Serum Albumen and 30-day Mortality

	B	S.E.	Wald	df	Sig. (p value)	Exp(B) (odds ratio)	95.0% C.I.for EXP(B)	
							Lower	Upper
Step 1 ^a Serum albumen	.475	.378	1.586	1	.208	1.609	.768	3.372
Constant	-1.536	.812	3.577	1	.059	.215		

a. Variable(s) entered on step 1: serum albumen.

4.2.9 CD4 cell count

The CD4 cell count of the patients that where HIV positive in the Study where found to be low 14.3% (n=5) and two of these had CD 4 cell count less than 200 cell/ ml as illustrated in Table 14.

Table 14. CD4 cell count of HIV Reactive Patients

CD4 Cell count.	Frequency	Percent	Valid Percent	Cumulative Percent
low	3	8.6	8.6	8.6
less than 200cells/ml	2	5.7	5.7	14.3
N/A- Non HIV reactive	30	85.7	85.7	100.0
Total	35	100.0	100.0	

4.2.9.1 Univariate linear regression analysis of CD4 cell count.

It was discovered that the patients CD4 cell did have a significant association with 30 day-mortality among the patient (p-value 0.001) as documented in Table 15. Binary logistic regression analysis could be done because all the patient with this variable died and there had one outcome for their dependent variable hence the use of univariate linear regression analysis.

Table 15. Univariate linear regression analysis of CD4 cell and 30-day Mortality

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95% Confidence Interval for B	
	B	Std. Error	Beta			Lower Bound	Upper Bound
1 (Constant)	2.972	.451		6.585	.000	2.054	3.890
CD4 Count	-.432	.118	-.537	-3.653	.001	-.672	-.191

a. Dependent Variable: 30-day post-operative Mortality.

4.3 Operation Findings and Post-operation Outcome

4.3.1 Site of Perforated peptic ulcer

The most frequent site of perforated peptic ulcer was found to be gastric 91.42% (n=32) as Figure 7, demonstrates.

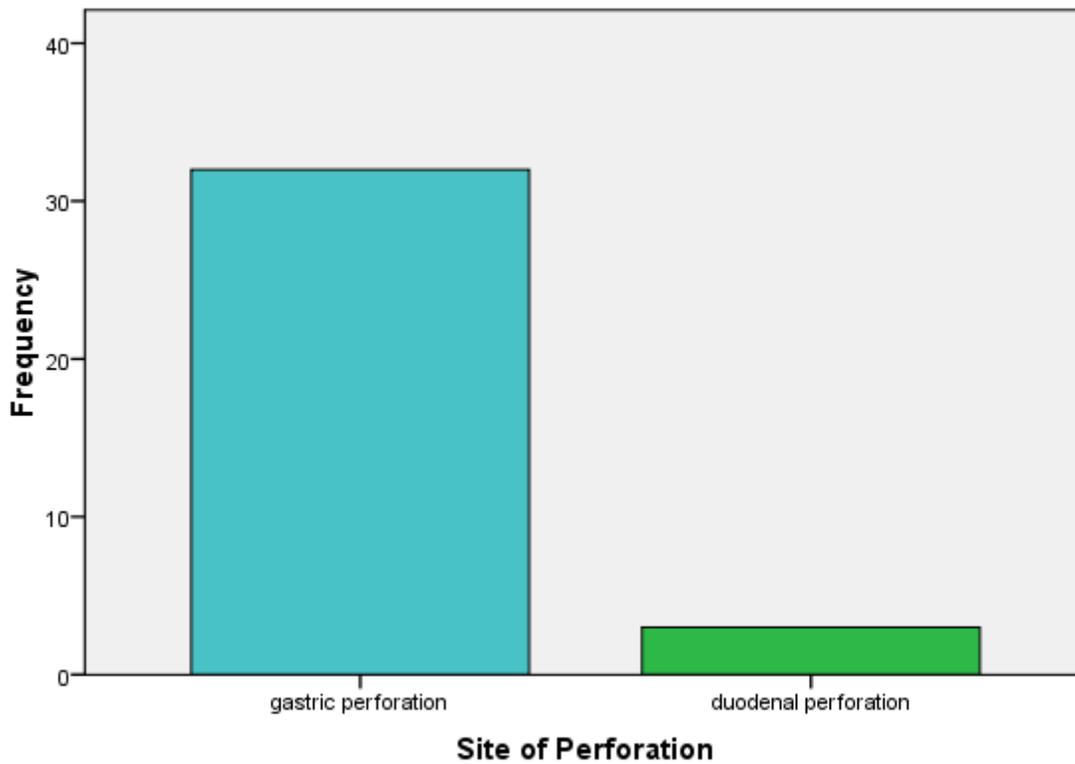


Figure 7. Shows frequency by site of peptic ulcer perforation

4.3.1.1 Univariate Logistic regression analysis of Site of perforation

The location of peptic ulcer perforation did not have a significant association with 30 day post-operation mortality (p-value 0.25; odds ratio 0.23) as Table 16 illustrates.

Table 16. Univariate logistic regression analysis of Site of perforation and 30-day Mortality

	B	S.E.	Wald	df	Sig. (p value)	Exp(B) (odds ratio)	95.0% C.I. for EXP(B)	
							Lower	Upper
Step 1 ^a Site of perforation(1)	-1.482	1.283	1.334	1	.248	.227	.018	2.808
Constant	.693	1.225	.320	1	.571	2.000		

a. Variable(s) entered on step 1: site of perforation.

4.3.2 Estimated Size of PPU

The mode and median size of perforated peptic ulcer was found to be in the range five (5) to 10 millimeters. Figure 8, below shows the percentages of different ranges of peptic ulcer perforations.

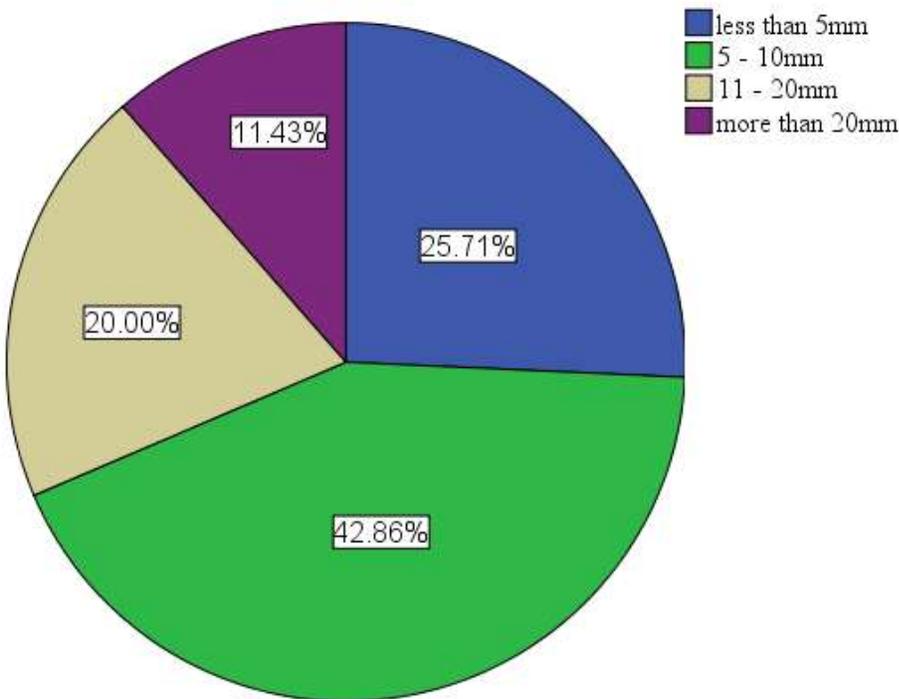


Figure 8. Shows the percentage of estimated size range of Peptic Ulcer perforation

4.3.2.1 Univariate binary logistic analysis of estimated size of perforation

The size of perforated peptic ulcer was significantly associated with 30 day post-operation mortality (p-value 0.035, odds ratio 2.49 at 95% C.I.), illustrated in Table 17.

Table 17. Univariate logistic regression analysis of perforation size and 30-day Mortality

	B	S.E.	Wald	df	Sig. (p value)	Exp(B) (odds ratio)	95.0% C.I. for EXP(B)	
							Lower	Upper
Step 1 ^a Estimated perforation size	.914	.434	4.431	1	.035	2.494	1.065	5.841
Constant	-2.726	1.086	6.296	1	.012	.065		

a. Variable(s) entered on step 1: estimated perforation size.

4.3.3 Type of Operation Done

Nearly all the patient had peptic ulcer repair and omental patch 94.3% (n=33) as Table 18 shows.

Table 18. Type of Operation Done

Operation Done	Frequency	Percent	Valid Percent	Cumulative Percent
gastric repair + omental patch	33	94.3	94.3	94.3
other operation	2	5.7	5.7	100.0
Total	35	100.0	100.0	

4.3.3.1 Univariate binary logistic regression analysis of type of operation done.

The type of operation done was not significantly associate with 30 day post-operative mortality (p value 0.64; odds ratio) as indicated in Table 19.

Table 19. Univariate logistic regression analysis of Type of operation done and 30-day Mortality

	B	S.E.	Wald	df	Sig. (p value)	Exp(B) (odds ratio)	95.0% C.I.for EXP(B)	
							Lower	Upper
Step 1 ^a Operation done	.693	1.462	.225	1	.635	2.000	.114	35.089
Constant	-1.386	1.595	.755	1	.385	.250		

a. Variable(s) entered on step 1: operation done.

4.3.4 Post-Operative Care

Post-operative care for the patients was done on the general ward 97.14% (n=34), only one patient was admitted to ICU representing 2.86% (n=1) as illustrated in Figure 9.

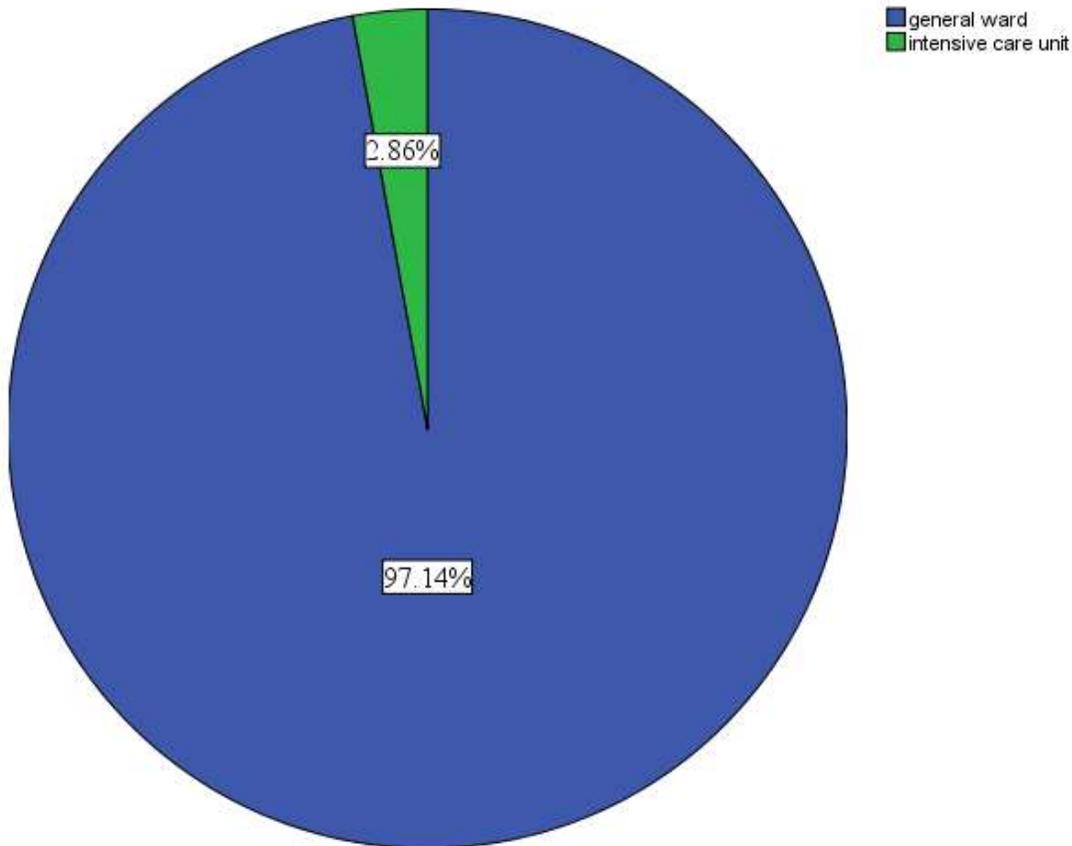


Figure 9. Shows patients' ward of admission for post-operative care with 97.1% admitted to the General Wards.

4.3.4 Length of Hospital Stay

The patients had a post-operative length of stay range of 12 days with a mean LOHS of 7.29 days.

Figure 10 demonstrates the length of the participants.

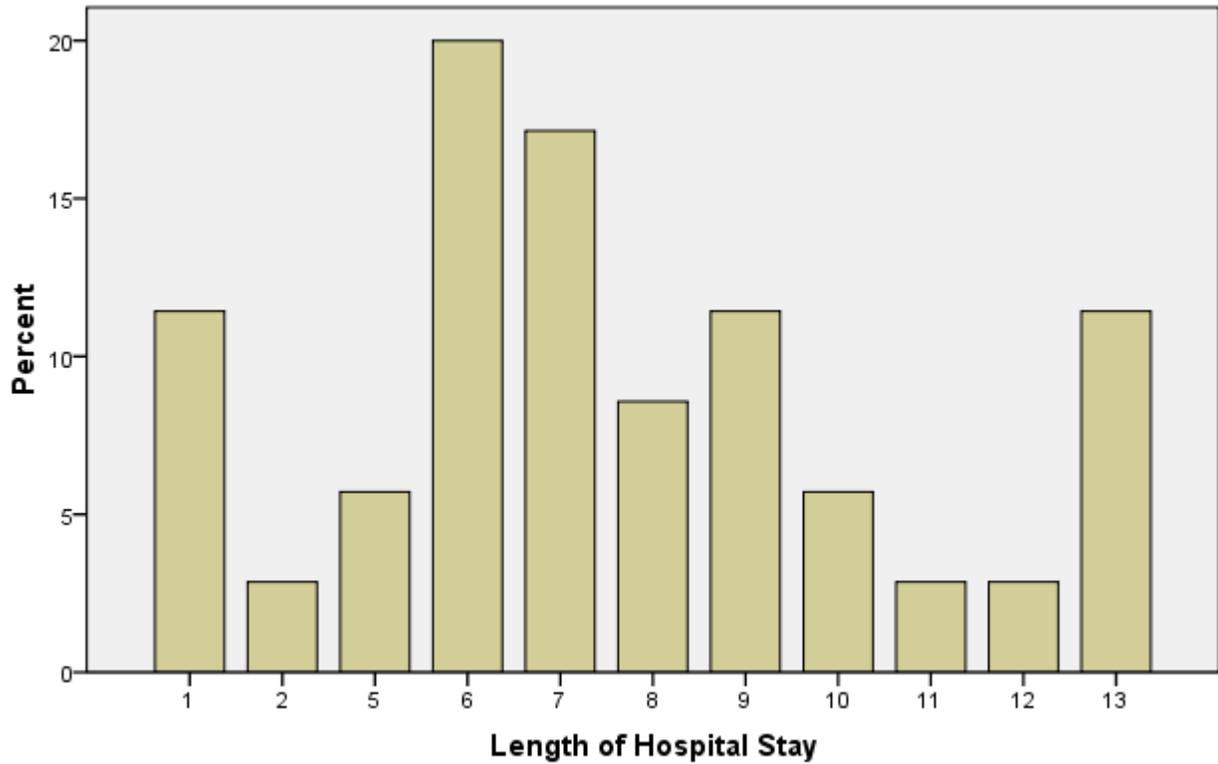


Figure 10. Shows post operative length of hospital Stay in days and the corresponding percentage of patients.

4.3.4 Post-Operative Complication

Complication developed in 40% (n=14). This is depicted in Figure 11.

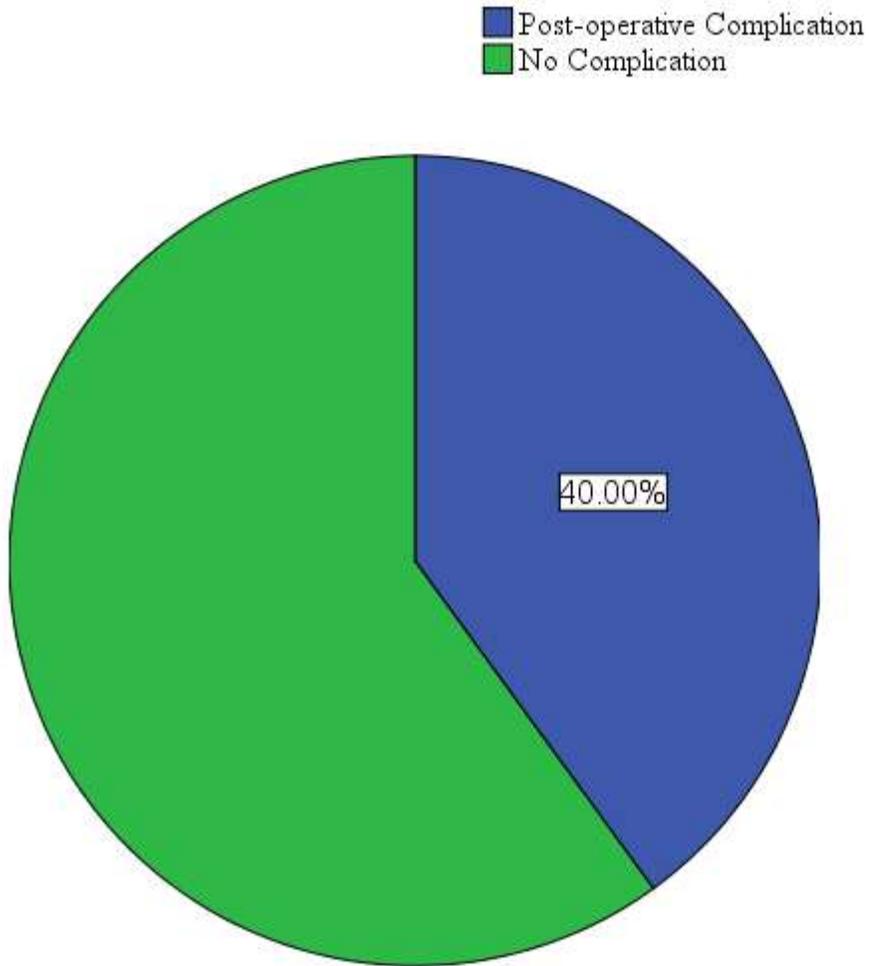


Figure 11. Shows percentage of patients that developed post-operative complications. It stood at 40%.

4.3.5 30 day post-operation mortality

The mortality rate at 30 post-operation days was found to be 34.29% (n=12) as Figure 12, shows.

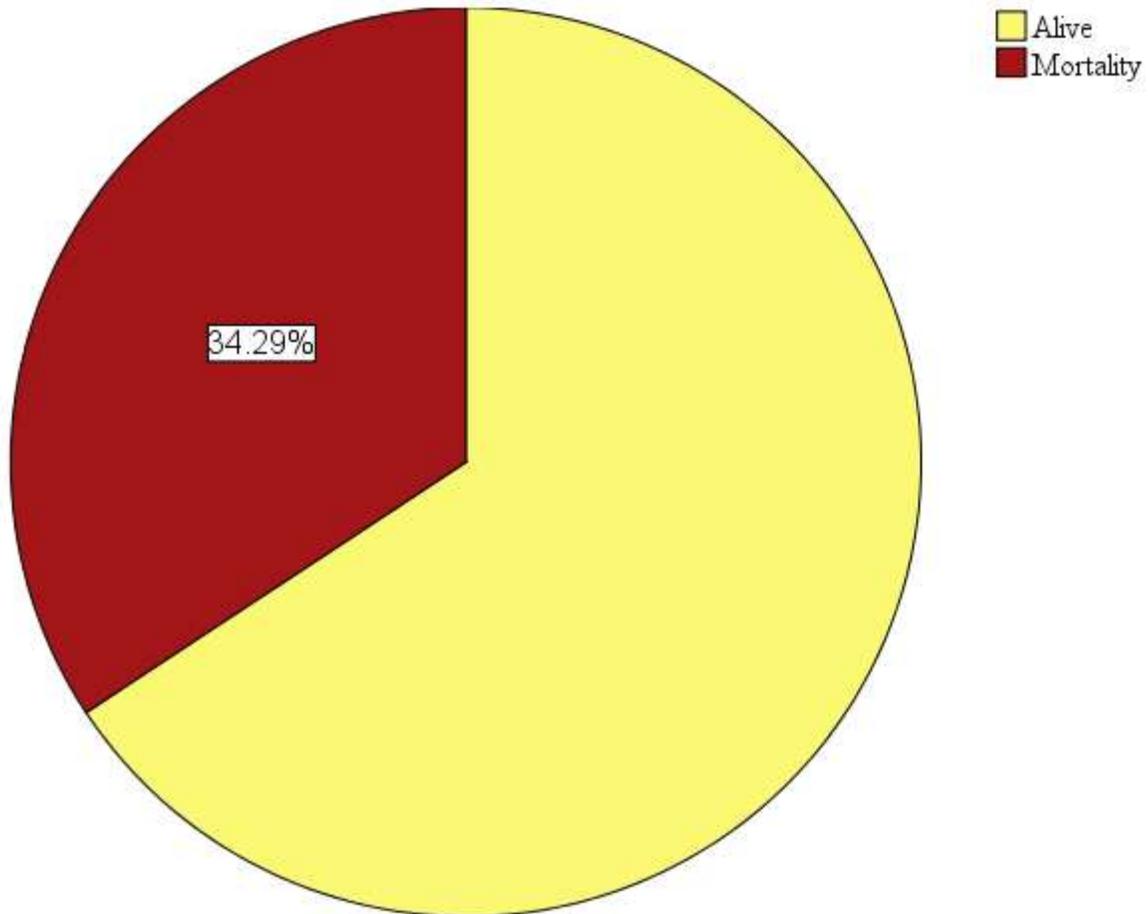


Figure 12. Shows 30 day post-operative Mortality and it was found to be 34.29%.

4.3.6 Duration Post operatively to Mortality

Mortality was 2.9% (n=1) in the period less than 24hours following surgery, 11.4% (n=4) for the period 1-2 days and 2-10 days after surgery and 8.6% (n=3) for the period 10-30 days after surgery. Look at Table 20.

Table 20. Duration to Death

Duration to Death	Frequency	Percent	Valid Percent	Cumulative Percent
less than 1 day	1	2.9	2.9	2.9
1-2 days	4	11.4	11.4	14.3
2 - 10 days	4	11.4	11.4	25.7
10 - 30 days	3	8.6	8.6	34.3
alive after 30 days	23	65.7	65.7	100.0
Total	35	100.0	100.0	

4.3.7 Multivariate Linear Regression Analysis of variables

Multivariate analysis of the factors statistically significant on univariate analysis found that no single variable was statistically significantly associated with mortality as shown in Table 21.

Table 21. Multivariate logistic regression analysis of significant Variables on Univariate analysis

	B	S.E.	Wald	df	Sig.	Exp(B)
Step 1 ^a Age	.749	.491	2.327	1	.127	2.115
ASA score	-.152	.606	.063	1	.802	.859
Serum creatinine	2.916	1.602	3.311	1	.069	18.459
Estimated perforation size	.739	.736	1.007	1	.316	2.094
HIV status	-18.604	3.207E4	.000	1	1.000	.000
CD4 count	-1.631	1.400E4	.000	1	1.000	.196
Constant	33.940	3.106E4	.000	1	.999	5.495E14

a. Variable(s) entered on step 1: Age, ASA score, serum creatinine, estimated perforation size, RVD status, CD4count.

CHAPTER FIVE: DISCUSSION

5.1 Discussion

This study was conducted to investigate factors associate with mortality in patients that presented with perforated peptic ulcers and had emergency laparotomy done in the Department Surgery at UTH- Adult Hospital. The participants in the study were prospectively enrolled and met the inclusion criteria set out in the methodology section. The study enrolled 38 participants, three were excluded because they failed to meet the inclusion criteria leaving 35 participants in the study. Two participants of the three excluded were lost to follow up and therefore, had incomplete data and one participant had a suspicious histology and a repeat biopsy was requested to exclude gastric malignancy.

Of the 35 participants 88.6% (n=31) were male and 11.4 % (n=4) were female. The age ranged from 14 years to 84 years old but most of the patients were blow the age of 50 years (82.9%; n=29) with two peak age ranges, 20 years- 30 years and 40 years-50 years consisting 25% (n=9) and 28.6% (n=10) respectively. This finding is in agreement with result from an earlier study done at UTH (Sondashi, 2010) and results from studies done Sub-Sahara Africa.(Chalya, 2011; Moses, 2015; Ugochukwu, 2013). This is in contrast from data from the developed world where patients are mainly elderly (Thorsen, 2013). The age of the patient was found to be significantly associate with 30 day post-operation mortality in this study on univariate binary logistic regression analysis (p-value 0.023, odds ratio 2.06 at 95% C.I.) but not on multivariate logistic binary regression analysis (p-value 0.13; odds ratio 2.12 at 95% C.I.). This in agreement with results from studies in developed world and Sub-Sahara Africa (Chalya, 2011; Moses, 2015; Thorsen, 2013). In this study, the age at which mortality raised significantly was clinically taken to be > 40 years old.

Patients were received either as self-referrals or referred from health facilities within Lusaka district and province catchment area mostly (85.71%; n=30) and the reminder (14.29 n=5), were referrals from neighboring provinces particularly Central and Southern provinces. Of note, is that the two (2) patients that were self-referrals presented within 24 hours of onset of symptoms. More than half of patients (54%; n=19) resided in high density areas, followed by medium density (22.9%; n=8), rural (17.14; n=8) and low density areas (5.7%; n=2).

In terms of education level of the patients, 48.6 % (n=17) had secondary level education, 34.3 % (n=12) had primary level education, 11.4 % (n=4) had never had any formal education and a meager 5.7 % (n=2) had tertiary level education. These findings suggest that the patients presenting PPU are mostly of low social economic status, looking at the areas they reside in is commonly high density and few of them patients had tertiary level education. Secondly, the fact that neighboring province still refer their patient needing surgery for PPU to UTH, shows that there is a gap that needs to be filled in the provision of surgical services in these provinces.

PPU patients presented to the department of surgery with a mode of two complaints (40.00%; n=14) on admission, followed by four or more (31.43%; n=11) and three (25.71%; n=9) complaints. The commonest complaint was abdominal pain that was present in all the patients in the study and for one (1) patient, it was the only complaint they presented with. However, the other commonly encountered complaints at presentation were nausea and or vomiting, abdominal distension and constipation (not opening bowels for varying period of time). Most patient presented after 24 hours after onset of symptoms, only 6 (17.16%) patients presented within the first 24 hours of onset of their symptoms. Frequently, patients presented in the period 24 hours to 48 hours of onset of symptoms (n=12; 34.32%), and 8 patients (22.88%) presented in the periods 48 hours to 72 hours and 72 hours to 96 hours after onset of symptoms respectively. One patient (2.86%) presented more than 96 hours after the onset of symptoms. These findings are agreeing to the previous study done at UTH and the study done by Chalya in Tanzania (Chalya, 2011; Sondash 2010). Late patient presentation has been noted to be a common feature among African population with PPU and often at the time they present the disease process had progressed significantly (Moses, 2015; Ugochukwu, 2013).

When binary logistic regression analysis was done for duration of symptoms and 30 day post-operation mortality after laparotomy for PPU, no statistically significant association (p-value 0.23, odds ratio 1.50 at 95% C.I.) was found between the duration of symptoms at presentation and 30 day post-operation mortality.

This was a surprising finding, previous studies done in Africa and the western world have consistently found that duration of symptoms to be a significant predictor of 30 day post-operation

mortality.(Mäkelä, 2002; Moses, 2015). Interestingly, a recent study in Turkey by Unver (2015), agrees with our finding.

They discovered that duration of symptoms had no significant effect on mortality, p-value 0.73, odds ratio 0.83 at 95% confidence interval (Unver, 2015).

More than a third of the patients (42.9%; n=15) were in shock (systolic BP < 100 mmHg and pulse rate of > 100 bpm) on presentation. This was expected since most patients presented late from the onset of their symptoms. However, the finding on univariate binary logistic regression analysis of shock on presentation and 30 day post-operation mortality was unexpected. There was no significant association (p value 0.87; odds ratio 2.63 at 95% C.I.) between shock on presentation and 30 day post-operation mortality. Boey (1982), in his study found that shock on admission to a significant factor in predicting mortality after surgery for PPU and many follow up studies have had similar findings since (Møller 2012; Noguiera 2003; Singh 2011). The reason for this finding, one can speculate is that, probably our patient were in early stage of shock and this condition was reversed by fluid management they received. However, due to the relatively small sample size in this study compared to the above previous studies it is difficult to draw any new conclusion.

The HIV incidence among this cohort was found to be 17.14% (n=6) and has shown a reductions when compared to the finding of Sondashi (2010), in his study. The fall of the HIV incidence among the patients that presented with PPU is in tandem with the fall in the national HIV prevalence rate from about 16.4% in 2010 to about 11.6% in 2016 (Unaids.). However, as noted the incidence is still above the national average. The CD4 count of all HIV reactive patient was low (<500cells/ml) and two of the patients had CD4 count lower than 200cell/ml. Four patients were known to be HIV reactive and where on treatment and two where newly diagnosed. All the patients who were HIV positive died within 30 days post-operatively. The HIV-status and the CD4 cell count where found to be statistically significantly associated with 30-day post-operative mortality on univariate linear regression analysis (p-value 0.000 and p-value 0.001 at 95% C.I.) respectively. This agrees with the finding of Chalya (2011) from his study in Tanzania.

When the patients were assessed according to their ASA Score on presentation, patients were frequently graded in descending order as ASA III (45.71%), ASA II (37.14%), ASA I (8.57%), ASA IV (2.86%) and ASA V respectively.

This finding compares well with the finding of Buck in his study, where 45.6 % of the participants in his study were graded ASA III or greater (Buck 2013). Binary logistic regression analysis of ASA and 30 day post-operation mortality revealed a statistically significant association (p-value 0.48; odds ratio 2.96 at 95% C.I.) between a rise in ASA and 30-day post-operative mortality. This finding is unsurprising, as it has been well documented in studies done in Asia and Europe and ASA score of patient before surgery has been well known to be an independent predictor for morbidity and mortality following Surgery (Møller 2012; Thorsen 2013).

A look at the chemistry results of the patients on admission, 40.00 % (n=14) had an elevated serum creatinine level and 37.1% (n=) had a low serum albumen level. Univariate binary logistic regression analysis of serum creatinine level on admission showed a statistically significant association (p-value 0.033; odds ratio 4.63 at 95% C.I.) between serum creatinine level and 30-day post-operation mortality. This discovery endorses finding from earlier studies that have found that elevated serum creatinine is predictor of 30 day post-operation mortality in patients with PPU (Singh 2011; Thorsen, 2013). Univariate binary logistic regression analysis of serum albumen on admission found no statistically significant association (p-value 0.21; odds ratio 1.61 at 95% C.I.) between serum albumen level 30 day post-operative mortality. This is in dispute with results from a study in Turkey that found low serum albumen to be the strongest single factor in predicting 30 day post-operation mortality after surgery for PPU (Menekse 2015).

At operation, the site of perforation was found to be gastric in 32 (91.14%) of the patients and only 3 (8.57%) patients had duodenal perforation. For gastric perforation, the commonest location was the antral and pyloric region. All duodenal ulcers were located to the first part of the duodenum. Most perforations were estimated to be between 5mm-10mm (42.86%, n=15), followed, in descending order by those estimated to be less than five (5mm) (25.71%; n=9), 11mm-20mm (20.00%; n=7) and > 20mm (11.43%; n=4) respectively. This finding concurs with the finding of Sondashi (2010), who also found that gastric perforation among our population occur mostly on the gastric region.

The operation that was commonly done was primary perforation repair plus omental pedicle patchy in 94.29% (n=33) cases and lavage with normal saline. This procedure has widely been accepted to be the standard in emergency management of PPU especially were patient present so late. It has proven to be an effective management of PPU with acceptable morbidity and mortality. The other operation performed was partial gastrectomy plus primary gastrojejunostomy in 5.71% (n=2) cases for large ulcer.

On univariate binary regression analysis of site of perforation and 30 day post-operation mortality did not yield any statistically significant association (p-value; odds ratio) between the two. This finding is in conflict with the finding of Chalya in Tanzania, who found that gastric location of PPU was significantly associated with mortality(Chalya 2011). However, size of PPU was found to be significantly associated with 30-day post-operative mortality, p-value 0.035; odds ratio 2.49. This results reinforces the finding of one European study that found that Size of perforation was a significant predictor of mortality and agrees with the finding of Lee, were his study did find a significant relation between perforation size and mortality on univariate analysis but not on multivariate analysis.(Lee 2001). Univariate binary logistic regression analysis of type of surgery done and 30 day post-operation mortality found no significant association between type of operation performed and 30 day post-operation mortality. This finding agrees with a study done in India, which found no significant difference between simple closure and definitive surgery (vagotomy plus drainage procedure) in the management of PPU (Chandra 2009). Kocer (2007), found that definitive operation in patients with PPU was significantly associated with mortality and this disagrees with the finding in this study.

Post operatively, almost all the patient (97.14%; n=34) were nursed on the general surgical wards. The mortality rate was found to be 34.31% and 40% of the patient developed a post-operative complication. The average length of hospital stay was 7.26 days with a standard deviation of +/- 3.45 days. The mortality rate has remained almost static with somewhat a slight reduction compared to the finding of Sondashi in 2010 which was at 37%. Half of the mortalities happened within the first 48 hours after operation. There is room for improvement when it comes to post-operative mortality outcome in patients with PPU in our hospital especially if care for these patients in the perioperative period is strengthened. Our usage of ICU care for PPU patients post-

operatively is quite very low, considering that most of our patients present late and in shock. There is evidence from Aga (2012), that increased usage of ICU and HDU facilities in the post-operative care PPU patient has been associate with improved survival among these patients.

We need to find a way for PPU patients to have increased access to ICU care despite the very high demand for bed space in our ICU if mortality among these patients is to be reduced.

After univariate binary logistic regression analysis of the independent (predictor) variable and univariate linear regression analysis of HIV status and CD4 cell count, outlined in the methodology section, age, ASA score, serum creatinine, peptic ulcer perforation size, HIV status and CD4 Cell count were found to have statistically significant association with 30 day post-operative mortality in patients with PPU in this study. However, on multivariate logistic regression analysis of the above factors, no statistically significant association was found between them and 30 day post-operation mortality. The strongest looking predictor among the above variable on multivariate logistic regression analysis was serum creatinine (p-value 0.69; odds ratio 18.46).

From the findings of the research, four (4) out of eight (8) of the variable constituting the PULP score were found to significantly associated with 30 day post-operation mortality on univariate regression analysis and these are age, raised serum creatinine, ASA score, AIDS. Compared to the variable used in the Boey score, only the co-morbidity factor was found to significant, that is HIV positive status, among our patients. Therefore, it would not be prudent to adopt any of the two popularly used scores to predict mortality in patients with PPU at UTH based on these research findings.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

PPU is a common finding among patient presenting with peritonitis and undergoing emergency laparotomy in the department of surgery, UTH-Adult Hospital. Most of the patient present late and are in shock at presentation. 30 day post-operation mortality was found to be 34.29% and 40.00% of the patient developed post-operative complications. Univariate binary logistic regression and univariate linear regression analysis revealed that age, raised serum creatinine, HIV positive status, low CD4 cell count and size of peptic ulcer perforation were significantly associated with 30 day post-operation mortality. However, none of the above variables was found to be significantly associated with 30 day post-operation mortality on Multivariate binary logistic regression analysis.

6.2 Recommendations

1. Improve post-operative ICU admission for selected patients with PPU.
2. Develop a Local Clinical tool to help identify patient in need of post-operative ICU care with the aim of reducing mortality among patients with PPU.
3. Formulate local Protocol on the management of patients with PPU, this will ensure uniform standard of care among Firms.
4. Establish HDU for post-operative care of patients with PPU and other surgical patients that need close post-operative. This will improve perioperative care of patient with PPU and ultimately post-operative outcome.

REFERENCES

Aga, H., Readhead, D., MacColl, G., Thompson, A., 2012. Fall in peptic ulcer mortality associated with increased consultant input, prompt surgery and use of high dependency care identified through peer-review audit. *BMJ Open* 2, e000271. <https://doi.org/10.1136/bmjopen-2011-000271>

Anbalaka, et. al., 2015. Five year experience in management of perforated peptic ulcer and validation of common mortality risk predicting models- Are existing models sufficient? A retrospective cohort Study. *International Journal of the surgery*, Volume 14, pp. 38-44.

Buck, et. al., 2013. Surgical delay is a critical determinant of survival in perforated peptic ulcer. *British journal of surgery*, Volume 100, pp. 1045-1049.

Chalya, P.L., Mabula, J.B., Koy, M., Mchembe, M.D., Jaka, H.M., Kabangila, R., Chandika, A.B., Gilyoma, J.M., 2011. Clinical profile and outcome of surgical treatment of perforated peptic ulcers in Northwestern Tanzania: A tertiary hospital experience. *World Journal of Emergency Surgery* 6, 31. <https://doi.org/10.1186/1749-7922-6-31>

Kelly, P., Katema, M., Amadi, B., Zimba, L., Aparicio, S., Mudenda, V., Baboo, K.S., Zulu, I., 2008. Gastrointestinal pathology in the University Teaching Hospital, Lusaka, Zambia: review of endoscopic and pathology records. *Trans R Soc Trop Med Hyg* 102, 194–199. <https://doi.org/10.1016/j.trstmh.2007.10.006>

Kocer, B., Surmeli, S., Solak, C., Unal, B., Bozkurt, B., Yildirim, O., Dolapci, M., Cengiz, O., 2007. Factors affecting mortality and morbidity in patients with peptic ulcer perforation. *Journal of Gastroenterology and Hepatology* 22, 565–570. <https://doi.org/10.1111/j.1440-1746.2006.04500.x>

Kim, et. al., 2012. Analysis of Risk Factors for Postoperative Morbidity in Perforated Peptic Ulcer. *Journal of Gastric Cancer*, 12(1), pp. 26-35.

Leeman, et. al, 2013. The management of perforated Gastric ulcers. *International Journal of Surgery*, Volume 11, pp. 322-324.

Mäkelä, J.T., Kiviniemi, H., Ohtonen, P., Laitinen, S.O., 2002. Factors That Predict Morbidity and Mortality in Patients with Perforated Peptic Ulcers. *The European Journal of Surgery* 168, 446–451. <https://doi.org/10.3109/110241502321116424>

Menekse, E., Kocer, B., Topcu, R., Olmez, A., Tez, M., Kayaalp, C., 2015. A practical scoring system to predict mortality in patients with perforated peptic ulcer. *World Journal of Emergency Surgery* 10, 7. <https://doi.org/10.1186/s13017-015-0008-7>

Møller, M.H., Adamsen, S., Wøjdemann, M., Møller, A.M., 2009. Perforated peptic ulcer: How to improve outcome? *Scandinavian Journal of Gastroenterology* 44, 15–22. <https://doi.org/10.1080/00365520802307997>

Moses, J.F., Hughes, C.D., Patel, P.B., Chao, T.E., Konneh, S.A., Jallabah, T.Y., Kikubaire, M.K., Meara, J.G., Hagander, L.E., 2015. Surgical outcomes for perforated peptic ulcer: A prospective

case series at an academic hospital in Monrovia, Liberia. *African Journal of Emergency Medicine* 5, 60–65. <https://doi.org/10.1016/j.afjem.2014.11.002>

Munir, et. al., 2014. Frequency of high boey score and its one month mortality after surgery for perforated peptic. *Kashmir journal of medical science*, 6(2), pp. 253-257.

Nichakankitti, et. al., 2016. The accuracy of prognostic Scoring systems for post- operative morbidity and mortality in patients with perforated peptic ulcer.. *International Surgery Journal*, 3(1), pp. 386-290.

Nogueira, C., Silva, A.S., Santos, J.N., Silva, A.G., Ferreira, J., Matos, E., Vila, H., 2003. Perforated Peptic Ulcer: Main Factors of Morbidity and Mortality. *World Journal of Surgery* 27, 782–787. <https://doi.org/10.1007/s00268-003-6645-0>

Ojuka, et. al., 2014. Causes and Patterns of Peritonitis at St. Francis Hospital Nsambya, Kampala Uganada. *East and Central African Journal of Surgery*, p. 19(3).

Proctor, et. al., 2014. Complication of Peptic Ulcers. *Surgery (Oxford)*, 32(11), pp. 599-607.

Ramakrishnan, et. al., 2007. Peptic Ulcer Disease. *American Family Physician*, 76(7), pp. 1005-1012.

Sarath Chandra, S., Siva Kumar, S., 2009. Definitive or conservative surgery for perforated gastric ulcer? – An unresolved problem. *International Journal of Surgery* 7, 136–139. <https://doi.org/10.1016/j.ijvsu.2008.12.037>

Sarosi, et. al., 2005. Surgical therapy of peptic ulcers in the 21st century: more common than you think.. *The American journal of surgery*, Volume 190, pp. 775-779.

Singh, et. al., 2011. Preoperative predictors of mortality in adults with perforation peritonitis. *Indian journal of critical care medicine*, 15(3), pp. 157-163.

Sondashi, et. al., 2010. A pilot study to determine the various clinical and epidemiological factors associated with Peptic ulcer perforation at UTH. *Medical Journal of Zambia*, 38(2), pp. 15-22.

Søreide, K., Thorsen, K., Harrison, E.M., Bingener, J., Møller, M.H., Ohene-Yeboah, M., Søreide, J.A., 2015. Perforated peptic ulcer. *Lancet* 386, 1288–1298. [https://doi.org/10.1016/S0140-6736\(15\)00276-7](https://doi.org/10.1016/S0140-6736(15)00276-7)

Søreide, K., Thorsen, K., Søreide, J.A., 2014. Strategies to improve the outcome of emergency surgery for perforated peptic ulcer. *British Journal of Surgery* 101, e51–e64. <https://doi.org/10.1002/bjs.9368>

Thorsen, K., Søreide, J.A., Kvaløy, J.T., Glomsaker, T., Søreide, K., 2013. Epidemiology of perforated peptic ulcer: Age- and gender-adjusted analysis of incidence and mortality. *World J Gastroenterol* 19, 347–354. <https://doi.org/10.3748/wjg.v19.i3.347>

Tolonen, et. al., 2016. Preoperative prognostic factors for severe diffuse secondary peritonitis: a retrospective study. *Langenbecks Archive Surgery*, Volume 401, p. 611–617

Ugochukwu, A.I., Amu, O.C., Nzegwu, M.A., Dilibe, U.C., 2013. Acute perforated peptic ulcer: on clinical experience in an urban tertiary hospital in south east Nigeria. *Int J Surg* 11, 223–227. <https://doi.org/10.1016/j.ijsu.2013.01.015>

unaid, <http://www.unaids.org/en/regionscountries/countries/zambia> (accessed 5.9.18).

Unver, M., Fırat, Ö., Ünalp, Ö.V., Uğuz, A., Gümüş, T., Sezer, T.Ö., Öztürk, Ş., Yoldaş, T., Ersin, S., Güler, A., 2015. Prognostic Factors in Peptic Ulcer Perforations: A Retrospective 14-Year Study. *International Surgery* 100, 942–948. <https://doi.org/10.9738/INTSURG-D-14-00187>.

APPENDICES

APPENDIX A

Participants Information Sheet

TITLE: A Study to investigate factors associated mortality in patient managed for perforated peptic ulcer at University Teaching Hospital, Lusaka Zambia.

Introduction

I am Dr. Edward N. Nyimbili, from the University of Zambia, school of medicine, department of Surgery, doing Master of Medicine in general surgery. I am carrying out a study investigating factors that are associated with morbidity and mortality in patient treated for perforated peptic ulcer in this hospital.

Purpose of the study

The purpose of the study is to find factors that can be used to tell which patients are at risk of dying that present with perforated peptic ulcer following surgery for a perforated peptic ulcer. The result of the study will help the Department of Surgery see if they any factors that can be acted on to help prevent or reduce number deaths and complications arising from perforated peptic ulcer disease.

Procedure

The study will involve you answering few questions on your demographic and those specific to your condition. This is done as a routine part of your work up for your condition. You will be required to sign a consent form to take part in the study. Blood will be drawn for routine investigation for your condition i.e. Full blood Count, Urea and electrolytes and liver function test. The treatment of your condition requires an abdominal operation to confirm and the repair the perforated ulcer. Additionally you will be required to do an HIV if your HIV status is not known and CD4 cell count will be done if required, to give you a holistic treatment. Participation in this study will not any way affect the quality of care you receive or delay the time you will be operated.

Potential Benefits

The study will cover the cost of the investigations. You will not receive any payment for participating in this study. There are no other benefits for participating in the study but information gained from the study will be used to improve the quality of care for patients with this condition in future.

Potential Risks

There is no risk attributed to participating in this study as all procedures done are part of the standard of care for patients with this condition.

Rights of a research Participant

Your participation in this is voluntary. You have the right to withdraw from the study at any time and such a decision will not in any way affect the quality and standard of care given to you.

Confidentiality

All the information obtained from you will only be used for the purpose of this study. Personal information about you will not be released to anyone and will not be used in any publication.

Further information

If you have any other question about this study or you wish to have further clarification about the study you may contact:

The Principal Investigator

Dr. Edward N. Nyimbili

University of Zambia

School of Medicine

Department of surgery

Lusaka, Zambia

Tel: +260979391951

For concerns regarding ethical issues in conducting this study contact.

ERES CONVERGE IRB

33Joseph Mwilwa Road

Rhodes Park

Lusaka.

Tel: 0955 155633/4

E-mail: eresconverge@yahoo.co.uk

APPENDIX B

Consent Form

By signing below, I give consent to participate in this study and that the purpose of this study has been explained to me and I understand the purpose of this study. I also give consent to the principle investigate to contact my next of Kin if he is unable to reach me during the course of the Study. In addition, I understand that participation in this study is purely voluntary and I can withdraw from the study at any time without giving any explanation. I am aware that my rights and privacy will be maintained throughout the study period and beyond.

I _____ (Names)

Agree to participate in both the interview and study

Sign/thumbprint _____ Date : ___/___/_____(Participant)

Sign _____ Date: ___/___/_____(Witness)

Sign _____ Date: ___/___/_____(Researcher)

APPENDIX C
QUESTIONNAIRE

A. DEMOGRAPHIC DATA

1. Participant Number _____
2. Age: 1. >20 ; 2. 20-30; 3. 31-40; 4. 41-50; 5. 51-65; 6. >65
3. Sex: 1. M 2. F
4. Marital Status 1. Single 2. Married 3. Divorced 4. Widow
5. Address _____ 1. Low 2. Medium 3. High 4. Rural
6. Education level: 1. None 2. Primary 3. Secondary 4. Tertiary

B. CLINICAL (History)

7. Referral from; 1. Low 2. Medium 3. High 4. Rural
8. Presenting complaint (1) Abd. Pain
- (2) Nausea/Vomiting
- (3) Abd. Distension
- (4) Others _____
9. Duration of Symptoms: ____ 1. <24hrs 2. 24-48hrs 3. 48-72hrs 4. >72hrs
10. Does patient know their HIV Status? 1. NR 2. Unknown 3. R
11. Any AIDS defining Disease. 1. Yes 2. No

C. CLINICAL (Examination)

12. Vitals at Presentation: BP _____ Pulse _____ RR _____ Temp. _____ x
- Pt in shock. 1. Yes 2. No
13. What is the ASA Score: 1. 2. 3. 4. 5.

D. INVESTIGATION

- 14. What is Serum Creatinine? x _____ 1. Normal 2. Elevated 3. Low
- 15. What is the Serum Albumen? _____ 1. Normal 2. Elevated 3. Low
- 16. What is CD4 count if appropriate? x _____ 1. Normal 2. Low 3. >200cell/ml

E. INTRA OPERATIVE FINDING:

- 17. Site for perforation 1. Gastric perforation 2. Duodenal perforation
- 18. Estimated perforation size. _____ 1. >5mm 2. 5-10mm 3. 10-20mm 4. >20mm
- 19. Operation done.
 - 1. Gastric repair + omental Patch 2. Other operations. Specify _____ x
- 20. Post-operative nursing of patient done in: 1. General ward 2. ICU
If in ICU reason for ICU admission? _____ x
- 21. Length of stay in hospital. _____ 1. <5days 2. 5-10days 3. 11-30days 4. >30days
- 22. Was there any additional surgery needed? 1. Yes 2. No
If yes; what was the indication? _____ x
- 23. Other complication Post op. _____ 1. Yes 2. No
- 24. Histopathology diagnosis; 1. Non Malignant 2. Malignant
Specimen#: _____
- 25. Is patient Alive 30 day's Post initial operation for PPU? 1. Yes 2. No
- 26. If NO how many days post operatively did the patient die? _____ x