THE UNIVERSITY OF ZAMBIA

SCHOOL OF MEDICINE

DEPARTMENT OF SURGERY

A CROSS-SECTIONAL STUDY ON FACTORS ASSOCIATED WITH PERFORATED PEPTIC ULCER DISEASE IN ADULTS PRESENTING TO THE UNIVERSITY TEACHING HOSPITAL, LUSAKA.

By

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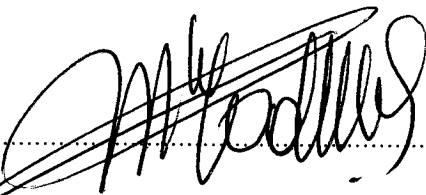
LUSAKA, ZAMBIA

JULY, 2010

DECLARATION

I hereby declare that the work presented in this study for the degree of Master of Medicine in general surgery represents my work and has not been presented either wholly or in part for any other degree by myself or any other person and is not being currently submitted for any other degree at the University of Zambia or any other university.

Signature of candidate..

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Signature of supervisor...

PROF.BFK ODIMBA

CERTIFICATE OF APPROVAL

This dissertation entitled "A cross-sectional study on **factors associated with perforated peptic ulcer disease in adults presenting to the University Teaching Hospital**" by Dr Kitanda J. Sondashi has been approved by the board of examiners as fulfilling part of the Surgery by the University of Zambia.

Examiner1: Signature...

Prof.BFK Odimba
Consultant general surgeon, UTH

Date..................... **27.02.12** ....

DEDICATION

This study is dedicated to my wife and the children Virginia, Ludwig and Sheba without

whose support I could not have finished this work.

ACKNOWLEDGEMENTS

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LIST OF ABBREVIATIONS

Hb   Haemoglobin

H2   Histamine type 2

HIV   Human immunodeficiency virus

NSAID   Non-steroidal anti-inflammatory drugs

SPSS   Statistical package for social sciences

UNZA   University of Zambia

UTH   University Teaching Hospital

ABSTRACT

Objective: To determine the various clinical and epidemiological factors associated with peptic ulcer perforation in adults at UTH.A pilot study for an impending broader controlled study.

Design: A hospital-based cross-sectional study

Participants: 35 adult patients all of whom were diagnosed at laparotomy as having perforated, benign peptic ulcers, confirmed histologically.

Setting:, University Teaching Hospital, Lusaka, Zambia.

Results: It was shown that there was a male preponderance (85.7%). The mean age was 39.9 years and the peak range to perforate was 16-45 years (68.6%). Most patients were Lusaka –based (82.8%),and came from a middle income background(62.8%).Clinically, the most frequent presenting complaint was abdominal pain(62.8%),and 57.2% of patients had symptoms lasting 24 hours or less. Furthermore, the commonest blood group was group O+ (33.2%), with 40% confirming history of use of NSAIDs. 57% were regular alcohol drinkers and 34% were cigarette smokers. Also, a further 32% of patients were found to be HIV positive and 84.2% had no previous peptic ulcer history. Gastric perforations were by far the commonest anatomical site (82.8%) followed by duodenal (14.3%). Postoperative hospital stay prolonging 10 days was 51.4% and 37% died after surgery.

Conclusion: Perforated peptic ulcers occur more in males below 45 years old, most of whom are middle income earners and Lusaka -based. A third of the study group tested positive for HIV and more than half confirmed being regular alcohol drinkers. About a third confirmed smoking cigarettes. The majority of patients denied history of previous peptic ulcer disease. Nearly half the group confirmed usage of NSAIDs and about a third were Blood group O+. Gastric perforations were in the greater majority with half the

patients prolonging hospital stay for more than 10 days. Mortality following surgery was high (37%). A larger study group ought to be recruited for definitive conclusions to be made.

1. __INTRODUCTION__

Acute perforations of peptic ulcers continue as one of the real emergencies of surgery requiring immediate attention and prompt operation. Studies have shown that of patients presenting with perforated peptic ulcers nearly half have no history of the disease(Kocer B et al2007). On endoscopy, unsuspected ulcers have been found in people who were taking non-steroidal anti-inflammatory drugs (NSAIDS),(Svanes C et al 1993).

In elderly patients, signs and symptoms may be minimal. In one series that looked at perforated peptic ulcers in patients over 60 years, 84% had only mild abdominal pains(Christensen et al 2007). Other reported symptoms were dyspepsia, anorexia, nausea and vomiting. Severe abdominal pain was only present in 16%. Duration of symptoms ranged from 4 hours to 10 days. Also, most patients had abdominal tenderness, with 66% exhibiting the classical signs of peritonitis. About 6% had no abdominal findings.

Due to the effective medical management with H2 receptor blockers and proton pump inhibitors, and eradication of Helicobacter pylori, the incidence of peptic ulcers and hospitalization rate have decreased. However, the rate of complicated peptic ulcers remains the same. In recent years, patients presenting with perforated peptic ulcers have tended to be elderly, chronically ill and taking one or more ulcerogenic drugs. Several studies have shown the mean age to be more than 60 years(Christensen et al 2006). A history of ulcer disease or symptoms of an ulcer is important .In one study, one-third of patients had history of peptic ulcers and 32% of patients who presented with perforation were taking H2 receptor blockers, anti acids or both. A significant percentage of patients had a history of smoking, alcohol abuse, and postoperative stress (Sharma SS et al 2006).

In most cases of perforation, gastric and duodenal content spills into the peritoneal cavity. This content includes gastric and duodenal secretions, bile, ingested food, and swallowed bacteria. The leakage results in peritonitis, with an increased risk of infection and abscess formation. Subsequent third-spacing of fluid in the peritoneal cavity due to perforation and peritonitis leads to inadequate circulatory volume, hypotension, and decreased urine output. In more severe cases, shock may ensue. Abdominal distention as a result of peritonitis and subsequent ileus may interfere with diaphragmatic movement, impairing expansion of lung bases. Eventually, atelectasis develops, which may compromise oxygenation of the blood, particularly in patients with co-existing lung disease. (Sharma S et al 2006).

2. **JUSTIFICATION**

There is no data on the epidemiological characteristics of perforated peptic ulcers in Zambia. What is more, there is an increased incidence of adult patients presenting with peptic ulcer perforation at UTH but data on predisposing or risk factors is lacking.

Also, morbidity and mortality associated with peptic ulcer perforation is very high. The post-operative mortality for emergency surgery nears 50% compared to elective surgery for unhealing ulcers which is below 5%.Thus,the study is meant to streamline the referral links between the endoscopy or medical unit and the surgical unit to manage refractory cases of peptic ulcers early. Lastly the study will provide a basis upon which further research can be undertaken.

3. OBJECTIVES

3.1. GENERAL OBJECTIVE

To determine the clinical and demographic characteristics associated with the high numbers of perforated peptic ulcers in adults presenting to the University Teaching Hospital.

3.2. SPECIFIC OBJECTIVES:

The specific objectives of this study are to:-
1. Determine the rate of peptic ulcer perforation at UTH
2. Study the demographic factors associated with perforated peptic ulcers in adults presenting to UTH.
3. Determine the clinical presentation associated with perforated peptic ulcers in adults at UTH.
4. Examine the roles of HIV, alcohol, smoking and NSAID usage as associated factors to peptic ulcer perforation.

4. LITERATURE REVIEW

Peptic ulcer, was until, recently regarded as an "Un African" disease. It has, however, been reported that the problem then was one of recognition unlike incidence.

Palmar. D et al (1994) in Cameroon found 35% (33 of 93) incidence of perforated peptic ulcers with a ratio of duodenal to gastric of 5:1.

In Ethiopia, Tedla .Z (1990), reported a 20% incidence of perforated peptic ulcers in the patients he studied.

Perforated peptic ulcers are fairly common in Zambia. Bem (1991) reported perforated peptic ulcers to be the third commonest cause of generalized peritonitis for which surgery was indicated between November 1988 and April 1990, by the surgical department of the UTH, Lusaka. He found it in 16 %(18 of 109) of patients, third after perforated terminal ileum and perforated appendicitis.

Furthermore, it was shown by Mulia. C (1998) in Zambia that of 87 patients who had undergone endoscopy at UTH, 14.9 %(13 of 87) had peptic ulcers.

Tukli.J (1977) in Zambia showed that of 60 patients with upper gastrointestinal bleeding, 55% (33 of 60) had chronic duodenal ulcers whilst 1.7 %(1 of 60) had gastric ulcers.

Mundia .S (1978) reported a 42 %(22 of 50) incidence of peptic ulcers.

Kelly P et al (2008) at UTH, found duodenal ulcers(17%)and gastric ulcers(12%) in a review of endoscopy and pathology reports.

At UTH, a two-year retrospective pilot survey between December 2005 and December 2007 revealed a total of 674 patients presenting with peritonitis requiring surgery. Of these patients 9.7% (66 of 674) had perforated peptic ulcers. Furthermore, it was found that 77%(51 of 66) of these had perforated gastric ulcers as opposed to 23%(15 of 66) with perforated duodenal ulcers, giving a ratio of gastric to duodenal of 3.3:1.

Svanes.C et al (1993) at the Haukeland University Hospital in Norway studied 1483 patients with perforated peptic ulcers from 1935-1990 to discover time trends in age, sex, disease characteristics, treatment and outcome. The male to female ratio fell from 5:1to 1.2:1, median age increased from 41 to 62, most perforations were duodenal (52%) followed by pyloric (30%) and prepyloric (10%).He reported 10% incidence of gastric perforations throughout the study period. Ulcer site was related to age (more gastric and

less duodenal with increasing age) and sex (more pyloric and less duodenal among women). There were twice as many perforations in the evening than in the morning. Treatment delay increased from a median five hours to nine hours, infective complications and mortality fell with the introduction of antibiotics in the 1950's

Several risk factors have been associated to peptic ulcer perforation, These include alcohol, cigarette smoking, NSAID usage, and blood group O+.

A study was done in Japan to assess risk and exposure to alcohol, cigarettes and NSAIDs in relation to development of ulcers and perforation (Kurata J, 1997).It was shown that the attributable risk percentage to ulcerate and perforate due to alcohol and cigarettes was 34%.Also the study further attributed risk percentage for regular NSAID usage to be 24%.

A Nigerian study to assess the association between blood group subtype and peptic ulcer perforation revealed that 69.2% of patients had blood group O+(Ajao OG,1989).

There is very limited literature on the relationship between HIV and perforated peptic ulcers locally and world-wide. A randomized controlled study was done at UTH to examine gastric mucosal barrier impediment to supplementation in HIV positive cases. It was shown that there was marked reduction in gastric acid production in these patients compared to HIV negative controls (Kelly P et al, 2009).Since over-production of gastric acid has been shown to predispose to peptic ulceration, it is assumed that HIV may offer a protective role in formation of peptic ulcers.

Marshall P et al (1984) showed that 60% of gastric and 90% of duodenal ulcers were due to H.pylori, and that 4% of gastric ulcers were due to gastric cancer.

While H. pylori is well recognized as a causative factor in peptic ulcers, its exact role in cases of perforated ulcer has not been established. Chowdry SK et al (1998) reported on a series of 45 patients, of which 15(33%) had duodenal perforation. None of these 15 patients had evidence of H. pylori infection. Reinbach DH et al (1993) also concluded that there was no clear association between H.pylori infection and duodenal ulcer perforation. In a series of 80 patients with perforated duodenal ulcers, 47% had H.pylori infection, which was similar to the 50% rate in the control group.

Plain chest and erect abdominal x-rays have been used to diagnose perforated peptic ulcer. However, in 30% to 50% of patients, the x-ray may be negative for free air, particularly in the elderly. A left lateral decubitus film is most sensitive in detecting pneumoperitoneum. Placing the patient in the upright or left lateral decubitus position for 10 minutes prior to x-ray may help detect the condition. Similarly, use of a water-soluble contrast medium with an upper gastrointestinal tract series or computed tomography scan may increase the diagnostic yield (Kocer B et al 2007).

Sharma SS et al (2006) in a prospective study of 96 patients looked at predictive risks for postoperative complications in perforated peptic ulcers. The patients were treated using Graham's omentoplasty patch or gastrojejunostomy. It was observed that the risk of developing postoperative complications was significantly influenced by the presence of concomitant medical illness (OR=8.9,p=0.001), abdominal distention (OR=3.8,p=0.048) and a need for blood transfusion (OR=4.2,p=0.027). Using Poisson regression, it was observed that the risk for a higher number of complications was influenced by the same factors (RR=2.6,p=0.015;RR=4.6,p=0.001;RR=2.4,p=0.002;respectively). However, the rate of development of complications was influenced by a history suggestive of shock (RH=3.4,p=0.002) and A- blood group (RH=4.7,p=0.04).

There has been a relative increase in cases of perforated peptic ulcers in elderly patients. Higher morbidity is due to several factors, often there's delay in diagnosing perforated peptic ulcers leading to treatment delay. Elderly patients are likely to have other medical problems, which increase preoperative risk and contribute to a higher rate of post operative complications. Werbin N et al (1990) reported a 50% mortality in patients over age 70 with duodenal perforation presenting over 24 hours from the onset of symptoms. In this same series, patients presenting early and were operated within 24 hours had 0% mortality. .

Kocer B et al (2007) showed that increasing age (>65), associated medical illness, increased ASA scores (3 and 4), smoking, presence of shock, and diagnostic and treatment delay accounted for higher mortality. He found a mortality rate with conservative surgery (simple closure and omental patch) of 8.6%. Boey et al found a mortality rate of 7.8% in 2558 patients with simple closure.

Christensen et al (2007) in a cohort of 2061 patients, found 743(36%) were between 65-79 years and 513(25%) were 80 and above. Standardized 30 day mortality was 8.9% amongst patients less than 65 rising to 44.6% among patients 80+ years. He concluded that ageing is a strong predictor for poor outcome in patients with perforated peptic ulcers independently of co-morbidity.

Chou NH et al (2000) in Taiwan studied 179 patients with perforated peptic ulcer to assess associated risk factors of mortality. The overall mortality was 15 %(26 of179).Of the 26 patients who died, the cause of death was overwhelming sepsis in 21(81%), hypovolemic shock in 2(7.7%), fatal arrhymia 1(3.3%) and heart failure 1(3.3%).15 of the patients who died of sepsis did not have fulminant abdominal sepsis. Most deaths occurred early after operation (1-96days), old age, preoperative shock, and type of operation seemed to be related to these deaths on univariate analysis, but multivariate analysis showed that coexisting medical illness, delayed treatment, and low albumin levels were independent risk factors for mortality. He concluded that to improve treatment outcome for perforated peptic ulcer, diagnosis and treatment should be prompt.

5. PATIENTS AND METHODS

5.1. STUDY DESIGN and DURATION

A snapshot cross-sectional study was done on patient medical records for the period covering the period 01st January to December 30th, 2009 .Thirty five (35) patients were enrolled in the study. The study is to serve as a pilot study as it is an analysis of initial data collected for a larger case-control study to be undertaken in due course.

5.2. STUDY SITE/AREA

The study was conducted in the department of surgery at the University Teaching Hospital in Lusaka, Zambia.

5.3 CASE DEFINITION

Refers to a perforated peptic ulcer at laparotomy whose histological findings confirm a benign, non-specific lesion.

5.4. INCLUSION CRITERIA

1 Patients over 16 years old

2 Patients presenting with generalized peritonitis in the surgical emergency ward

3 Positive histological diagnosis for benign ulcerative lesion.

4 Obtained informed consent

5.5. EXCLUSION CRITERIA

1 Patients under 16 years old

2 Patients presenting with other surgical emergencies other than peritonitis.

3 Histopathological diagnosis other than benign ulcerative lesion

4 Refusal to give consent.

5.6. SAMPLE SIZE

All patients that met the inclusion criteria for the study and gave consent were enrolled continuously during the study period and thus determined the sample size.

Of thirty-nine (39) histological diagnoses that were captured during the study period, thirty-five(35) were benign ulcerative lesions, two(2) were gastric cancer and two(2) were reported as indeterminate.

5.7. SAMPLING

All consented patients that met the inclusion criteria were enrolled in the study using a non-probability convenience method throughout the period of the study.

5.8. DATA COLLECTION

Data was collected using standardized data collection sheets at patient enrollment and on follow-up. Data was retrieved from case notes and manual registration recording systems in theatre, surgical admission wards, inpatient wards, outpatient clinics, endoscopy and histology laboratory. Data captured from case notes included patient characteristics, previous ulcer history ,time of perforation, admittance and operation, preoperative diagnostic procedures, treatment, complications and death. Other data were retrieved from operation notes and in-patient consecutive recordings of admitted and operated patients.

5.9. DATA ANALYSIS

Data on clinical and socio-demographic factors was captured on patient evaluation forms then entered into spreadsheets on Excel and imported to SPSS Version 17.0 for analysis. Frequency tables and cross tabulations were used to draw inferences.

LIMITATIONS

Study sample size was relatively small compared to the scope of the study as well as time limitations thereby making it difficult to produce definite conclusions.

6. **ETHICAL CONSIDERATIONS**

This study involving human subjects was approved by the University of Zambia Biomedical Research Ethics Committee (assurance no.FWA00000338, IRB00001131 of IoRG0000774).

Informed consent was obtained from every patient prior to inclusion. Absolute confidentiality was assured and the right to withdraw from the study reserved to the patient. For patients unable to understand English, vernacular was used to properly communicate various aspects about the study. All patients were treated humanely and with dignity.

7. <u>RESULTS:</u>

Relevant data was retrieved from standardized collection sheets and entered into an Excel spread-sheet then imported in SPSS Statistics 17.0 for analysis. The data was categorized into three groups (i).Rate of perforation at UTH (ii). Demographic variables representing socio- demographic factors and (iii). Clinical variables that represented clinical presentation, history and laboratory findings.

7.1. Rate of perforation at UTH

Of 118 patients operated for peritonitis between January to December 2009, thirty-five (35) had benign, perforated peptic ulcers accounting for 29.7% of emergency surgery.

7.2. Demographic variables (see table 1)

- *Gender* - Of 35 patients, thirty(30) were male(85.7%),and five(5)were female(14.3%).The male/female ratio being 5.9:1

- *Age* - a continuous variable representing patient age distribution. The mean age was 39.9 years while the age range was 16-82 years.

- *Province* of origin - UTH being a referral hospital caters for the entire country. Majority of patients were Lusaka-based(82.8%).

- *Occupation* - Stress is directly linked to occupation and is thus a known cause of peptic ulcer disease. Self-employed patients accounted for 40%,business people were 28.6%.

- *Monthly income*- a surrogate variable used to grossly categorize the study patients into social demographic strata. Most patients fell in the middle income bracket (34.2%)

7.3. Clinical variables

These were subdivided into signs and symptoms, medical history and laboratory findings.

7.3.1. SIGNS AND SYMPTOMS-

Commonest presenting complaint was abdominal pain only(62.8%),duration of symptoms ranging 25-48 hours(42.8%).Preoperative Hb ranged 10-13g/dl(57.2%).See table 2

7.3.2. MEDICAL HISTORY-

Included socio-behavioural history, and concurrent illness.57% of patients confirmed drinking alcohol regularly,34% smoked cigarettes,40% of patients used NSAIDs on a regular basis.Also,84.2% of patients had no history of prior peptic ulcer disease. See figure1&2

7.3.3. LABORATORY FINDINGS

The commonest blood group subtype was O +(33.2%),and 32% of patients tested positive for HIV. See figure 1& 3.

Gastric perforations were in the greater majority (82.8%), whereas duodenal perforations accounted for 17.2 %,(see figure 4). Of thirty-nine (39) perforations during the study period, thirty-five (35) were histologically classified as benign, chronic ulcerative lesions, two (2) were gastric carcinoma and two (2) were indeterminate. Thus 89.7% of perforated ulcers were due to benign, chronic lesions and 5.1% were as a result of cancer.

Most patients prolonged hospital stay for more than 10 days (51.4%) after surgery.(figure 5)

Table 1. Distribution of the patients' demographic variables thought to be associated with perforation, $n = 35$

| Variable total	f	% of
• *Gender*		
Female	05	14.3
Male	30	85.7
• *Subject Age*		
16 – 30yrs	12	34.3
31 – 45yrs	12	34.3
46 - 60yrs	07	20.0
>60yrs	04	12.4
• *Pt.[1] province of origin*		
C/B	02	05.7
Central	03	08.6
Lusaka	29	82.8
Southern	01	02.9
• *Pt[1]. occupation*		
Business	10	28.6
Civil service	03	08.5
Retired	01	02.9
Self-employed	14	40.0
Unemployed	07	20.0
• *pt.[1] Income*		
<0.5m	05	14.3
500 – 1.5m	12	34.2
1.5 – 2m	10	28.6
N/A	08	22.9

Pt.[1]=patient, Income recorded in millions of ZMK

The variables representing clinical signs and symptoms captured from patient files included the following.

Table 2: Distribution of the patients' signs and symptoms, *n = 35*

Variable		Freq.	%
Presenting Complaint	Abdominal Pain	22	62.8
	Abd. Distension + Vomiting	01	02.9
	Abd. Pain + Distension	07	20.0
	Abd. Pain + Vomiting	05	14.3
Duration of presenting symptoms	6 – 12hrs	10	28.6
	13 – 24hrs	10	28.6
	25 – 48hrs	15	42.8
Pre-Op Hb	<10.0g/dl	13	37.1
	10.0 – 13.0g/dl	20	57.2
Pre-Op Hb	<10.0g/dl	13	37.1
	10.0 – 13.0g/dl	20	57.2
	> 13.0g/dl	02	05.7

Figure 1: Distribution of (a) Medical History – HIV status & previous peptic ulcer history (b) Social/behavioural History – Alcohol intake & Smoking.

Blood Group
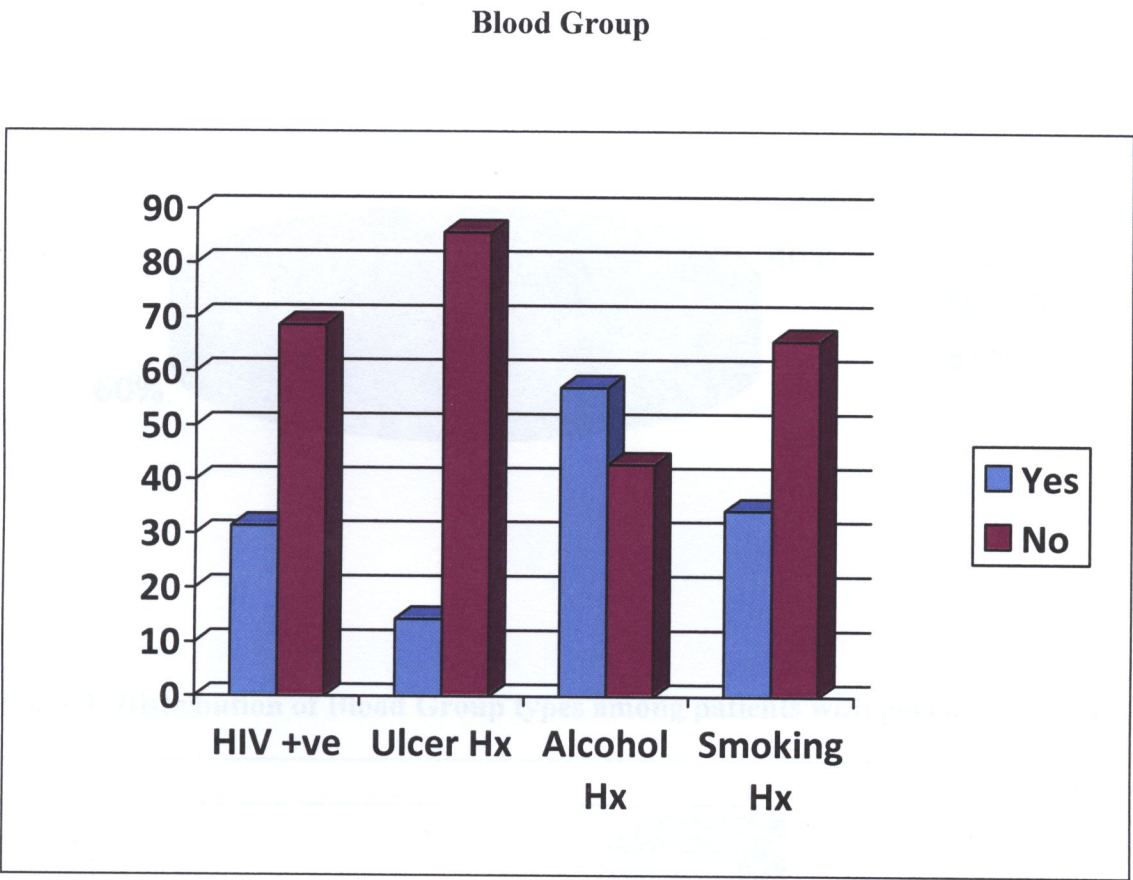
Non Steroidal Anti Inflammatory Drugs (NSAIDs) are over the counter medication in Zambia commonly bought by patients without a doctor's prescription to self medicate against pain which is a common symptom in peptic ulcer disease. Patients suffering from peptic ulcer disease in both medical and surgical wards including clinics are commonly prescribed non-steroidal-anti-inflammatory drugs for pain. Chronic use of NSAIDs is said to cause peptic ulcer disease especially in states of under nutrition and alcohol abuse both of which are common in Zambia.

The diagram below shows the distribution NSAIDs use among the all the study patients who also had perforated peptic ulcer disease.

Figure 2: Distribution of history of NSAIDs use among patients with perforated peptic ulcers
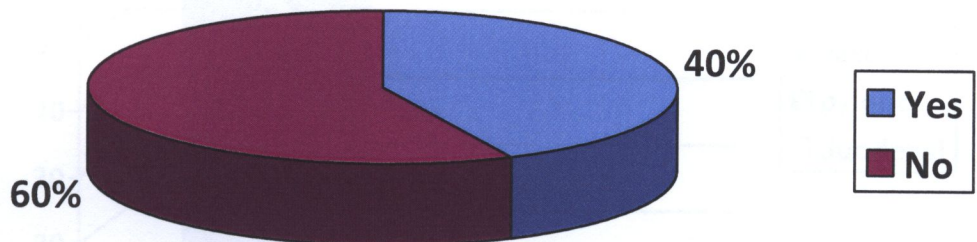

Figure 3: Distribution of Blood Group types among patients with perforated ulcers
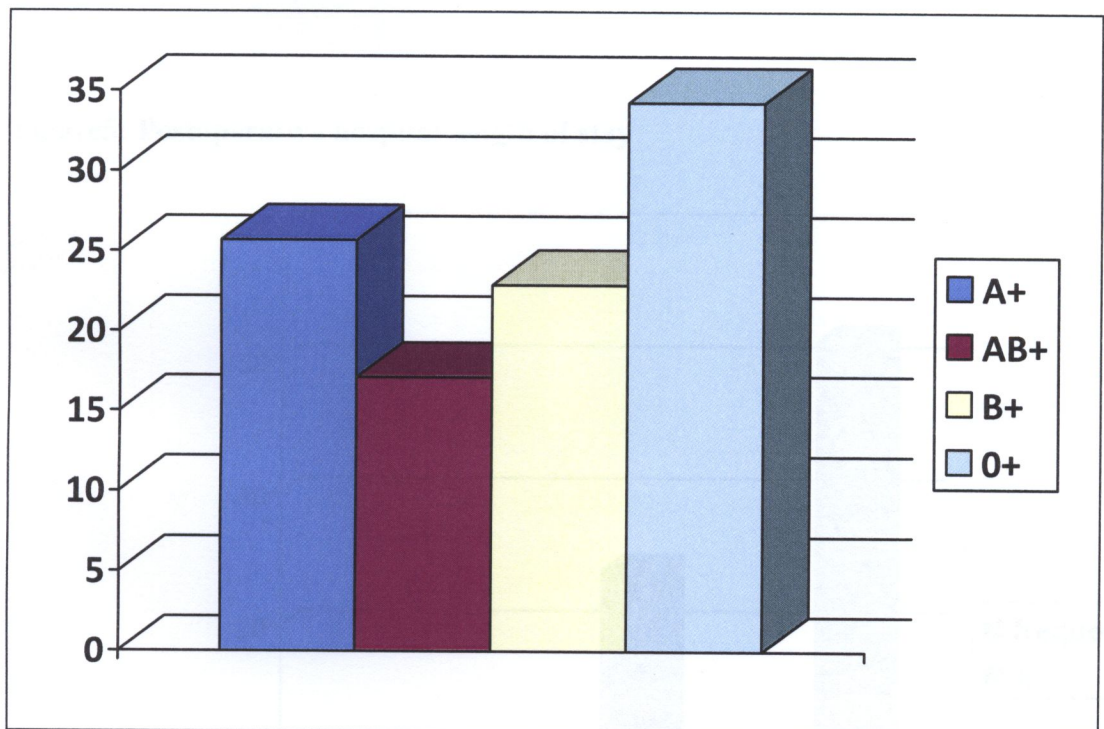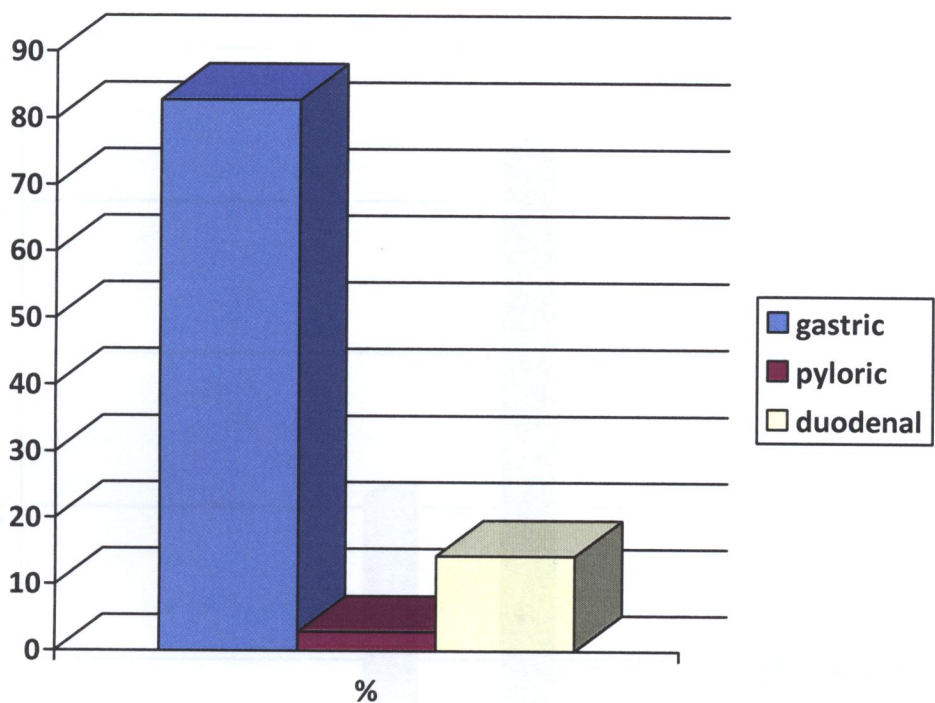
Figure4: Distribution of anatomical site of perforation of study patients

Gastric perforations were by far the commonest mode of ulcer perforation.

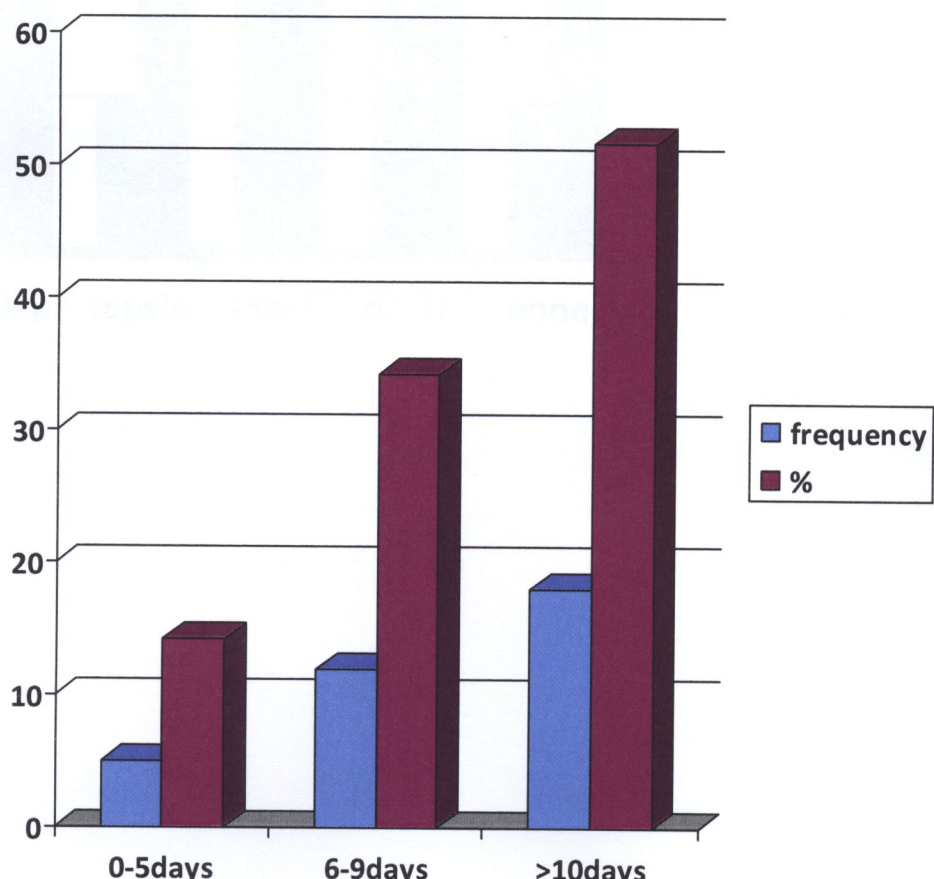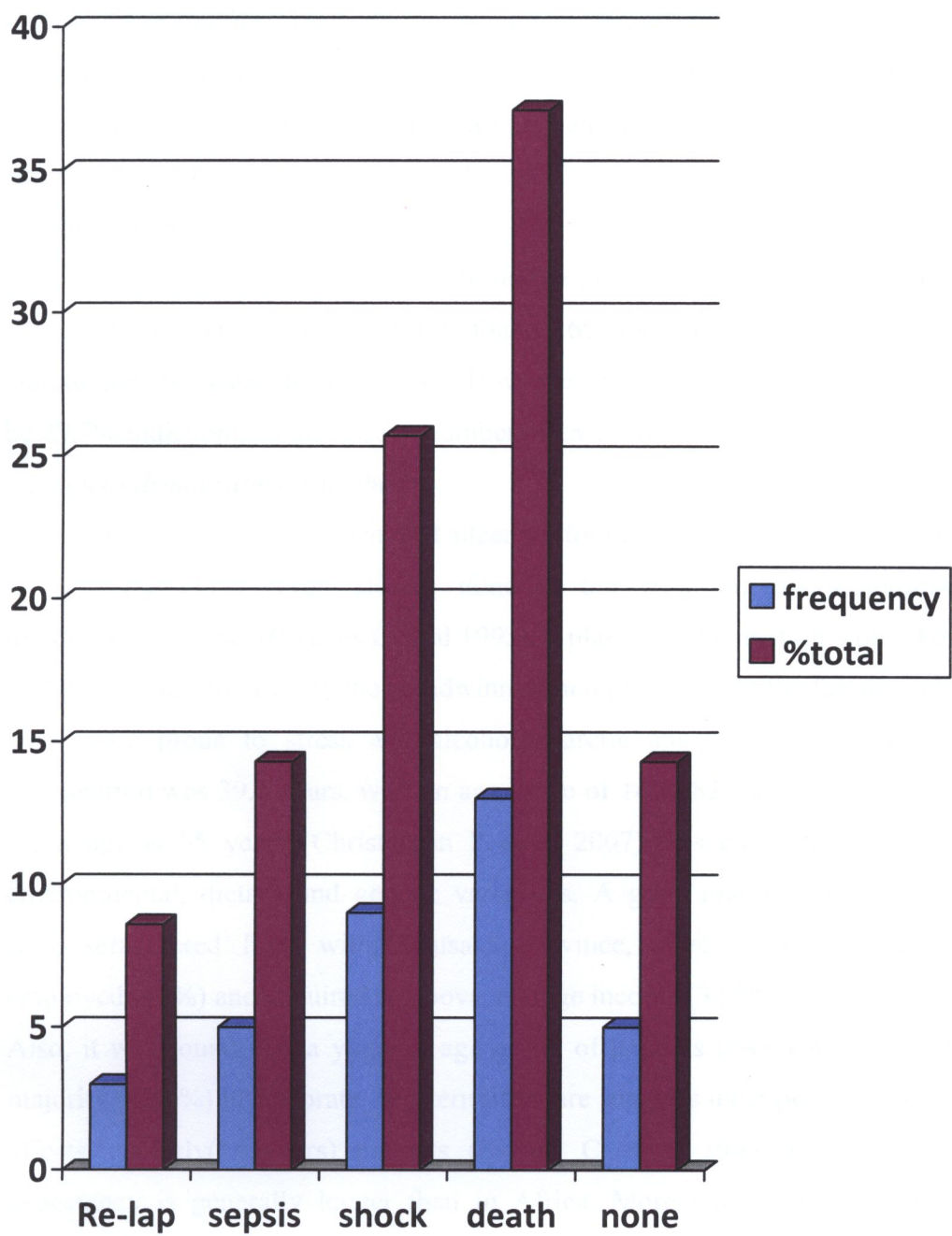**Figure5: Postoperative hospital length of stay**

Figure6; Complications arising after surgical operation.

8.   DISCUSSION

This study aimed at identifying socio- demographic features as well as clinical presentation and /or findings associated with patients found with perforation of peptic ulcers on surgery. It is a cross-sectional analysis of initial data comprising only cases for an impending larger case-control study. It will thus help in subject selection for controls and cases.

8.1. Incidence

It was shown that perforated ulcers are on the increase at UTH, thus the purpose for the study. Bem in 1991 at UTH, found 16% incidence for perforated ulcers among operated cases for peritonitis. However, our study shows the incidence to be 29.7% indicating an increase in number of cases over the years.

8.2. Socio-demographic variables

From our study, it was shown that ulcer perforation had a male preponderance (85.6%) (table1),however ,studies done in the west suggest perforation is irrespective of gender(Svanes C et al 1993).A plausible explanation would be that in Zambia, men are mostly the breadwinners and providers in the family and thus are more prone to stress and alcohol/cigarette abuse. The average age at presentation was 39.9 years, with an age range of 16 to 82 years. In the west, the mean age is 65 years (Christensen P et al 2007).This could be attributed to environmental, dietary and genetic variations. A good majority of the patients were self-refered from within Lusaka province, most of whom were self-employed (40%) and acquired an above average income (34.2%).

Also, it was found that a younger age group of patients (<45years) were in the majority (68,6%) to perforate. Western literature suggests ulcer perforation mostly affects elderly(>65years) patients (Svanes C et al 1993).In the west, life expectancy is generally longer than in Africa, More elderly patients are thus captured than in Zambia where the bulk of the population is youthful. Also, it is assumed that peptic ulcer disease is diagnosed earlier and treated promptly and effectively in the west rather than in Zambia where inadequacies in health service delivery are more prone leading to complications like perforation.

8.3.Clinical variables

The commonest presenting symptom was abdominal pain alone (62.8%), (Table2). This is in agreement with a study done in Norway(Christensen P,2007) where only abdominal pain was the presenting complaint(84%).Duration of symptoms ranged from 6-48 hours, with most patients presenting 24-48 hours after onset of symptoms(42.8%).Patient delay has a bearing on precipitation to perforate as well as poor outcome postoperatively(KocerB et al 2007).Furthermore, it was shown that 57.2% of patients had a preoperative Hb ranging 10-13g/dl, whereas anaemic patients(Hb <10g/dl) accounted for 37.1%, implying perforation does occur at a relatively normal Hb although this is bound to drop due to intrabdominal bleeding if surgery is delayed.

Furthermore ,it was found that blood group O+ was commonest(33.2%) seconded by group A+(24.3%),(seeTable2).This is in agreement with one study done in Nigeria where blood group O+ was found in 69.2% of patients with perforated peptic ulcers(Ajao OG ,1989).

Figure2 shows the use of NSAIDs in relation to perforation where 60% of patients denied usage and 40% confirmed taking some NSAIDs regularly.

NSAIDs have clearly been shown to predispose to peptic ulcer disease. A study done in Japan showed NSAIDs to be a risk factor for perforation in 24% of cases (Kurata J,1997). In our study the sample size may not be large enough for this finding to be conclusive. However, other factors like alcohol abuse with poor nutrition commonly found in a 39 year old Zambian male could be looked at.

HIV was a factor of interest to us. In Figure3 the study relates past medical and/or social history to perforation of peptic ulcers. Here it was found that 32% of patients tested positive for HIV whereas 68% were negative.HIV infected adults show reduced levels of gastric acid production in the stomach ,this may offer a physiological protection against peptic ulcer formation. This was shown in a study done at UTH where it was seen that HIV infection may actually curtail peptic ulcer formation due to acchlorhydria (Kelly P et al, 2009).Thus it would be expected that the rate of HIV in this study should be low, however a 32% infection rate is quite significant. This could squarely be as a result of the pre-existing high prevalence if HIV in the general population, or else a larger, controlled study ought to be employed to draw meaningful conclusions.

Most patients presenting with perforation had no history at all of previous ulcer disease

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(84.2%) making clinical diagnosis at presentation difficult. This is in agreement with a study done in Europe (Kocer B,2006) where half of cases had no history of ulcer disease.

On social history,57% reported to have been regular alcohol drinkers whereas 43% denied alcohol intake. Cigarette smokers accounted for 34% against 66% of non-smokers .Alcohol and smoking have been shown to predispose to peptic ulcer perforation, as seen in Japan where 34% was the population attributable risk to smoking and alcohol (Kurata J,1997).

Gastric perforations were the commonest anatomical site (82.8%) followed by duodenal (14.3%) and only one(1) pyloric perforation. Most studies done in the west suggest a predilection to duodenal perforations. In one study 52% of duodenal and 10% gastric perforations were recorded (Svanes C et al, 1993).The high numbers of gastric perforations in Zambia may be due to dietary or genetic factors, but other factors may be at play and this ought to be researched further.

Further it was shown that 51.4% of patients had stayed more than 10 days on the ward postoperatively for peptic ulcer perforation (Figure5).This clearly has implications on clinical and administrative costs due to associated morbidity.

Death was the commonest complication arising postoperatively accounting for37%.This high mortality rate could be attributed to diagnostic and treatment delay, as well as concomitant underlying medical illness, as noted with high rate of HIV infection in the study group.

9. CONCLUSIONS

The rate of peptic ulcer perforation at UTH is increasing as noted from the study where 29.7% incidence was noted compared to 16% incidence seen at UTH between 1988 to 1990 (Bem,1991).

The mean age for peptic ulcer perforation at UTH is 39.9 years, the peak age range for perforation is 16 to 45 years (68.6%).In Europe, the mean age remains above 62 years (Svanes C et al, 1993). A younger population is mostly affected in Zambia, whether this is due to dietary, environmental or genetic factors remains to be known.

A male preponderance for the disease has been shown accounting for 85.7% compared to 14.3% of females. The male to female ratio is 5.9:1. Most literature from Europe suggests perforation is irrespective of age. A Study done in Norway showed the male /female ratio as 1.2:1(Svanes C et al, 1993).

The commonest presenting complaint remains abdominal pain only as seen in 62.8% of cases, this ties in with a study done in Norway where 84% of cases presented with abdominal pain only(Christensen P ,2007).

84.2% of patients had no prior history of peptic ulcer disease. This is comparable to one study where about 50% of cases reported the same (Kocer B et al, 2007)

Patient delay has a bearing on diagnostic and treatment delay as is shown in our study where 42.8% of patients presented 24-48 hours after onset of symptoms. This has a bearing on morbidity and mortality (Kocer B, 2007).

Blood group subtype seems to favour ulcer perforation as shown where Group O+ accounts for 33.2% of cases. In a study done in Nigeria, it was shown that 69.2% of patients with perforated ulcers had blood Group O+.(Ajao OG,1989).

The use of NSAIDs appears to have an effect on tendency to ulcerate and perforate as shown where 40% of patients confirmed their usage. In one study, summary risk and exposure values were computed for the general population. General population attributable risk percentage for ulceration and perforation due to NSAIDs alone was24 %(Kurata J,1997).

The relationship between HIV and peptic ulcer perforation still remains unclear.32% of patients tested positive for HIV indicating that the rates are high among patients who perforate. However, HIV has been shown to offer a protective effect on the gastric mucosa as it limits production of gastric acid (Kelly P et al,2009).This is one aspect of the study that ought to be expanded to a broader, well- controlled study for meaningful conclusions to be made especially that review of literature is quite limited in this regard.

Regular alcohol use and cigarette smoking are linked to perforation of peptic ulcers as shown where 57% and 34% of patients confirmed use of alcohol and cigarette smoking respectively. A study done in Japan gave the calculated population attributable risk percentage to ulcerate and perforate due to alcohol and cigarettes as 34%(Kurata J,1997).

Gastric perforations are commoner at UTH(82.8%),duodenal perforations are less likely(14.3%).This is contrary to a study done in Norway where 52% of duodenal and 10% of gastric perforations were observed. There may be various factors at play including genetic, dietary and environmental. This scope of the study will need to be broadened.

Most patients prolong post-operative hospital stay for more than 10 days (51.4%) indicating the high morbidity associated with the disease. Also the mortality rate stands at 37% postoperatively, and this may be due to various factors such as underlying medical illnesses and patient delay translating to diagnostic and treatment delay.

10. RECOMMENDATIONS

Owing to the increase in the rate of peptic ulcer perforation at UTH and taking into account the various disparities obtaining locally and abroad, it is recommended that a broader, well-controlled study be undertaken to yield definite conclusions. This should take stock of factors such as H.pylori infection, dietary, environmental and genetic.

Due to the high morbidity and mortality associated with perforated peptic ulcers, it is recommended that a fast –track system be established between the endoscopist or physicians and the surgeons to refer cases of intractable peptic ulcers for elective surgery early enough. This is to avert complications like perforations which carry a high mortality even after emergency operation.

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APPENDIX A

RESEARCH EVALUATION FORM

1. CODE NO._____

    Address (Physical) _____

    Province_____

2. AGE: _____

3. SEX: M/F_____

4. OCCUPATION:_____

5. MONTHLY INCOME: (a)<500,000   (b)500,000-1000,000   (c)1,500,000-2,000,000   (d)>2,000,000

6 .Presenting Symptoms: (a) Abd. Pain

                (b) Nausea/Vomiting

                (c) Abd. Distention

                (d) Other

7. Admittance vital signs:(a) Temp_____

              (b) Pulse_____

              (c) Resp_____

              (d) BP_____

8. Duration of symptoms: (a)<6hrs (b) 6-12hrs (c) 12-24hrs   (d) 24-48hrs   (e) >48hrs

9. Treatment/operative delay: (a) <4hrs (b) 4-8hrs (c) 8-12hrs (d) >12hrs

10. Preoperative Hb:_____g/dl

11. Blood group:_____

12. Drug history:_____

13. Medical/ulcer history:Y/N _____

    If yes a) when diagnosed? -----------------------------------

        b) how diagnosed? Endoscopy/clinical (please tick)

        c) which drugs given--------------------

30

d) duration of treatment---------------

   e)compliance and outcome; Good/Bad/Poor (please tick)

14. HIV status known? Y/N, if yes state result.............

15. Drinks Alcohol?   Y/N, if yes how long----------

16. Smokes Cigarettes? Y/N, if yes how long--------

17. ASA Score: (a) 1 (b) 2   (c) 3   (d) 4

18. Peri-operative findings (ulcer location): (a) gastric (b) pyloric   (c) duodenal

19. Peri-operative blood transfusion? Y/N

20. Hospital length of stay: (a) 3-5days (b) 5-7 days   (c) 7-10days (d) >10days

21. Complications arising: a) re-laparotomy? Y/N

              b) Hypovolaemic Shock? Y/N

APPENDIX B

CONSENT TO PARTICIPATE IN RESEARCH

(Patient information sheet)

TITLE: FACTORS ASSOCIATED WITH PERFORATED PEPTIC ULCERS IN ADULTS AT UTH

PURPOSE OF STUDY

The purpose of this study is meant to highlight common factors linked to the high numbers of patients presenting with peptic ulcer perforation at UTH. The results of which are hoped to produce recommendations that may improve surgical treatment and possible prevention of peptic ulcer perforation.

SURGICAL PROCEDURE

Once perforation is suspected it is prudent to do an abdominal operation to confirm and then repair the ulcer. This will done whilst you have been put to deep sleep so that you feel no pain. Following the operation, we will administer anti-ulcer drugs and antibiotics to quicken the healing process. Routine Diagnostic Counselling and Testing (DCT) for HIV will be done and tissue biopsies (samples) from ulcers taken for histology exam. This will help in wholistic treatment.

RISKS, BENEFITS &COMPENSATION

The risks are few compared to benefits like a full recovery, rehabilitation and information on disease prevention. Patients will be compensated for transport as well as laboratory investigations. Participation is wholly voluntary.

CONFIDENTIALITY&RIGHT TO WITHDRAW

Participants are assured of total privacy and confidentiality in as far as dissemination of results is concerned. The participant reserves the right to withdraw from the study.

CONTACT PERSON

Please contact Dr. Kitanda Sondashi on 0977808686, or The Chairman-Research Ethics Committee, UNZA Tel:01-256067, for querries, clarification or translation.

APPENDIX C

CONSENT TO PARTICIPATE IN THE STUDY

I have been asked to participate in the above research and give my consent freely and willingly by signing this form after reading the patient information sheet;

I understand that:

1. If I do not volunteer, or decide to withdraw from the study, my decision will be accepted and this will not influence the continuing management of my condition.

2. I have read (or) and understood the information that has been read to me in my vernacular language and have had all my questions answered to my satisfaction.

3. I am further aware that information I divulge will be treated in a confidential manner and I will not be personally identified.

_____   _____

Signature or thumb print of patient   Signature of Investigator

_____   _____

Date   Place

N.B.:   In case of any questions, please contact Dr. Kitanda Sondashi Department of Surgery, University Teaching Hospital (UTH), Lusaka. Tel: 0977808686, Email: jaysondashi@yahoo.co.uk