FACTORS ASSOCIATED WITH PEPTIC GASTRODUODENAL ULCER PERFORATIONS IN ADULT PATIENTS AT MUHIMBILI NATIONAL HOSPITAL

BY

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A dissertation submitted in (partial) fulfillment of the requirements for the award of the degree of Master of Medicine (in General Surgery) of Muhimbili University of Health and Allied Sciences

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CERTIFICATION

The under signed certifies that he has read and hereby recommend for acceptance by Muhimbili University of Health and Allied sciences a dissertation entitled: **"Factors associated with peptic gastroduodenal ulcer perforations among emergency laparotomy adult patients with acute abdomen at Muhimbili National Hospital, from April 2010 to March 2011"** in partial fulfillment of the requirements for the degree of Master of Medicine (General surgery) of Muhimbili University of Health and Allied Sciences.

_____

Prof. Naboth Mbembati, MD, MMed

(Supervisor)

Date _____

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I, **Ngerageza Japhet**, declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

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DEDICATION

This dissertation is dedicated to my dear wife, Isabella and lovely children, Mazoya and Niyilagila. It is also dedicated to the memory of my late father, Gideon Misaago Ngerageza, who inspired me right from childhood to study medicine. He had had long standing epigastric pain and eventually died of gastric cancer.

ABSTRACT

Introduction: Peptic gastroduodenal ulcer disease results from an imbalance of acid secretion and mucosal defenses that resist acid digestion. Following developments in the medical treatment of peptic ulcer disease (PUD) in the last two decades, surgical intervention is currently confined to the treatment of complicated disease, namely, ulcer hemorrhage, perforation, penetration and obstruction. Simple closure or omental patch repair is the mainstay of treatment of perforated peptic ulcer (PPU), definitive surgery being rarely practiced, dependence now being on medical therapy to complete the healing process and prevent recurrence of the disease[1, 2] The main objective of the study was to evaluate the sociodemographic characteristics, types and risk factors for perforated gastroduodenal disease at Muhimbili National Hospital, in Dar es Salaam.

Methods: A case-control hospital based study with prospective data collection for one year, from April 2010 to March 2011. Cases were patients with gastroduodenal perforation enrolled following emergency laparotomy. Controls were gastroduodenal ulcer patients diagnosed by oesophagogastroduodenoscopy. The sociodemographic characteristics were age, sex, religion and area of residence. The risk factors evaluated included; cigarette smoking, alcohol consumption, use of nonsteroidal anti-inflammatory medications, stress, number of meals, serological status for Helicobacter pylori and human immunodeficiency virus.

Results: Cases had age range between 15 and 70 years, mean age of 33.8 years with male to female ratio of 9:1 and patients aged 20 – 39 years formed the majority of perforated

gastroduodenal ulcer disease. It was found that controls had age range between 17 and 85 years, mean age of 46.9 years with male to female ratio of 2:1 and patients in the age group 40 – 59 formed a large proportion of gastroduodenal ulcer disease. The ratio of gastric to duodenal perforation was 2.5:1 among cases while the ratio of gastric to duodenal ulcers was 1:1 among controls. Age was associated with perforated gastroduodenal disease and Moslems were significantly more affected than Christians. Area of residence and sex were not associated with perforated gastroduodenal disease. Current cigarette smoking, current alcohol drinking as well as coexistence of stressful condition within six months period were strong risk factors for perforation. It was noted that patients who presented with epigastric pain were less likely to perforate than those without epigastric pain. The use of NSAIDs for at least one week and number of meals per day were not associated with perforation. Moreover, H. pylori and HIV seropositivity were not associated with gastroduodenal perforation.

Conclusion: In our community perforated gastric ulcer was seen more often than perforated duodenal ulcer. Age and Moslem were the two sociodemographic characteristics strongly affected with gastroduodenal perforation. Recent histories of Cigarette smoking and alcohol consumption as well as psychological stress were the strong risk factors for perforation. However long standing history of epigastric pain was protective. There were no statistical associations for NSAIDs use, number of meals per day and seropositivity for H. pylori and HIV in relation to gastroduodenal perforation.

Recommendation: The management of patients with peptic gastroduodenal ulcer disease should include counseling on risk factors and maintaining medications to prevent complications such as perforation.

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LIST OF ABBREVIATIONS

ART – Antiretroviral treatment

CTC – Care and Treatment Clinic

MNH – Muhimbili National Hospital

EP – Epigastric pain

MOI – Muhimbili Orthopaedic Institute

CPL – Central Pathology Laboratory

NSAIDs – Nonsteroidal anti-inflammatory drugs

HIV – Human immunodeficiency virus

CMV – Cytomegalovirus

GDU – Gastroduodenal ulcer

DU – Duodenal ulcer

GU – Gastric ulcer

PUD – Peptic ulcer disease

SPSS – Statistical programme for social scientists

OGD – Oesophagogastroduodenoscopy

AD – Alcohol drinking

CS – cigarette smoking

INTRODUCTION

Definition

Peptic ulcer disease (PUD) results from an imbalance of acid secretion and mucosal defenses that resist acid digestion. Moreover, studies have confirmed the strong association between gastric antral infection with *H pylori* and peptic ulceration. More than 90% of patients with peptic ulcer disease are infected with *H pylori*, and eradication of this infection not only heals most uncomplicated ulcers but also significantly decreases the likelihood of recurrent ulceration [1, 2.]

Magnitude of the problem

The disease continues to have a substantial impact on our society's health care system. It occurs slightly more frequent in men. Although 70% of ulcer patients are between the ages of 25 and 64, the peak prevalence of complicated ulcer disease requiring hospitalization is in the age group 65 to 74 years[3, 4].

Although morbidity from PUD is decreasing in the west, the incidence of perforated ulcer remains relatively constant. Perforated ulcers are decreasing in incidence in younger age patients and are increasingly being observed in the elderly and in women. Perforation is typically a significant clinical event marked by abdominal pain, rigidity, the absence of bowel sounds and a sense of impending doom. Most duodenal ulcers perforate anteriorly, while gastric ulcers generally perforate along the anterior wall of the lesser curvature of the stomach. Elective surgery leads to 5 – 10% of mortality while in emergency situation it goes to 20 – 30% and may be as high as 30% to 50% particularly in elderly [1-3]

Current situation on the matter in World literature

Following developments in the medical treatment of PUD in the last two decades, surgical intervention is currently confined to the treatment of complicated disease, namely, ulcer hemorrhage, perforation, penetration and obstruction. Simple closure or omental patch repair is the mainstay of treatment of perforated peptic ulcer (PPU), definitive surgery being rarely

practiced, and dependence now being on medical therapy to complete the healing process and prevent recurrence of the disease[1, 2]

Situation in Tanzania

There are no formal statistics on the types, sociodemographic characteristics and locally documented risk factors for perforated gastroduodenal ulcer disease both at Muhimbili National Hospital and country at large. This study intends to address this concern and given a positive impact on the management of these patients.

LITERATURE REVIEW

Occurrence of complications

A study by Olubuyide[5], on autopsy survey of peptic ulcer disease at Ibadan University Hospital, Nigeria showed that bleeding was the most frequent cause of death from peptic ulcer disease and was responsible for 72.2 percent of the deaths due directly to ulcer disease. This was followed by ulcer perforation found in 25.9 percent of the deaths. Kuremu[6] found that perforations were the commonest complications (56.6%) followed by gastric outlet obstruction (34.0%).

Sociodemographic characteristics

Kuremu[6] did a study on surgical management of peptic ulcer disease at Moi Teaching and Referral Hospital, Eldoret, Kenya. The mean age was 47 years with a male/female ratio of 1.7:1. Ersumo[7] (a review of 74 cases of perforated peptic ulcer in Tikur Anbessa Hospital, Addis Ababa, Ethiopia) found that the mean age was 32.6 years, with a male to female ratio of 7.2 to 1.0. Dakubo[8] studied Gastroduodenal peptic ulcer perforation at the University of Ghana and reported that the mean age of 40.9 years, with male to female ratio was 4.5:1 Bin-Taleb[9] found that an overall mean age of 39.08 years, with male to female ratio of 8:1. In another study by Bas[10] the mean age of patients was 38.6 years. In the study by Ohene-Yeboah[11] the mean age was 52.2 years and more males were affected by a ratio of 3.3:1.

Aman[12] did a study on the frequency of Helicobacter pylori infection in patients with perforated duodenal ulcer, the age ranged from 20 - 80 years old with male to female ratio of 9:1. In a study by Nuhu[13] on intraoperative diagnosis of acute perforated duodenal ulcer the age range was 18-77 years and a mean age of 45.5 years male to female ratio of 4.8:1. Another study by Sarath[14] on gastric perforation the mean age of the patients was 44.5 years with male preponderance. In a study by Torab[15] on patients with perforated peptic ulcer disease admitted to Al-Ain Hospital,

UAE, the age range was 20 - 65 years; the mean age of patients was 35.3 years. In a study by Zangana[16] on risk factors for acute perforated duodenal ulcers in Erbil Governorate-Kurdistan, Iraq about 60% of patients were within their 4th and 5th decade of age and the male to female ratio was 8.5:1.

In the study by Zangana[16] patients residing in the rural areas had a lower incidence of perforation (39%) than those living in the urban areas (61%).

Ratio of peptic gastroduodenal ulcer disease

In the study by Kuremu[6] duodenal ulcer associated complications were the commonest with duodenal ulcer/gastric ulcer ratio of 11.5:1 and the study by Ersumo[7] reported that most patients had duodenal ulcer perforation at laparotomy. The study by Dakubo[8] showed that there were 88% duodenal, 7.1% prepyloric, and 4.9% type 1 gastric ulcer perforations. Another study by Bin-Taleb[9] reported that the perforated duodenal ulcer and perforated gastric ulcer ratio was 4.38:1. In the study by Ohene-Yeboah[11] the ratio of gastric to duodenal perforations of 2.8:1.

Symptomatology and medications

The study by Kuremu[6] found that most patients had chronic peptic ulcer symptoms with inadequate or no medical treatment. In the study by Ersumo[7] nearly 22.0% of the patients, no previous history of peptic ulcer disease was documented. Another study by Nuhu[13] reported that previous history of peptic ulcer disease was found in 78.6% of the patients. Zangana[16] found that 66 patients (53.2%) developed perforations during Ramadan fasting months (4 out of the total 48 months) and about 59.6% were asymptomatic before they developed the perforation. It has been reported that up to 50% or more of ulcer complications have been shown to occur without warning symptoms[3, 17] Ohene-Yeboah[11] studied on perforated gastric and duodenal ulcers in an

urban African population and found that some of the perforations were associated with prolonged fasting for religious reasons.

Risk factors for peptic gastroduodenal ulcer perforation

NSAIDS

Dakubo[8] reported that ulcerogenic substance intake was found in 67% patients. In the study by Torab[15] on patients with perforated peptic ulcer disease admitted to Al-Ain Hospital, UAE, the common risk factors for perforation were smoking, history of peptic ulcer disease (PUD) and use of non-steroidal anti-inflammatory drugs (NSAIDs). Ohene-Yeboah[11] reported that some of these perforations were associated with the intake of NSAIDS.

In a study by Horowitz[20] it was found that 50% of patients with perforated duodenal ulcer had a prior history of NSAIDs use. In another study by Lanas[21] it was found that use of aspirin was associated with 70% of upper gastrointestinal perforations versus 26.9% of controls (p=0.0001) Numerous studies have demonstrated that NSAID users are at a substantial risk for symptomatic PUD including complicated ulcers, bleeding and perforation. These studies demonstrate an increased risk of these complications from three to fourfold compared to patients not on NSAIDs or aspirin routinely[22] The risk of symptomatic and complicated ulcers remains continuous during drug exposure, and the relative risk of a complication has been noted to be highest in the first three months of therapy, likely due to the fact that patients with risk factors become symptomatic more quickly[23] The risk of developing symptomatic and complicated PUD has also become apparent with low dose aspirin. A recent meta-analysis by Derry[24] demonstrated an increased risk of bleeding by nearly two fold in persons taking aspirin at low doses (≤325mg/day)

Alcohol and Cigarette smoking

In a study by Svanes[18], on smoking and ulcer perforation, current smoking increased the risk for ulcer perforation 10-fold in the age group 15–74 years (OR 9.7, 95% CI 5.9 to 15.8) and there was a highly significant dose-response relationship ($p<0.001$). The results were similar in men (OR 9.3, 95% CI 4.9 to 17) and women (OR 11.6, 95% CI 5.3 to 25), and for gastric (OR 10.5, 95% CI 4.5 to 25) and duodenal (OR 8.6, 95% CI 4.9 to 15.4) ulcer perforation. No increase in risk was found in previous smokers (OR 0.8, 95% CI 0.2 to 2.2)

Andersen[19] in the year 2000, assessed the association between smoking, intake of alcohol and the risk of peptic ulcer perforation, and found that smoking more than 15 cigarettes per day increased the risk of perforation more than 3-fold. Drinking more than 2 litres of alcohol per week increased the risk of ulcer perforation.

In another study by Zangana[16] sixty five percent of the cases were smokers. Stress and smoking played a significant role in the occurrence of perforation in 83% of cases.

Helicobacter pylori

While *H. pylori* is well recognized as a causative factor in PUD, its exact role in cases of perforated ulcer has not been established. Chowdhary[25] reported on a series of 45 patients, of which 15 had a perforated duodenal ulcer; none of these 15 patients had evidence of *H. pylori* infection. Reinbach[26] also concluded that there was no clear association between *H. pylori* infection and duodenal ulcer perforation. In their series of patients with acute perforated duodenal ulcer, 47% of patients had evidence of *H. pylori* infection, which was similar to the 50% rate in the control group. In contrast, another study by Ng[27] suggested that *H. pylori* played an important role in the etiology of non-NSAID-related ulcers. Results obtained by Tokunaga[28] when evaluating H. pylori infection in patients operated for duodenal ulcer showed that H. pylori infection was more prevalent in perforated duodenal ulcer (92%) than hemorrhagic (55%) and stenotic ulcer (45%). The results were comparable to those obtained by Mihmanli[29] in which the prevalence of H. pylori infection in 16 patients operated for perforated duodenal ulcer was 88.8%.

HIV and CMV

Studies have shown that in Human immunodeficiency virus (HIV) disease, Cytomegalovirus (CMV) is one of the major causal agents of upper gastrointestinal bleeding. It is not clear if this factor plays a part in peptic ulcer perforation[30, 31]

Psychosocial factors (Stress)

Psychosocial factors can be estimated to contribute to 30% to 65% of ulcers, whether related to nonsteroidal anti-inflammatory drugs, *H. pylori*, or neither. Levenstein and colleagues reviewed the multifactorial origins of peptic ulcer, concluding, entirely plausibly, that stress increases vulnerability to other ulcerogenic agents like *H. pylori*, an assertion that makes good intuitive sense[32, 33] The study by Zangana[16] showed that stress and smoking played a significant role in the occurrence of perforation in 83% of cases.

PROBLEM STATEMENT

A large number of patients are admitted to our surgical department due to acute abdomen. Upon emergency surgery, a number of them are found to be due to perforated peptic gastroduodenal ulcer disease and pose a challenge on the perioperative management.

In the period of 6 months (July-December2009), a total of 45 patients, aged between18 and 50 years, were found to have perforated gastroduodenal ulcers at Muhimbili National Hospital (retrieved from Main theatre registry books). The majority of these patients were very sick on arrival at the hospital, demanding extensive preoperative care, and in most cases coupled with electrolyte disturbance posing a challenge to both anaesthesia and surgery. They needed supportive nutrition (enteral or parenteral nutrition) which is expensive and not readily available. The morbidity and mortality was significant and progressively increased with re-perforation or leakage following emergency repair in addition to prolonged hospitalization. The burden was primarily felt by family or relatives due to loss of productive and reproductive manpower and more challenging to the hospital which provided services on a limited budget.

Perforated peptic gastroduodenal ulcer disease currently carries a significant proportion of surgical patients undergoing emergency laparotomy at Muhimbili National Hospital. The sociodemographic characteristics and risk factors associated with perforated peptic gastroduodenal ulcer disease are locally not known.

RATIONALE/JUSTIFICATION

The study will show sociodemographic characteristics, types and risk factors associated with perforated peptic gastroduodenal ulcers which in turn will help in the following aspects;

- Early identification of patients with peptic gastroduodenal ulcer disease who are at risk of perforation in terms of their age and risk factors associated with perforation.
- May aid in creating follow up clinic for patients with peptic gastroduodenal ulcer disease thus effecting care and preventing complications.
- It will show the need of mobilizing both human resource and equipments to effect preoperative, intraoperative and postoperative care of patients with perforated peptic gastroduodenal ulcer disease.
- The study will have an overall impact in reducing complications (such as perforation), morbidity and mortality as well as the cost of treating patients with peptic gastroduodenal ulcer disease if the identified risk factors are averted.
- The study will contribute in improving the teaching on the matter.

OBJECTIVES

Broad Objective

To evaluate the sociodemographic characteristics, types and risk factors for perforated peptic gastroduodenal ulcer at Muhimbili National Hospital, in Dar es Salaam.

Specific Objectives

I. To determine the sociodemographic characteristics of patients presenting with peptic gastroduodenal ulcer disease attending MNH from April 2010 to March 2011

II. To assess the association between patients' sociodemographic characteristics and perforation of peptic gastroduodenal ulcer.

III. To obtain the ratio of peptic gastroduodenal ulcers (GU and DU) among patients attending MNH from April 2010 to March 2011.

IV. To find the risk factors associated with peptic gastroduodenal perforation among patients attending MNH from April 2010 to March 2011.

METHODOLOGY

I. Study area

Departments of Surgery, Internal medicine and Endoscopy unit at Muhimbili National Hospital (MNH)

II. Study design

Retrospective Case- control Hospital based study with prospective data collection from patients as they were diagnosed following emergency laparotomy due to acute abdomen or following upper gastrointestinal endoscopy. This design was sufficient to determine the sociodemographic characteristics, anatomical types of gastroduodenal ulcers as well as determining the factors associated with peptic gastroduodenal perforation.

III. Study population

Cases

All patients with the diagnosis of perforated peptic gastroduodenal ulcer disease following emergency laparotomy due to acute abdomen were taken as cases. The perforated ulcer considered was the one occurring in the gastroduodenal region only. Patients with perforations in other regions of the gastrointestinal tract were excluded from the study. All patients with penetrating traumatic perforations or established malignancy to the gastroduodenal region were excluded from the study.

Controls

The controls were patients with the diagnosis of gastroduodenal ulcer without perforation. The diagnosis of gastroduodenal ulcer in these patients was made by endoscopy. They were obtained at both inpatient and outpatient department for Surgical and Medical departments and at the endoscopy unit. They were not matched to the cases. Therefore this was a retrospective unmatched case-control study.

Sample size

Statistical programme for social scientists (SPSS) for sample size calculation in an unmatched Case-control study was used.

With Odds ratio of 5 (increased risk of peptic ulcer perforation), with power of the study of 80%, employing 95% Confidence Interval, with Case-control ratio of 1:1, then the number of cases was 64 patients with perforated peptic ulcer disease and 64 controls (patients with peptic ulcer without perforation)

Odds ratio different from 1 indicated the possibility of an association between exposure and disease. If odds ratio is greater than 1 exposure to the factor led to an increased risk of peptic ulcer perforation, and if odds ratio is less than 1 it showed a protective effect of the exposure under investigation.

IV. Sampling technique

There was no sampling. All patients with intraoperative diagnoses of perforation in the gastroduodenal region were included into the study as cases while those with gastroduodenal ulcers diagnosed at endoscopy were enrolled as controls.

In each case of gastric ulcer or perforation the biopsy of the edges had been performed and other specific causes of ulcers excluded by the Pathologist.

Research instruments

A structured Questionnaire for face to face interview technique with the patient was used. The questionnaire collected information on socio-demographic characteristics, history of cigarette smoking, alcohol consumption, chronic history of epigastric pain (prior to the acute episode of peptic gastroduodenal ulcer perforation), medical history on use of medications such as non-steroidal anti-inflammatory drugs or injections, psychological stress and number of meals.

The serostatus for human immunodeficiency virus and helicobacter pylori were obtained from laboratory tests of sera from the patients with respective reagents. Serological reagents for HIV and Heligo G kits of serological test for H. pylori were needed.

The researcher conducted interviews to all patients enrolled into the study.

Inclusion criteria were;

- Presence of peptic gastroduodenal ulcer which was confirmed by OGD or following laparotomy due to peritonitis.
- Patients who were able to recall past events and communicate normally were enrolled for interview and collection of blood sample.
- Critically ill patients were given a day or two for their condition to get better, and then they were enrolled into the study.
- Histological diagnosis of chronic inflammation for biopsied edges of gastric ulcers or perforations
- Patients' age of at least 15 years

Exclusion criteria were;

- Critically ill patients who did not improve following emergency repair
- Perforations or ulcers in areas of the gastrointestinal tract other than gastroduodenal region
- Patients who did not consent to participate in the study
- Established diagnoses such as malignancy, trauma
- Patients' age below 15 years

There were no any potential subjects who refused to participate in the study. However 12 patients with peptic gastroduodenal perforations died within 12 to 24 hours following emergency repair. It was also found that 7 patients with peptic gastroduodenal ulcers could not be found. All these patients were not included in the study.

Data collection procedures

Patients with gastroduodenal ulcers were enrolled and interviewed at the outpatient department (endoscopy room) and inpatient department at surgical as well as medical wards at Muhimbili National Hospital.

The researcher introduced himself and explained to patients about their problems of peptic gastroduodenal ulcer or perforations. He further explained the purpose of research and once patients agreed, they were given consent form to sign and then enrolled for interview and collection of blood sample.

The interviews were conducted in the endoscopy room following OGD or bed side in medical or surgical wards for admitted patients.

The researcher ensured that necessary materials for venopuncture (gloves, cotton wool swab, methylated spirit, syringes and red topped empty sterile bottles) were available in the endoscopy room and both medical and surgical wards. Blood sample collection was done immediately following interview at the endoscopy room or bed side in the respective ward. A tourniquet was applied on the arm; cubital area cleaned with spirit soaked swab, then venopuncture was done from engorged superficial veins of fore arm with a sterile syringe and 3mls of blood collected into a bottle. Then the tourniquet was removed, new swab applied at the puncture site until haemostasis was achieved.

The blood sample bottle was labeled with patient's ID number, name, age, sex, time and date of collection. The investigation form fully labeled as above was attached to the bottle and then sent to the clinical laboratory CPL or MOI within 2 hours of collection.

In the laboratory, the laboratory technologist centrifuged the sample to separate blood cells from serum. The latter was then stored in separate new bottles, fully labeled as above, at freezing temperatures (-16^0C to -20^0C). The bottles were kept in one large plastic bag, labeled as "PUD research".

At the end of data collection, the laboratory technologist allowed the samples to thaw and conducted serological tests for HIV, H. pylori and CMV for each serum. The serological results were then handed over to the researcher, after ensuring that the ID numbers on the bottle were the same to the ID numbers on the investigation form. Then the researcher

entered the laboratory results into the questionnaires. The researcher paid for laboratory services (laboratory tests and laboratory technologist)

The OGD was done by the endoscopists approved at Muhimbili National Hospital and the researcher, under the supervision of the endoscopist on duty. The double contrast barium meal was not routinely done at MNH, and the researcher did not rely on barium meal because it is inferior to OGD. The emergency laparotomy was done by the admitting surgical team (registrar, resident, specialist surgeon, consultant surgeon).

The researcher got all patients with gastroduodenal ulcer disease by attending and participating in daily endoscopic activities at endoscopy room and worked hand in hand with admitting surgical and medical teams. Moreover the endoscopist phoned or sent messages to the researcher who followed up patients either in hospital premises or to their areas of residence. This was done to all those patients with peptic gastroduodenal ulcer who were not seen within the hospital premises, and the researcher had to follow up them to their areas of residence for enrollment and interview. Moreover there were inadequate controls so following up the diagnosed patients was extremely important.

The researcher categorized the status of cigarette smoking into previous smoking, current smoking and none smoking. Previous smoking meant that the patient used to smoke and stopped smoking more than three months prior to enrollment into the study. Current smoking meant that the patient was still a smoker during the enrollment into the study and/or stopped smoking in the period of less than 3 months. Nonsmokers were individuals who had never smoked during their life time.

Alcohol consumption was categorized into previous drinking, current drinking and none alcohol drinking. Previous drinkers had quitted alcohol consumption more than three month ago. Current drinkers were those still drinking at the time of enrollment and/or stopped drinking in the period of less than 3 months. Nonalcohol drinkers were those who had never drunken alcohol in their life time.

The use of NSAIDs was categorized as previous, current and nonuser. Previous user was the one who had used NSAIDs than three months ago. Current user was the one who had used NSAIDs within three months of enrollment and/or stopped using NSAIDs in the period of less than 3 months and nonuser of NSAIDs was the one who had had not used NSAIDs for the past three months. “The risk of symptomatic and complicated ulcers remains continuous during drug exposure, and the relative risk of a complication has been noted to be highest in the first three months of therapy, likely due to the fact that patients with risk factors become symptomatic more quickly[23]”.

Psychological stress was categorized as present or absent. The former meant that the stressful event had occurred within six months and the patient admitted to suffer from the event. The latter was considered when there were no stressful events prior to the current illness. The stressful events included; Loss of spouse/ Loved one, Loss of job/ no job, domestic violence/ divorce/ separation, copying with chronic illness etc. They were assessed on their effect to daily activities.

Data management

Data quality was ensured by checking twice for completeness in the filling of the questionnaire, had which clear unambiguous questions that were understood by patients. In addition to that, the researcher repeated the questions after completing the

questionnaire to ensure consistency in the responses. Testing of the questionnaire was done during the month of March 2010 to ensure quality of data.

The researcher ensured that all responses in the questionnaire were filled as required then prepared data base in the SPSS version 17 for data entry and analysis. Questionnaires were given serial numbers from 1 onwards regardless of being case or control.

Variables such as age in years were continuous variables. These variables were summarized by mean and standard deviation, and then handled by student t- test.

All other variables as shown by the questionnaire were categorical variables (binary data). Categorical variables were summarized in frequency tables. Then the difference in proportions was handled by Chi square or Fisher's exact test. Thereafter, multivariate analysis was done.

The age range was obtained from the difference between youngest and oldest patient and mean age calculated from the sum of all ages of the individual patients divided by the number of patients. The sex ratio was obtained from number of males to females.

V. Ethical issues

The ethical clearance was sought from the Ethical Clearance Committee of Muhimbili University of Health and Allied Sciences. There was careful handling of patients' information and informed consent requested prior to being enrolled into the study as being a case or control.

The patients who refused to participate in the interview continued to be managed normally but did not participate in the study.

Critically ill patients with inability to recall the past events were not enrolled into the study until their clinical condition improved.

VI. Limitations of the study

Failure to enroll very sick patients into the study led to loss of potential cases to have larger sample size.

There were loss of blood samples in the laboratory (14.0% of cases and 20.6% of controls) and this has affected the sample size.

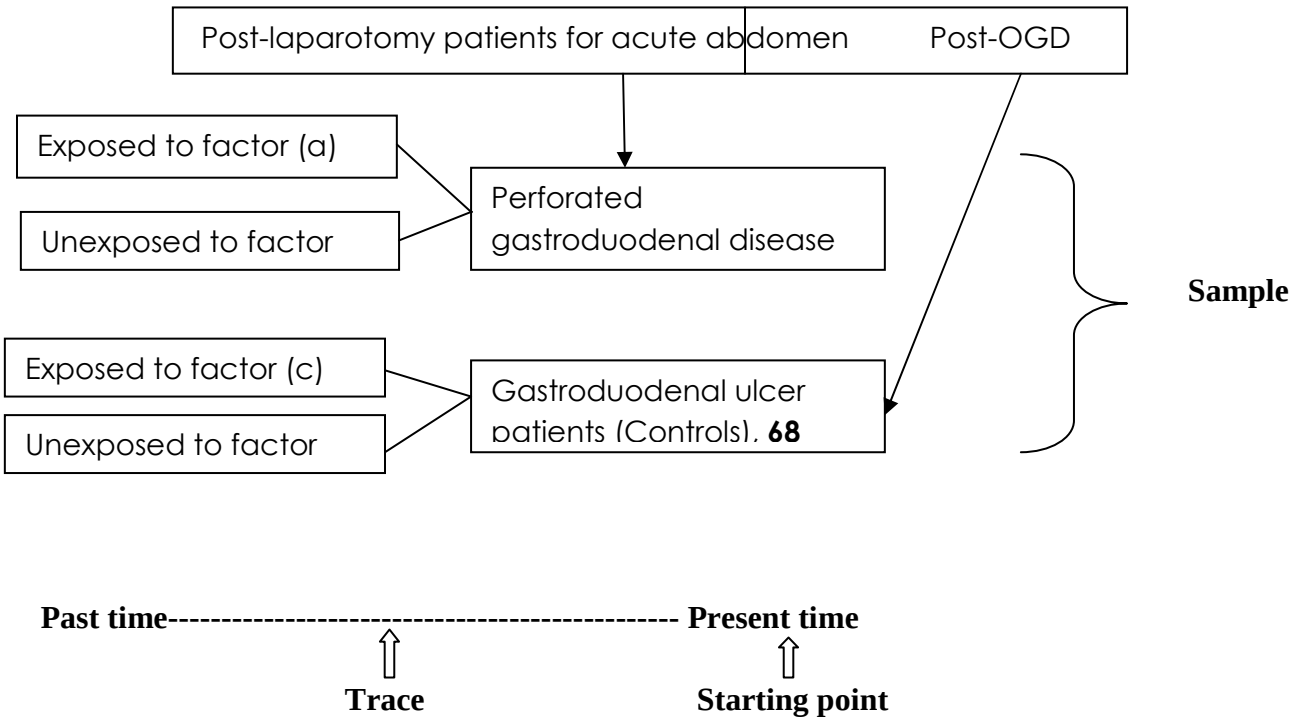
Unavailability of serology kits for cytomegalovirus, led to inability to find the association of CMV and peptic gastroduodenal ulcer perforation.

RESULTS

I; Sociodemographic characteristics of the study population

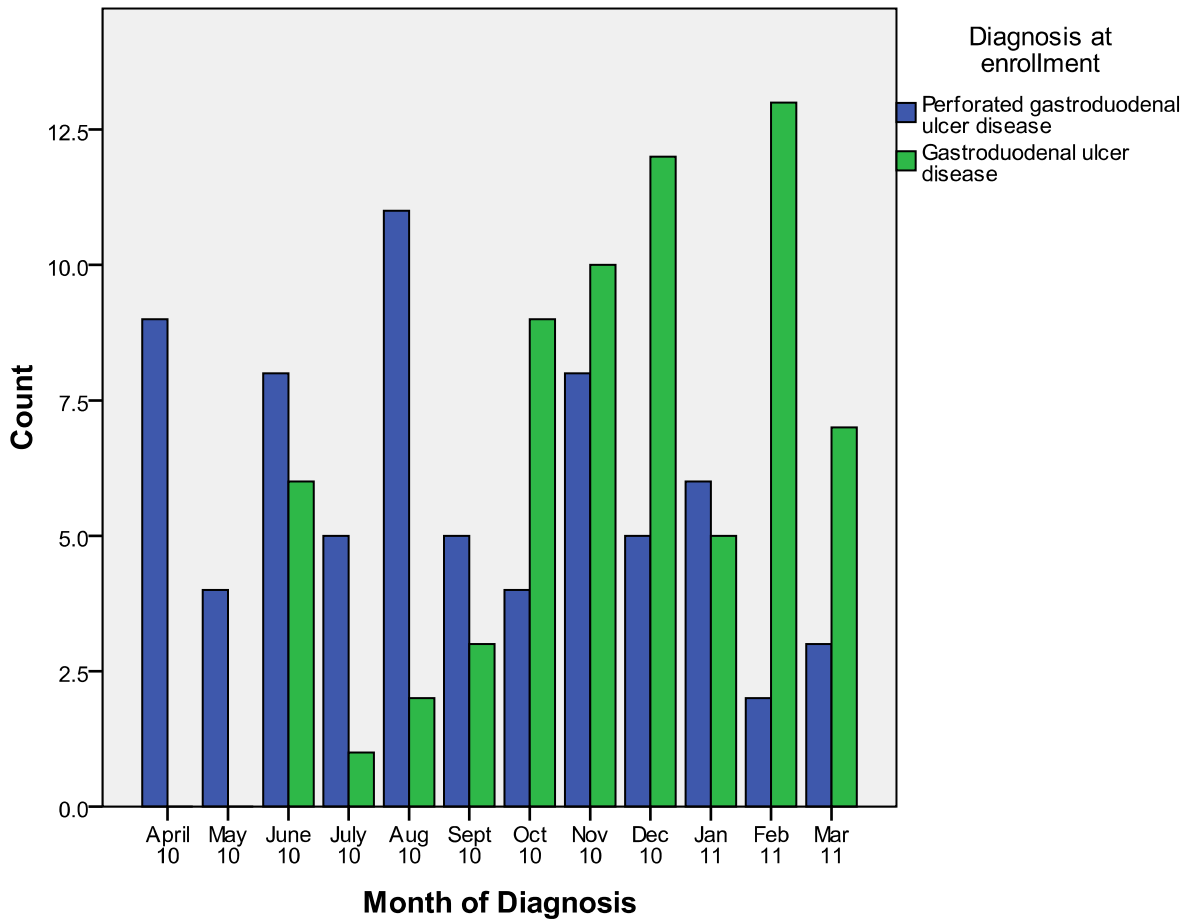
During this study period, from April 2010 to March 2011 a total of 138 patients (70 cases and 68 controls) were enrolled into the study and interviewed. By definition, cases were patients with the diagnosis of gastroduodenal ulcer perforation following emergency laparotomy for acute abdomen while controls were patients diagnosed to have gastroduodenal ulcer by endoscopy (**Figure I**).

Figure I: Flow diagram of the Case-control study



This was an incident case-control study as the both cases and controls were enrolled into the study immediately after being diagnosed as perforated gastroduodenal disease and gastroduodenal ulcer respectively.

Figure II: Distribution of study population by the month of diagnosis



There were more patients with perforated gastroduodenal ulcer disease during the month of August 2010, followed by April 2010. The former corresponded with the month of Ramadan. There were no controls enrolled during the months of April and May 2010 and very few patients (on average less than three per day, two to three days per week) underwent endoscopy. From June 2010 more endoscopies (with average of six to eight per day, four days per week) were done. This could explain the steady increase in control enrollment during those months.

Table1: Frequency of complications of Gastroduodenal ulcer disease of the study population

Complication	Frequency	Percentage %
Perforation	70	51.0
Bleeding	22	16.0
Obstruction	0	0.0
Penetration	0	0.0
No complication	46	33.0
Total	138	100.0

It was found that perforation was the commonest complication followed by bleeding. Neither penetration nor obstruction was found as complications of gastroduodenal ulcer disease.

Cases had age range between 15 and 70 years with a mean age of 33.8 years while controls had age range between 17 and 85 years with the mean age of 46.9 years with male to female ratio of 9:1 and 2:1 respectively.

Tables 2: Distribution of sociodemographic characteristics of the study population

Table 2a: Distribution of study population by Age groups

Age groups in years	Cases	Controls	Total
< 20 years	2 (2.9%)	2 (2.9%)	4 (2.9%)
20 – 39 years	50 (71.4%)	20 (29.4%)	70 (50.7%)
40 – 59 years	16 (22.9%)	30 (44.1%)	46 (33.3%)
≥ 60 years	2 (2.9%)	16 (23.5%)	18 (13.0%)
Total	70 (100.0%)	68 (100.0%)	138 (100.0%)

The majority of cases (71.4%) were in the age group 20 – 39 years while a large proportion of controls (44.1%) were the age group 40-59 years. Teenage and elderly age groups in both populations composed of the minority of patients. The two groups were not similar by age distribution (X^2 27.984, 3df p=0.000).

Table 2b; Distribution of study population by sex

	Cases	Controls	Total
Male	63 (90.0%)	44 (64.7%)	107 (77.5%)
Female	7 (10.0%)	24 (35.3%)	31 (22.5%)
Total	70 (100.0%)	68 (100.0%)	138 (100.0%)

The majority of cases were males (90.0%) as compared to controls where males comprised 64.7%. It was found that the male to female ratio was 9:1 among cases and 2:1 among controls. The two populations were not similar by sex (X^2 =12.67, 1df p=0.000).

Table 2c; Distribution of study population by Area of residence

	Cases	Controls	Total
Urban	47 (67.1%)	46 (61.8%)	89 (64.5%)
Rural	23 (32.9%)	22 (38.2%)	49 (35.5%)
Total	70(100.0%)	68 (100.0%)	138 (100.0%)

The majority of cases (67.1%) resided in urban areas, which was relatively similar to 61.8% of controls. The two groups were similar by area of residence (X^2= 0.436, 1df p=0.509).

Table 2d; Distribution of study population by Religion

	Cases	Controls	Total
Moslems	43 (61.4%)	29 (42.6%)	72 (52.2%)
Christians	27 (38.6%)	39 (57.4%)	66 (47.8%)
Total	70 (100.0%)	68 (100.0%)	138 (100.0%)

The majority of cases (61.4%) were Moslems which was contrary to controls, in which Christians formed the larger proportion (57.4%). The two populations were not similar by religion (X^2 4.876, 1df p=0.027)

Tables 3: Determining risk factors for Gastroduodenal ulcer perforation

Table 3a: Association of status of cigarette smoking and perforation of gastroduodenal ulcer

Status of cigarette smoking	Cases	Controls	Total
Current smokers	33	8	41
Previous smokers	11	19	30
Non smokers	26	41	67
Total	70	68	138

Current smokers were about seven times at higher risk of gastroduodenal perforation as compared to nonsmokers [OR=6.50, 95% CI (2.60, 16.25) with a p-value of 0.000].

There was no statistically significant difference between previous smokers and non smokers [OR=0.91, 95% CI (0.37, 2.22) with a p-value of 0.980].

Table 3b: Association of Alcohol consumption and perforation of gastroduodenal ulcer

Status of alcohol consumption	Case	Control	Total
Current drinking	25	7	32
Previous drinking	25	33	58
None alcohol drinking	20	28	48
Total	70	68	138

The risk for gastroduodenal perforation was increased five times in current alcohol drinkers as compared to nondrinkers [OR=5.00, 95% CI (1.81, 13.81) with a p-value of 0.003].

There was no statistically significant difference between previous alcohol drinkers and nondrinkers [OR=1.06, 95% CI (0.49, 2.30) with a p-value of 0.961].

Table 3c: Association of NSAIDs use and perforation of gastroduodenal ulcer

Status of NSAIDs use	Case	Control	Total
Current users	62	52	114
Previous user	2	7	9
Non users	6	9	15
Total	70	68	138

There was no statistically significant difference between current use of NSAIDs and nonusers in relation to perforation of gastroduodenal ulcer [OR=1.79, 95% CI (0.60, 2.81) and a p-value of 0.439].

There was no statistically significant difference between previous NSAIDs user and nonuser [OR=0.43, 95% CI (0.07, 2.81) with a p-value of 0.655].

Table 3d; Association of Psychological stress and perforation of gastroduodenal ulcer

Psychological stress	Case	Control	Total
Present	34	7	41
Absent	36	61	97
Total	70	68	138

The risk of gastroduodenal perforation increased eight times in a stressed patient as compared to an unstressed patient [OR=8.23, 95% CI (3.31, 20.48) with a p-value of 0.000].

Table 3e: Association of number of meals with perforation of gastroduodenal ulcer disease

Meals per day	Case	Control	Total
1 – 2 meals	35	29	64
≥ 3 meals	35	39	74
Total	70	68	138

There was no association between the number of meals taken per day and risk of gastroduodenal perforation [OR=1.34, 95% CI (0.69, 2.69) with a p-value of 0.487].

Table 3f: Association of Epigastric pain and perforation of gastroduodenal ulcer

Epigastric pain	Case	Control	Total
Present	41	57	98
Absent	29	11	40
Total	70	68	138

Experiencing epigastric pain appeared to be protective in the sense that patients who presented with epigastric pain were three times less likely to perforate as compared to those without epigastric pain [OR=0.274, 95% CI (0.122, 0.608) with a p-value of 0.001].

Table 3g: Association of serostatus for Helicobacter pylori and perforation of gastroduodenal ulcer

H. pylori serology	Case	Control	Total
Positive	24	29	53
Negative	34	25	59
Total	58	54	112

It was observed that the serum samples for 10 cases ad 14 controls were lost or misplaced in the laboratory and in addition to that the serological results for H. pylori for two patients were lost or misplaced in the laboratory. There was no association between H. pylori seropositivity and gastroduodenal perforation [OR=0.61, 95% CI (0.29, 1.29) with a p-value of 0.264].

Table 3h: Association of serostatus for HIV and perforation of gastro duodenal ulcer

Serostatus for HIV	Case	Control	Total
Positive	4	6	10
Negative	56	48	104
Total	60	54	114

Serology for HIV was not done in 10 cases and 14 controls because the samples were lost in the laboratory.

There was no association between HIV seropositivity and gastroduodenal perforation [OR=0.57, 95% CI (0.15, 2.14) with a p-value of 0.613].

Table 4: Analysis of Potential determinants for perforation of gastroduodenal ulcer disease by Forward Binary Logistic regression model

Parameter	Wald	p-value	Estimated OR	95% CI for Estimated OR	
				Lower	Upper
Age	14.001	0.000	1.085	1.040	1.132
Sex	0.845	0.358	1.838	0.502	6.375
Religion	3.947	0.047	3.097	1.015	9.448
Current CS	4.967	0.026	3.270	1.154	9.271
Current AD	5.003	0.025	3.421	1.164	10.050
Stress	9.837	0.002	5.982	1.956	18.923
EP	9.465	0.002	0.157	0.049	0.511
Constant	21.596	0.000	0.007		

It was found that age had the higher Wald in the model than the rest, which signified the larger contribution of age in the model. This was followed by stress and epigastric pain (EP), then current alcohol drinking (AD), current cigarette smoking (CS) and the least was religion (Moslem).

The predictor model showed that age and Moslem were important and independent sociodemographic characteristics associated with perforation of gastroduodenal ulcer disease. The current cigarette smoking, current alcohol consumption and stress were important and independent risk factors for perforation of gastroduodenal ulcer disease (p-value was less than

0.05) while history of chronic epigastric pain was protective. However it was found that sex was not a sociodemographic characteristic associated with peptic gastroduodenal ulcer perforation.

Since age is a quantitative numerical variable, an increase in one-year in age had an 8.5% (95% CI 4.0% to 13.2%) increase in odds of having gastroduodenal ulcer perforation.

The Moslems were at three times higher risk of gastroduodenal ulcer perforation than Christians. The current smokers were at three times higher risk of perforation than nonsmokers. The current alcohol drinkers were at least three times at increased risk of perforation as compared to nonalcohol drinkers. Stressed individuals were at about six times higher risk of perforation than unstressed patients. Patients who had history of epigastric pain were less likely to perforate as compared to asymptomatic patients.

DISCUSSION

Background

Peptic gastroduodenal ulcer disease results from an imbalance of acid secretion and mucosal defenses that resist acid digestion. Surgical intervention is currently confined to the treatment of complicated disease, namely, ulcer hemorrhage, perforation, penetration and obstruction. Simple closure or omental patch repair is the mainstay of treatment of perforated peptic ulcer (PPU), definitive surgery being rarely practiced as dependence is now on medical therapy to complete the healing process and prevent recurrence of the disease[1, 2]

Occurrence of complications

In this study it was found that perforation (51.0%) was the commonest complication followed by bleeding (16.0%). Neither penetration nor obstruction was found as complications of gastroduodenal ulcer disease. It showed similar findings to the study by Kuremu[6] who found that perforations were the commonest complications (56.6%) but differed in that in the latter it was followed by gastric outlet obstruction (34.0%).

This study showed that gastroduodenal perforation was the commonest complication in our community. The two studies showed similar findings probably because of their close geographical location and similar sociodemographic characteristics.

Sociodemographic characteristics of the study population

I: Age

The study found that cases had age range between 15 and 70 years, mean age of 33.8 years and controls had age range between 17 and 85 years, mean age of 46.9 years. Majority of cases

(71.4%) had had ages around the mean making it important age group of patients with peptic gastroduodenal perforations. Forward binary logistic regression confirmed that age had the higher wald in the model than the rest, which signified the larger contribution of age in the model. Along with that age was an important and independent risk factor for perforation of gastroduodenal disease (p=0.000). In addition to that an increase in one-year in age had a 8.5% (95% CI 4.0% to 13.2%) increase in odds of having gastroduodenal perforation.

It was different from the following studies: Kuremu[6] reported the mean age was 47 years. Dakubo[8] reported that the mean age of 40.9 years. Bin-Taleb[9] found that an overall mean age of 39.08 years. Bas[10] found that the mean age of patients was 38.6 years. Nuhu[13] reported that that age range of 18-77 years and a mean age of 45.5 years. Sarath[14] reported that the mean age of the patients was 44.5 years. Zangana[16] reported that about 60% of patients were within their 4th and 5th decade of age. Ohene-Yeboah[11] found that the mean age was 52.2 years.

In this study, the mean age was lower and young patients were more affected by perforated gastroduodenal disease than in the quoted studies. The difference could probably be explained by premature self dependence or lack of parental guidance in our community thus predisposing to risk factors associated with gastroduodenal ulcer perforation.

It was similar to the following studies: Ersumo[7] found that the mean age was 32.6 years and Torab[15] whose findings showed that the age range was 20 - 65 years, the mean age of patients was 35.3 years.

II: Sex ratio

This study found that the male to female ratio was 9:1 among cases and 2:1 among controls. However it was demonstrated by Logistic regression that sex was not the sociodemographic characteristic associated with gastroduodenal ulcer perforation (p=0.358).

In this study there was a male preponderance similar to the following studies: Kuremu[6] reported the male/female ratio of 1.7:1. Dakubo[8] reported a male to female ratio was 4.5:1. Bin-Taleb[9] reported a male to female ratio of 8:1. Nuhu[13] reported a male to female ratio of 4.8:1 Sarath[14] showed that there were male preponderance. Zangana[16] found that a male to female ratio was

8.5:1. Ohene-Yeboah[11] reported the male to female ratio of 3.3:1. Ersumo[7] found that a male to female ratio of 7.2 to 1.0. Aman[12] found that age ranged from 20 - 80 years old with male to female ratio of 9:1.

The magnitude of male preponderance could probably be explained by the fact that males were more aggressive and thus predisposed to risky behavior more than females leading to gastroduodenal perforation.

III: Area of residence

This study showed that majority of cases (67.1%) resided in urban areas while 32.9% of cases resided in rural areas and 61.8% and 38.2% of controls were residing in urban and rural areas respectively. The two groups (cases and controls) were similar by area of residence. However it was found that there was no statistically significant difference between the area of residence and perforation of gastroduodenal ulcer (p=0.509).

The above findings were similar to those of Zangana[16], who reported that patients residing in the rural areas had a lower incidence of perforation (39%) than that living in the urban areas (61%).

This could probably be explained by having more risky behavior and stressful life in the urban population than rural population leading to more gastroduodenal perforations in the urban than rural population. In addition to that, the sample size was probably too small to elicit the statistical difference between urban and rural populations.

IV: Fasting religious seasons and number of meals

There were more patients [11 patients (16.0%)] with gastroduodenal perforation during the month of August 2010 which corresponded with the Ramadan fasting month.

Similar findings were reported by Zangana[16] who found that 66 patients (53.2%) developed perforations during Ramadan fasting months (4 out of the total 48 months) and Ohene-Yeboah[11] who found that some of the perforations were associated with prolonged fasting for religious reasons.

However, this study showed that there was no association between the number of meals taken per day and risk of gastroduodenal perforation (p=0.487).

Ratio of GU to DU

In this study the ratio of gastric to duodenal perforation was 2.5:1 among cases while the ratio of gastric to duodenal ulcers was 1:1 among controls.

The results of this study were different from the following studies: Kuremu[6] reported that a duodenal ulcer/gastric ulcer ratio of 11.5:1. Ersumo[7] reported that most patients had duodenal ulcer perforation at laparotomy. Dakubo[8] showed that there were 88% duodenal, 7.1% prepyloric, and 4.9% type 1 gastric ulcer perforations. Bin-Taleb[9] reported that the perforated duodenal ulcer and perforated gastric ulcer ratio was 4.38:1.

The findings of this study were similar to those by Ohene-Yeboah[11] who reported that the ratio of gastric to duodenal perforations of 2.8:1.

The risky behavior characterizing this study population could probably be implicated more in the gastric than duodenal perforations. These included; premature self dependence, Alcohol drinking, Cigarette smoking, drug abuse, stressful life accompanied by poverty.

Symptomatology and medications

In this study 59.0% of cases had chronic history of epigastric pain and 41.0% were asymptomatic while the majority of controls (84.0%) had chronic history of epigastric pain and 16.0% were asymptomatic. Epigastric pain had a significantly large Wald in the Logistic regression model and an independent risk factor for gastroduodenal perforation (p=0.049). Patients who had chronic history of epigastric pain were less likely to perforate than asymptomatic patients (estimated OR=0.157), and probably increased health seeking behavior. It was also noted that none of the cases had been on medications and only 7.0% of controls had been on medications.

The findings of this study were comparable to those of the following studies: Kuremu[6] who found that most patients had chronic peptic ulcer symptoms with inadequate or no medical treatment. It was reported that 41.0% of patients were asymptomatic prior to perforation and comparable results had shown that up to 50% or more of ulcer complications have been shown to occur without warning symptoms[3, 17]. According to Zangana[16] about 59.6% were asymptomatic before they developed the perforation which supported the fact that epigastric pain was protective as shown by this study.

The findings of this study were different from those of the following studies: Ersumo[7] reported that nearly 22.0% of the patients there was no previous history of peptic ulcer disease. A larger proportion (78.6%) of symptomatic patients was reported by Nuhu[13] than the findings of this study.

The similarity and difference could possibly be explained by lack of enough health education, poverty and tolerance to pain among patients in our community.

Risk factors associated with perforations of peptic gastroduodenal ulcer

I: Use of NSAIDs

This study showed that the majority of cases (91.0%) and controls (87.0%) were users of NSAIDs.

Dakubo[8] reported that ulcerogenic substance intake was found in 67% patients and Horowitz[20] found that 50% of patients with perforated duodenal ulcer had a prior history of NSAIDs use. The quoted studies showed comparative results to those of this study.

Torab[15] reported NSAIDs as one of the common risk factors for perforation. Lanas[21] found that use of aspirin was associated with 70% of upper gastrointestinal perforations versus 26.9% of controls (p=0.0001) but none of patients in this study reported to have used aspirin. Numerous studies demonstrated that NSAID users are at increased risk of complications from three to

fourfold compared to patients not on NSAIDs or aspirin routinely[22]. Ohene-Yeboah[11] reported that some of these perforations were associated with the intake of NSAIDS. The results of the quoted studies were contrary to those of this study.

In this study there was neither statistical difference between current use of NSAIDs and nonusers (p=0.439) nor between previous NSAIDs user and nonuser (p= 0.655) in relation to perforation of gastroduodenal ulcer. A recent meta-analysis by Derry[24] demonstrated an increased risk of bleeding by nearly two fold in persons taking aspirin at low doses (≤325mg/day). Thus NSAIDs could probably be associated with ulcer bleeding more than perforation.

II: Cigarette smoking

In this study the majority of cases (63.0%) were smokers as compared to smokers in the control group (40.0%) and current smoking was strongly associated with gastroduodenal perforation. It was found that the wald for current smoking was a significant contributor in the logistic regression model and an independent risk factor for cigarette smoking. The current smokers were at three times increased risk of perforation as compared to nonsmokers.

Comparable findings were reported by Zangana[16] in which 65% of the cases were smokers. Stress and smoking played a significant role in the occurrence of perforation in 83% of cases. Svanes[18]reported that current smoking increased the risk for ulcer perforation 10-fold and there was a highly significant dose-response relationship (p<0.001). No increase in risk was found in previous smokers. Andersen[19] assessed the association between smoking and the risk of peptic ulcer perforation and found that smoking more than 15 cigarette per day increased the risk of perforation more than 3-fold.

Silverstein[34] documented effects of the toxic constituents of cigarette smoke particularly nicotine, carbon monoxide, and hydrogen cyanide and suggested potential mechanisms by which smoking may undermine expeditious wound repair. *Nicotine* is a vasoconstrictor that reduces

nutritional blood flow to the skin, resulting in tissue ischemia and impaired healing of injured tissue. Nicotine also increases platelet adhesiveness, raising the risk of thrombotic microvascular occlusion and tissue ischemia. In addition, proliferation of red blood cells, fibroblasts, and macrophages is reduced by nicotine. *Carbon monoxide* diminishes oxygen transport and metabolism, whereas *hydrogen cyanide* inhibits the enzyme systems necessary for oxidative metabolism and oxygen transport at the cellular level. This could also explain the toxic effects of cigarette smoking leading to perforation of gastroduodenal ulcer.

III: Alcohol consumption

The studies showed that majority of cases (71.4%) were alcohol drinkers as compared to 59.0% of controls. The wald for current alcohol consumption was a significant contributor in the logistic regression model, and an independent risk factor for perforation of gastroduodenal ulcer (p=0.025). The current alcohol drinkers were at least three times increased risk of perforation as compared to nonalcohol drinkers.

Similar findings were reported by Andersen[19] who assessed the association between intake of alcohol and the risk of peptic ulcer perforation, and found that drinking more than 2 litres per week increased the risk of ulcer perforation.

Alcohol is known to impair wound healing through a variety of mechanisms: nutritional deficiencies leading to impaired wound healing and disinhibition caused by alcohol leads to increased risk behavior hence more predisposition to gastroduodenal ulcer perforation than in abstainers.

IV: Stress

This study showed that 48.6% of cases were stressed as compared to 10.3% of controls. The wald for stress is significantly high in the logistic regression model. Moreover, stress was an

independent risk factor for perforation (p=0.002). Stressed individuals were at about six times increased risk of perforation as compared to unstressed patients.

Comparable results were reported by Zangana[16] in which stress and smoking played a significant role in the occurrence of perforation in 83% of cases.

The mechanisms underlying stress as the risk factor for gastroduodenal ulcer perforation includes; Neuro-endocrine mechanism leading to a cascade of elevated levels of stress hormones, reduced inflammatory response and matrix degradation processes in early wound healing and increased vulnerability to risk behavior, hence more predisposed to peptic gastroduodenal ulcer perforation.

V: H. pylori seropositivity

This study showed that H. pylori seropositivity among cases and control were 41.0% and 54.0% respectively. There was no association between H. pylori seropositivity and gastroduodenal perforation (p=0.264).

Reinbach[26] concluded that there was no clear association between *H. pylori* infection and duodenal ulcer perforation. In their series of patients with acute perforated duodenal ulcer, 47% of patients had evidence of *H. pylori* infection, which was similar to the 50% rate in the control group. Chowdhary[25] reported on a series of 45 patients, of which 15 had a perforated duodenal ulcer; none of these 15 patients had evidence of *H. pylori* infection. The quoted studies showed comparable results to this study.

Different results were reported by Tokunaga[28] in which H. pylori infection was more prevalent in perforated duodenal ulcer (92%) than hemorrhagic (55%) and stenotic ulcer (45%). Ng[27] suggested that *H. pylori* played an important role in the etiology of non-NSAID-related ulcers. Mihmanli[29] reported that the prevalence of H. pylori infection in 16 patients operated for perforated duodenal ulcer was 88.8%.

VI: HIV seropositivity

The study showed that the HIV seropositivity was 6.7% and 11.1% among cases and controls respectively. There was no association between HIV seropositivity and gastroduodenal ulcer perforation (p=0.613). However reports from other studies showed that Cytomegalovirus (CMV) is one of the major causal agents of upper gastrointestinal bleeding in HIV positive individuals and it was not clear if this factor played a part in peptic ulcer perforation[30, 31] It was the intention to do CMV serology in this study but it could not be done because the appropriate reagent could not be obtained.

CONCLUSION

The occurrence of perforated gastroduodenal ulcer disease has been shown to be multifactorial and was the commonest complication of gastroduodenal ulcer disease. In our community perforated gastric ulcer was seen more often than perforated duodenal ulcer. Age and religion (Moslem) were the two sociodemographic characteristics strongly associated with gastroduodenal ulcer perforation. Recent histories of cigarette smoking and alcohol consumption as well as psychological stress were the strong risk factors for perforation. However, history of chronic epigastric pain prior to the acute episode was protective. All patients with perforated disease were not on medications (proton pump inhibitors and/or antibiotics) prior to surgical repair. There were no statistical associations for NSAIDs use, number of meals per day and seropositivity for H. pylori and HIV in relation to gastroduodenal ulcer perforation.

RECOMMENDATION

1. A study should be designed to evaluate in depth the role of psychosocial factors in patients with perforated gastroduodenal ulcer disease.

2. Along term study should be designed to find the possible causes of increased gastroduodenal ulcer perforation during the fasting religious seasons.

3. The management of patients with peptic gastroduodenal ulcer disease should include counseling on risk factors and maintaining medications to prevent complications such as perforations.

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APPENDIX I
QUESTIONNAIRE

Registration number ----------

Religion ----------

Age --------

Sex ----------

Diagnosis; DU…

GU…

Complication……..

Q1. Residence

(a) Urban

(b) Rural

Q2. Have you ever smoked cigarettes for prolonged period of time? (>3months)

(a) Yes

(b) No

Q3. Are you currently smoking cigarettes? (<3months)

(a) Yes

(b) No

Q4. How many pieces do you smoke?

(a) < 5 pieces per day

(b) > 5 pieces per day

Q5. Have you ever drunk alcohol for a prolonged period of time? **(>3months of enrollment)**

(a) Yes

(b) No

Q6. Are you currently drinking alcohol? **(≤3months)**

(a) Yes

(b) No

Q7. How much do you drink per day?

(a) 1-2 bottles per day

(b) > 2 bottles per day

Q8. Did you have any history of upper abdominal pain/discomfort? (epigastric pain prior to acute episode of perforation)

(a) Yes

(b) No

Q9. Have you ever been on prolonged use of steroids?

(a) Yes

(b) No

Q10. Are you currently taking steroids?

(a) Yes

(b) No

Q11. Have you ever been on long standing use of NSAIDs? **(> 3months of enrollment)**

(a) Yes

(b) No

Q12. Are you currently on NSAIDs? **(≤ 3 months of enrollment)**

(a) Yes

(b) No

Q13. What is the dose?

(a) 1-2 daily

(b) 3 or more per day

Q14. Did you have any history of psychological stress? **(≤ 6 months of enrollment)**

(a) Yes

(b) No

Q15. What types of food you commonly ate prior to illness?

(a) Hard food

(b) Soft food

Q16. How many meals do you eat per day?

(a) 1-2 main meals

(b) >2 main meals

Q17.What is the spacing time in between meals?

(a) 4-6 hours, regular

(b) >6 hours, irregular

Q18. Serological test results for H. pylori is

(a) Positive

(b) Negative

Q19. The serostatus for HIV is

(a) Positive

(b) Negative

Q20. The serological test for CMV is

(a) Positive

(b) Negative

DODOSO

Namba ya usajili ----------

Dini ----------

Umri----------

Jinsia---------

Tatizo; DU--------

GU---------

1.Makazi

(a)Mjini

(b) Kijijini

2.Je umewahi kuvuta sigara kwa muda mrefu? **(zaidi ya miezi 3 iliyopita)**

(a) Ndio

(b) Hapana

3. Je unavuta sigara sasa? **(katika miezi 3 iliyopita)**

(a) Ndio

(b) Hapana

4. Unavuta sigara ngapi?

(a) < 5 kwa siku

(b) > 5 kwa siku

5.Umewahi kunywa pombe kwa muda mrefu? **(zaidi ya miezi 3 iliyopita)**

(a) Ndio

(b) Hapana

6. Unakunywa pombe sasa? **(katika miezi 3 iliyopita)**

(a) Ndio

(b) Hapana

7. Unakunywa kiasi gani?

(a) Chupa 1-2 kwa siku

(b) Zaidi ya chupa 2 kwa siku

8. Umewahi kupata maumivu sehemu ya juu ya tumbo?

(a) Ndio

(b) Hapana

9. Umewahi kutumia vidonge vya steroid?

(a) Ndio

(b) Hapana

10.Unatumia vidonge vya steroid sasa?

(a) Ndio

(b) Hapana

11. Umewahi kutumia vidonge vya kutuliza maumivu(NSAIDs)? **(zaidi ya miezi 3 iliyopita)**

(a) Ndio

(b) Hapana

12. Je unatumia vidonge vya kutuliza maumivu sasa? **(katika miezi 3 iliyopita)**

(a) Ndio

(b) Hapana

13. Unatumia vidonge vya kutuliza maumivu kiasi gani?

(a) Vidonge 1-2 kwa siku

(b) 3 au zaidi

14. Je umepata tatizo lolote la linalokupa mawazo sana? **(Katika miezi 6 iliyopita)**

(a) Ndio

(b) Hapana

15. Ulikula chakula cha aina gani kabla ya kupatamaumivu makali ya tumbo?

(a) Chakula kigumu

(b) Chakula laini

16. Unakula mara ngapi kwa siku?

(a) Mara 1-2

(b) > 2

17. Ni muda gani hupita kati ya mlo mmoja na mwingine?

(a) Masaa 4-6

(b) Zaidi ya masaa 6

18. Kipimo cha H. pylori kinaonyesha kuwa;

(a) Umewahi kupata maambukizi

(b) Hujawahi kupata maambukizi

19. Kipimo cha VVU kimeonyesha kuwa;

(a) Umepata maambukizi

(b) Hakuna maambukizi

20. Kipimo cha CMV kinaonyesha kuwa;

(a) Umepata maambukizi

(b) Hakuna maambukizi

APPENDIX II

BUDGET ESTIMATE

Laboratory technologist and sample preservation	Serological tests(HIV & H. pylori) @ 2,000shs per sample Sample preservation	350,000shs 50,000shs
Heligo G kits & CMV kits	1kit for 50 samples (H. pylori) @ 150,000shs. Then 3 kits were purchased. Serological reagents (ELISA) for HIV	450,000shs 100,000shs
Stationaries	Papers, typing, printing and photocopying from proposal to report writing	150,000shs
Active tracing of controls	Air time & transport	250,000shs
Contingency funds	10% of the budget	150,000 shs
Total budget		1,500,000 shs

The source of the fund was the Government of Tanzania through the Ministry of Health & Social welfare, 1,500,000shs

APPENDIX III

Consent Form

ID no _____

Consent to participate in the study assessing the clinical epidemiology of perforated peptic ulcer disease at Muhimbili National Hospital

Greetings! My name is Dr Japhet Gideon Ngerageza, a postgraduate student at Muhimbili University of Health and Allied Sciences

The purpose of the study

To evaluate the distribution and risk factors for perforated Peptic ulcer disease at Muhimbili National Hospital, in Dar es Salaam.

What participation involves

If you agree to participate in the study, a pre-test counseling will be offered and a sample of blood collected for HIV, Cytomegalovirus (CMV) and H. pylori testing. Post-test counseling will be offered if you are willing to receive back results. You can decide not to receive back your results, it's OK but it is useful for you to receive them.

If you happen to test positive for HIV infection, you will be linked with CTC at MNH for continuum of care, including assessment for fitness for ART. In addition once tested positive for H. pylori, you will be advised on use of triple therapy for eradication of H. pylori

Confidentiality

All information collected on questionnaires will be entered into computer with identification number. The questionnaires will be handled with great secrecy in order to maintain confidentiality throughout the study.

Risks

There is no direct risk associated with this study.

Right to withdraw and alternatives

Taking part in this study is completely voluntary. If you choose not to participate in the study, you will continue to receive all services that you would normally get from the hospital.

Benefits

If you agree to take part in this study, you will benefit from knowing your current HIV status.

Currently medication for HIV infection/AIDS is available at various governmental and non-governmental facilities. If you test positive then you'll be linked with care and treatment centre where you can get ART as needed and follow-up.

On the other hand, knowing that you are negative help in being more protective.

In case of any injury

Apart from you providing us with blood sample, we do not expect any harm from your participation. However, in case of injury, blood from both the injured individual and the patient will be tested for HIV serostatus. The he will be started on post exposure prophylaxis for HIV within 2 to 8 hours of injury for duration of one month and may stop medication once blood results from the patient are negative for HIV.

Who to contact

If you have any question about the study, you should contact Dr Japhet G. Ngerageza on +255784-653148.

If you have any questions/concerns about your rights as a participant, you may contact Prof E. Lyamuya, Chairman of MUHAS Research and Publications Committee. P.O.BOX **65001 Dar es Salaam. Tel 2150302-6**

Signature

I …… have read the content of this form .My questions have been answered. I agree to participate in this study**.**

Signature of participant …….

Signature of witness ……..

Date of signed consent …/…/ 2010 or 2011

Participant agrees☐ / Participant does NOT agree ☐

Kiswahili version of consent form

ID no _____

Hati ya ukubali wa kushiriki kwenye utafiti unaoangalia uhusiano baina ya kutoboka kwa vidonda vya tumbo na virusi vya ukimwi (HIV), virusi vya Cytomegalovirus (CMV), bacteria aina ya H. pylori, Uvutaji wa sigara, unywaji wa pombe, na mengineyo.

Salaam! Naitwa Daktari Japhet Gideon Ngerageza, mwanafunzi wa uzamili katika chuo kikuu cha Tiba za Afya cha Muhimbili.

Lengo la utafiti

Uhusiano baina ya kutoboka kwa vidonda vya tumbo na virusi vya ukimwi (HIV), virusi vya Cytomegalovirus (CMV), bacteria aina ya H. pylori, Uvutaji wa sigara, unywaji wa pombe, na mengineyo.

Ushiriki wako ni wa namna gani?

Ukikubali kushiriki, utapewa unasihi kwa ajili ya kupima VVU, CMV na H. pylori. Damu itachukuliwa na kupelekwa maabara kwa ajili ya kupima VVU, CMV na H. pylori. Ushauri wa kupokae matokeo ya kipimo utatolewa, lakini kama utakuwa tayari kuupokea. Unaweza kuamua usipokee matokeo yako, haina taabu, lakini ni muhimu ukapokea.

Usiri

Taarifa zote zilizochukiliwa kupitia dodoso letu, pamoja na vipimo vitatambulika kwa namba na siyo jina ili kuongeza usiri. Usiri huo utalindwa hata baada ya kukamilika kwa utafiti huu.

Madhara

Mbali na maumivu kidogo wakati wa kuchukua damu, hatutegemei kwamba utapata madhara yoyote.

Faida

Kama ulikuwa haujui hali yako ya maambukizi ya VVU, utapata bahati ya kufahamu.

Endapo utapatikana na VVU, dawa za kufumbaza VVU zinatolewa bure na utaweza kuzipata na kufuatiliwa afya yako kwenye kliniki maalum. Utaandikiwa dawa endapo itaonekana kuwa na bakteria wa aina ya H. pylori.

Mwisho, kufahamu ya kuwa hauna VVU kunasaidia kuongeza jitihada katika kujikinga dhidi ya maambukizi.

Haki ya kujitoa

Ushiriki wako ni wa hiari, unaweza kujitoa wakati wowote katika utafiti huu. Ukiamua kutokushiriki, utaendelea kupatiwa huduma kama kawaida.

Mawasiliano

Ukiwa na maswali kuhusu utafiti huu, au umeshindwa kuhudhuria cliniki, wasiliana nami , Dr. Japhet G. Ngerageza kwa nambari ya simu +255784 653148

Ukiwa na maswali kuhusu haki yako kama mshiriki, wasiliana na Prof. Eligius Lyamuya, mwenyekiti wa Kitengo cha Utafiti wa Chuo Kikuu cha Afya ya Tiba Muhimbili S.L.P **65001 Dar es Salaam. Tel 2150302-6**

Sahihi

Mimi _____ nimekubali kushiriki utafiti huu baada ya maswali yangu yote kujibiwa.

Sahihi ya mshiriki _____

Sahihi ysa shahidi _____ Tarehe __/___/2010 au 2011

Mshiriki amekubali ☐/ Amekataa ☐