



ST. PAUL'S HOSPITAL MILLENNIUM MEDICAL COLLEGE

CLINICAL CHARACTERISTICS OF ENDOSCOPICALLY PROVEN PEPTIC ULCER DISEASE AND ASSOCIATED FACTORS OF PEPTIC ULCER DISEASE COMPLICATIONS, A CROSS-SECTIONAL STUDY AT SAINT PAUL'S HOSPITAL MILLENNIUM MEDICAL COLLEGE, ADDIS ABABA, ETHIOPIA.

BY- EDEN MULUNEH (MD, INTERNAL MEDICINE RESIDENT)

A RESEARCH THESIS TO BE SUBMITTED TO DEPARTMENT OF INTERNAL
MEDICINE AND PUBLIC HEALTH, SPHMMC, IN PARTIAL FULFILLMENT OF
THE REQUIREMENT FOR SPECIALTY CERTIFICATE IN INTERNAL MEDICINE

FEB, 2024G.C

ADDISABABA, ETHIOPIA

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ETHIOPIA

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Abbreviations and acronyms

ASA-acetylsalicylic acid

EGD-Esophagogastroduodenoscopy

GBD-global burden of disease

GI-gastrointestinal

GOO-gastric outlet obstruction.

HBSAg – Hepatitis B surface Antigen

HIV-human immune deficiency virus

H. pylori- Helicobacter Pylori

IBD-inflammatory bowel disease.

IBS-irritable bowel syndrome.

IPUD-Idiopathic peptic ulcer disease

NSAID-nonsteroidal anti-inflammatory drugs

NUD-non ulcer dyspepsia

ODK-Open Data kit

PPI -proton pump inhibitor

PsA- psoriatic Arthritis

PUD-peptic ulcer disease

RA -Rheumatoid Arthritis

RVI- Retro viral infection

SLE- Systemic Lupus Erythematosus

SPHMMC-saint Paul's hospital millennium medical college

SPSS-Statistical Package for the Social Sciences

USA- United states of America

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Abstract

Background: Peptic ulcer disease is one of the world's major GI problems, globally affecting millions of people in their everyday life. Regarding complications, the commonly encountered are bleeding, perforation, gastric outlet obstruction, penetration, and fistula formation. Majority of deaths attributed to complications are related to multi-organ failure.

Objective: To assess the clinical characteristics of peptic ulcer disease, and associated factors with endoscopically proven Peptic ulcer disease complications in saint Paul millennium medical college, Addis Ababa, Ethiopia.

Method: A cross-sectional study was conducted among 227 participants who had undergone endoscopic evaluation between March and June 2023. The participants were selected using a convenience sampling method. Data collection involved reviewing the participants' medical charts using a structured checklist. The collected data included demographic information, risk factors, comorbidities, and complications associated with endoscopically proven Peptic Ulcer disease. In cases where data were incomplete, phone calls were made, and outpatient visits were conducted over a period of four months. The data were then entered into Kobo Toolbox version 4.4 and exported to Statistical Package for the Social Sciences, window version 27 for analysis. Descriptive statistics were summarized using frequencies, tables, and figures. Bivariable and multivariable logistic regression analyses were performed. Variables with a p-value < 0.05 in the multivariable analysis were considered to have a statistically significant association with Peptic Ulcer disease complication.

Result: The average age of the patients was 42 ± 14.8 years, with more than half of them being above 40 years old. Males comprised two-thirds (68.2%) of the study participants. Among the patients, 70 (31.4%) tested positive for *Helicobacter pylori* while less than 5% of them had non-steroidal anti-inflammatory drug use and 9% of them had history of cigarette smoking. The majority of them had Abdominal pain and danger sign (92.8%,76.7%) respectively. Duodenal

ulcers were encountered in 74.4%. Out of 223 PUD subjects who underwent endoscopy, 110 (44.8%) experienced complications. It was found that the age group of 40-50 [AOR=3.004; 95%CI (1.098, 8.2232)], patients over 50 years old [AOR=12.06; 95%CI (4.261, 34.146)], positive *Helicobacter pylori* infection [AOR=5.914; 95%CI (2.878, 12.151)] and smokers [AOR=3.907; 95%CI(1.224, 12.472)] were identified as predictors for Peptic ulcer disease complications. .

Conclusion and recommendation: This study presents evidence that individuals who are above 40 years old test positive for *Helicobacter pylori*, and smokers were more likely to experience complications from peptic ulcer disease. It is crucial to promptly diagnose and treat patients with peptic ulcer before it becomes more complicated. Stakeholders should focus on expanding the availability of endoscopic centers across the country to enable early diagnoses. Additionally, educating the general population about the significant risk factors and prevention methods should be prioritized.

Keywords: peptic ulcer disease, H.pylori, complications, Ethiopia

1. Introduction

1.1 Background

PUD is a common disorder of the digestive system which is defined as digestive tract injury that results in mucosal break of 3-5mm or more with visible depth reaching the submucosa(1, 2). PUD occurs mostly in the stomach and first part of duodenum but also in the distal esophagus, jejunum and Meckel's diverticulum (2). Accordingly based on the location of the ulcer, its broadly classifies as Duodenal ulcer and Gastric ulcer.

PUD is one of the world's major GI problems, globally affecting millions of people in their everyday life. It affects about 4 million people each year (3). According to a Study on Global Burden of Disease of PUD, which was conducted from 1990-2019, the prevalence of PUD which was 8.09 million in 1990, increased by 25.8%, at the end of the study period,2019. Likewise the incident cases of PUD raised from 2.82 Million to more than 3.59 million(increased by 27.3%)at the end of study period(4). According to previous studies, peptic ulcer disease occurred in 2.4–3.5% of the Western population, 12–15% of Asian population, and 24–28% of sub-Saharan African dwellers(5-10) .Worldwide Age-standardized PUD-associated death rates varied from 0.46 to 22.48 per 100,000 population(4) .

The two major etiologies of PUD are H. pylori infection and the consumption of nonsteroidal anti-inflammatory drugs (NSAIDs). Other causes of peptic ulcer disease include Physical and psychologic stress ,drugs other than NSAID, such as acetaminophen (in doses greater than 2 or 3 g daily), bisphosphonates, cocaine, glucocorticoids, selective serotonin reuptake inhibitors, clopidogrel, and erlotinib, Infections such as , Non-pylori helicobacter and Cytomegalovirus, mechanical factors such as post-obstruction, foreign body, surgery, ischemia, inflammatory and infiltrating diseases of the stomach (eg, IBD), and acid hypersecretory states (e.g., Zollinger-Ellison syndrome). peptic ulcer with no definite causes such as H. pylori infection, NSAIDs use or hypergastrinemia are termed as Idiopathic PUD (IPUD) (11).

The global difference in the magnitude of the H. pylori infection rate could be explained by the difference in socio-economic status, environmental sanitation, living conditions, and personal hygiene(12).

Approximately 70 percent of peptic ulcers are asymptomatic(13). Patients with silent peptic ulcers may later present with ulcer-related complications such as hemorrhage or perforation, which usually is seen in Gastric ulcer. Upper abdominal pain or discomfort is the most prominent symptom in patients with peptic ulcers accounting for 80 percent of patients with endoscopically diagnosed ulcers (14). Other associated symptoms include abdominal fullness, nausea, and early satiety that may be provoked by eating.

The risk of complications in patients with chronic PUD is 2 to 3 percent per year(15, 16).Complications may be heralded by new ulcer symptoms or a change in symptoms or may occur in the absence of typical symptoms. peptic ulcer bleeding, perforation, GOO, Penetration and fistula formation are the commonly encountered complications. H.pylori ,NSAID use , previous ulcer, age ,and chronic debilitating disorder, especially cardiovascular disorder are found to be the determinants of peptic ulcer bleeding and perforation(17-19).

The diagnosis of peptic ulcer disease is suspected in patients with dyspepsia, especially in the setting of nonsteroidal anti-inflammatory drug (NSAID) use or a history of Helicobacter pylori (H. pylori) infection. The diagnosis of peptic ulcer disease is definitively established by direct visualization of the ulcer on upper endoscopy (20, 21).

Low socio-economic status, environmental sanitation, and living conditions contribute to the high prevalence of H. pylori as well as PUD (13). Majority(52.2%) of Ethiopian population are H.pylori infected according to national study done in 2019(22). Among dyspeptic patients who undergone endoscopic evaluation,35% of them had PUD, of which H. pylori followed by NSAID were the attributing etiologies. Duodenal ulcer were more prevalent compared to gastric Ulcer(23).

1.2 Statement of the problem

Though the different underlying etiologies for PUD have led to difference in the prevalence of PUD from one world region to the other ,overall the burden of PUD is growing in developing countries(4).

With regard to Risk factor, H.pylori is found to be the major factor for PUD as seen in local and worldwide studies(23, 24) ,this contradict with few studies that revealed NSAIDs use as the major factor (25, 26) .The cooccurrence of h.pylori and NSAIDs use has synergistic effect for the occurrence of PUD and the complications (17, 27-29) .

Other risk factors, smoking are risk factors for PUD(19, 30).A Systematic Review of the Epidemiology of Complicated Peptic Ulcer Disease showed that Prior use of NSAIDs was the most commonly identified risk factor for peptic ulcer hemorrhage.in addition an association between H. pylori infection, ulcer size and alcohol use and peptic ulcer bleeding was seen. Smoking had association with PUD perforation(19)

Overall, on Endoscopic findings, duodenal ulcer is more prevalent than Gastric ulcer, in contrast to few studies which showed equal prevalence and higher prevalence of gastric ulcer. (25, 31)

In Ethiopia there are limited facilities with Endoscopic service and well trained personnels that the studies done on Endoscopic proven PUD are limited(32).

In Ethiopia, according to a recent Study done in Gondar, Northern Ethiopia it was found that the prevalence of endoscopically diagnosed PUD was 35%. H. pylori followed by NSAID use were described as the major underlying etiologies. The majority of them were duodenal ulcers (23).

Decades ago there was one study conducted at Southern Ethiopia ,that detected that 93% of the PUD patients had h.pylori infection, but details on the endoscopic finding and complications are lacking(33).

Few years back a population-based study conducted in Ethiopia stated that the burden of H. pylori infection in Ethiopia is as high as 52.2%. but it did not describe the relation to PUD prevalence (10).

As to my knowledge there are limited Data on Ethiopian study regarding the association between risk factors and type of ulcer, ulcers magnitude, comorbidities and rate of complications Among PUD patients .

This study aims to fill the gap in assessing the underlying risk factor, the comorbidities and the complications of PUD. It also aims to show the association of the risk factors, comorbidities and endoscopic findings with the complications. This study will help to take action to tackle the risk factors.

1.3 Significance of the study

The studies conducted in our setup on endoscopically proven PUD are limited. This may be due to the absence of Endoscopy machine and scarcity in professionals in most health facilities of Ethiopia. There is only one recent study that is conducted upon Endoscopic diagnosis of PUD. Since this study is to be conducted in SPHMMC, which is one of the tertiary referral hospital located in the central part of the country, it will better represent the country as a whole and be applicable for the general population.

Determining the risk factors, comorbidity and complications will add to the existing knowledge about the problem for clinicians in local setup. Health authorities can use the findings of this research for development of policies and guidelines and for adequate resource allocation. Future researchers can use this study as a baseline to investigate the issue in the same or different contexts.

2. Literature review

Despite sharply decreasing rate of PUD related hospital admission, an estimated 15000 deaths occur each year because of peptic ulcer. Worldwide annual incidence estimates of peptic ulcer hemorrhage and perforation were 19.4–57 and 3.8–14 per 100,000 individuals, respectively (34).

There is a change in prevalence rate of PUD, dropping off among developed and growing among developing countries with relation to the underlying etiologies. The contributing factors for the increment in developing world is delayed detection and treatment of the underlying risk factor, poor hygiene and poor awareness (35).

It commonly affects young adults as seen both in global and local study (4, 23). The incidence of PUD increases with age, especially the occurrence of complication is higher as age advances(36).

Worldwide the lifetime risk of developing peptic ulcer disease is about 4% for females and 10% for males (35). Studies done on general population of the world, decades ago showed that The prevalence of peptic ulcer disease has shifted from male predominance to similar occurrences in males and females (18, 37). According to study done on global burden of disease of PUD, conducted from 1990 to 2019, globally males are predominately affected (2:1) compared to females, but since the prevalence rate in males is decreasing faster than those of females, the male to female ratio is getting lower, (1:0.94). when its seen with regard to global regions, most of them showed male predominance with the exception of Western sub-Saharan Africa, South Asia, North Africa and the Middle East, High-income North America and Central sub-Saharan Africa, where females were majorly affected (4). A study done At tertiary care teaching hospital in Dhaka, Bangladesh the majority of PUD patients were females(55.6%) (25). A recent study in Gondar, Northern Ethiopia showed male predominance (23). Globally among elderly PUD patients females were majorly affected. (4).

According to health facility based recent study done in Gondar hospital, Gondar, Ethiopia among adults with complaints of dyspeptic symptoms who underwent endoscopic evaluation, the mean age of patients was 42, from which more than half of them were males and urban

dwellers (54%,58% respectively). Regarding endoscopic findings,1/3rd (35%) of the patients had PUD, of which 2/3rd (72%) of them were duodenal ulcer. The other endoscopic findings were gastritis/duodenitis ,gastric mass, and pyloric obstruction in descending order(19%,6%,4%),the remaining 1/3rd patients had functional dyspepsia (23).

The majority (70 percent) of those PUD patients were asymptomatic, of those who are symptomatic, abdominal pain account for approximately 80 % of cases. Patients may have associated symptoms of bloating, abdominal fullness, nausea, and early satiety that may be provoked by eating (13, 14). Duodenal ulcer is highly prevalent compared to gastric ulcer and occur 2 decades earlier than Gastric ulcer (36). A study from Bangladesh revealed higher prevalence of gastric ulcer. (25). gastric ulcer has higher complication rate compared to Duodenal ulcer due to less symptoms and delayed diagnoses usually after complication have already occurred (25).

2.1 Risk factor

NSAID use and H. pylori infection represent independent and also synergistic risk factors for peptic ulcer disease. A systematic review of H. pylori prevalence around the world showed that the highest reported H. pylori prevalence areas were Africa (70.1 percent), South America (69.4 percent), and Western Asia (66.6 percent). Regions with the lowest reported H. pylori prevalence were Oceania (24.4 percent), Western Europe (34.3 percent), and Northern America (37.1 percent)(12). A study done in Nigeria showed that the prevalence of h. pylori was 38.3%. The majority of the patients in this study were NSAID users (26).

According to study done Yirgalem ,southern Ethiopian 1999,among patients with PUD, majority of them(93%),had active h.pylori infection (38).In a recent study done in Ethiopia, Gondar among dyspeptic patients who undergo endoscopic evaluation, h.pylori was found in 71.1 % and 40% were NSAID users (23).

A recent study in Ethiopia in 2019, the overall prevalence of H. pylori is 52.2%, H. pylori being highly prevalent in Somalia (71%) followed by Amhara 54.6%, SNNPR 53.6%, Benishangul Gumuz 48.7%, Addis Ababa 48.1%, and Oromia Region 39.9% (10).

Even though NSAID and H.pylori were said to be the etiologies for PUD, the yearly incidence of clinical ulcer disease among subjects who are NSAID users or H.pylori infected is only approximately 1% , indicating that there are many other contributing factors (39-41).

Likewise, the determined associated factors for H. pylori infection in Ethiopia were environmental factors, such as lack of hand washing before meal and after toilet use and behavioral factors such as smoking and drinking alcohol, that showed the synergistic effect. chat chewing didn't show significant association. patients with GI symptoms due to other GI diseases were also more likely to be infected by H.pylori, (22).

The prevalence of H. pylori infection rises with age: 29.7% in those less than 30 years old and 63% at age 55-65 (42).

Low educational level is a high risk for asymptomatic PUD, due to increased prevalence of H. pylori, psychological stress and hard physical work. Aggressiveness of H. pylori is determined by virulent H. pylori genotype, environmental and dietary factors. helminthiasis and chili pepper due to capsaicin are shown to have protective effect against h.pylori (43, 44).

NSAID use is associated with a fourfold increase in the risk of peptic ulcer disease (45). In addition, NSAIDs are associated with an increased risk of complications from peptic ulcer disease which include gastrointestinal bleeding, perforation, and pyloric obstruction. NSAID-induced ulcers may also be more refractory to conventional therapy (46).

As Health facility based Study in United states of America reveal Gastric Ulcer has become more commonly associated with the use of nonsteroidal anti-inflammatory drugs and acetylsalicylic acid (ASA) while Duodenal Ulcer is associated with age and smoking (47). PUD risk progressively increases with increasing pack-years of cigarette smoking (48). Besides Alcohol intake is a risk factor and it predicts the occurrence of complications(19).

Physical and psychologic stress are considered one of the risk factor for PUD, Nutritional deficiencies have been regarded as etiologic factors in peptic ulcers However, malnutrition does not appear to have any causative role in peptic ulceration in European countries and the north America (49, 50).

2.2 Comorbidities

The point prevalence and lifetime prevalence of PUD in cirrhotic patient are point prevalence are 11.7% and 24.2% and it is usually asymptomatic as seen in most studies. Its more frequently seen in HBSAg Positive cirrhotic patients. The majority patients have gastric ulcer, at the antrum. There were no association between PUD and H. pylori, age, sex, child-Pugh score, model for end-stage liver disease score, and Complications of Cirrhosis such as Hepatic Encephalopathy and ascites. Compared with the general population, patients with cirrhosis have higher bleeding complications, delayed healing, and greater ulcer recurrence rates(51).The prevalence of symptomatic PUD in cirrhosis have increased hospital burden as well as poor outcome in terms of higher in hospital mortality(52) (53) (54) (55) (56) .

Hypertension and other Cardiovascular Diseases Such as ischemic stroke and Ischemic heart disease are seen in patients with PUD ,association to the use of Aspirin and h.pylori infection were noted (23) (57, 58). In Rheumatologic diseases such as Rheumatoid Arthritis and Psoriatic Arthritis ,PUD is one of the comorbidity seen (23, 59, 60). Among HIV patients ,CMV was the major underlying cause (61).

2.3 Complications

The risk of complications in patients with chronic PUD is 2 to 3 percent per year. There has been a consistent decrease in the incidence of bleeding and perforation and hospitalization rates due to complications of PUD, presumably reflecting the fall in *Helicobacter pylori* prevalence(15) (16). Hemorrhage occurs four times more often than perforation and penetration. High age and the use of nonsteroidal anti-inflammatory drugs (NSAID) are the most important risk factors(62). The incidence of rebleeding is twice as high after a first complication (63). A Systematic Review of the epidemiology of complicated Peptic Ulcer Disease showed that Prior use of NSAIDs was the most commonly identified risk factor for peptic ulcer hemorrhage.in addition an association between H. pylori infection, ulcer size and alcohol use and peptic ulcer bleeding was seen. Smoking had association with PUD perforation(19).PPI use had shown protective effect against complication of PUD(64).

In patients with bleeding peptic ulcer, the majority of deaths are related to multi-organ failure or cardiopulmonary causes rather than to bleeding itself (65). Not surprisingly, in patients with gastrointestinal bleeding requiring endoscopic therapy, hypovolemic shock, multiple comorbidities, and rebleeding in the hospital were predictive of mortality. (66)

2.4 Conceptual framework

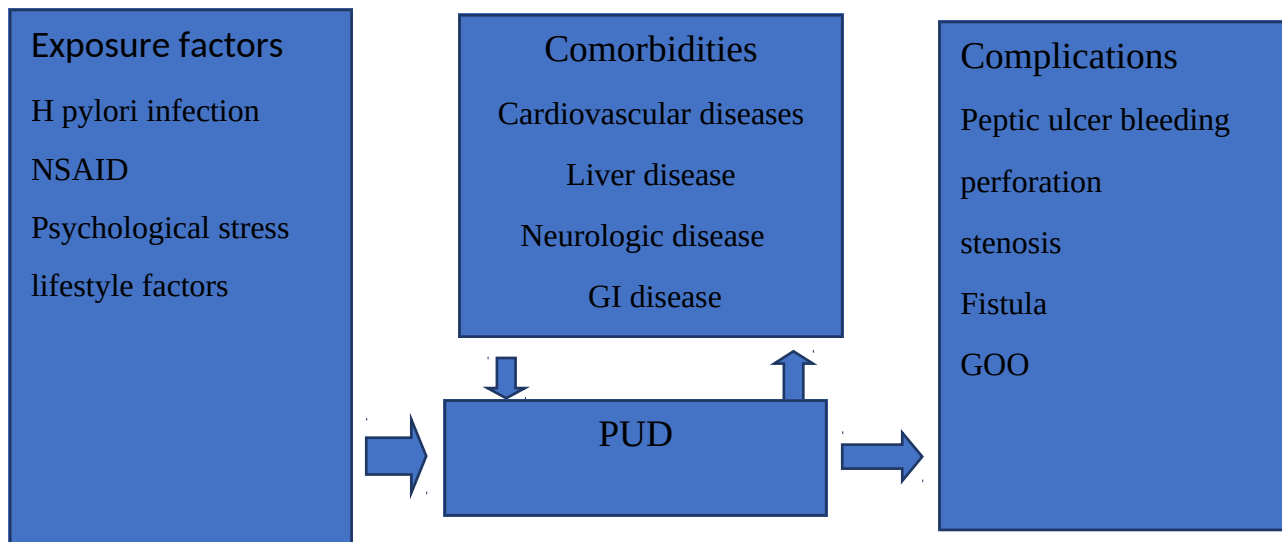


Figure 1: Conceptual framework on associated factors of complication of PUD

- Risk factors(16, 23, 38, 50, 67)
- Comorbidities(23, 51, 57, 60)
- Complications(29, 68, 69)

3. Objectives

3.1 General objective

- ❖ To assess the clinical characteristics of PUD, and associated factors of patients with endoscopically proven PUD complications in SPHMMC, Addis Ababa, Ethiopia, 2024.

3.2 Specific objective

- ❖ To assess the clinical characteristics of endoscopically proven PUD patients in SPHMMC
- ❖ To assess the comorbidities in subjects with endoscopically proven PUD in SPHMMC
- ❖ To assess the prevalence of complications of endoscopically proven PUD in SPHMMC.
- ❖ To assess the associated factors with complications of endoscopically proven PUD patients in SPHMMC

4. Methods and materials

4.1 Study design.

A hospital based cross-sectional descriptive study was conducted among endoscopically proven PUD.

4.2 Study area and period.

4.2.1 Study area.

This study was conducted in St Paul's Hospital Millennium Medical College, the second largest tertiary hospital in Addis Ababa, Ethiopia.

The college has more than 2800 clinical, academic, and administrative and support staffs that provide medical specialty services to patients who are referred from all over the country, teaching medicine and nursing students and

doing basic and applied research. While the inpatient capacity is more than 700 beds, The College sees an average of 1200 emergency and outpatient clients daily(70). SPHMMC's Endoscopy unit is the first African Endoscopic center to be accredited by the world Endoscopy organization/European society of GI Endoscopy. On Average 40 to 50 Endoscopic procedures per week have been done at the GI unit, with growing capacity.

4.2.2 Study period.

The study was conducted at SPHMMC Endoscopy unit from March to June 2023.

4.3 Population

4.3.1 Source population.

Patients with clinically diagnosed PUD at SPHMMC GI unit from January, 2018 to February 2023.

4.3.2 Study population.

All patients who have endoscopic proven PUD and who fulfill the inclusion criteria.

4.4 Eligibility criteria

4.4.1 Inclusion Criteria

Those adult (≥ 18 years of age) patients from SPHMMC GI clinic, who undergone Endoscopy from January, 2018 to February 2023.

4.4.2 Exclusion criteria

patients with incomplete sociodemographic history and phone number and Charts without endoscopy record were excluded.

4.5 Study variables.

4.5.1 Independent Variables

- ❖ Sociodemographic status: Age, sex, place of residency
- ❖ H. pylori infection

- ❖ NSAID /ASA use→ total duration and last use.
- ❖ Lifestyle(behavior)→ cigarette smoking, alcohol, khat
- ❖ psychological stress
- ❖ preexisting GI and hepatobiliary Disease
- ❖ previous history of Endoscopically proven PUD
- ❖ preceding use of PPI and duration of use
- ❖ symptoms of PUD and Danger sign
- ❖ Comorbidities: Cardiovascular Disease, hepatobiliary disorder except cirrhosis, cirrhosis, GI disease Genitourinary, HIV, genitourinary, rheumatologic disease
- ❖ Endoscopic finding
(Ulcer size, site, Forrest class (if bleeding)
Other endoscopic findings)

4.5.2 Dependent Variables

- ❖ complications of endoscopically proven PUD

4.6 Sample size determination and Sampling Technique

4.6.1 Sample size determination.

The sample size was determined using single population estimation formula using the assumptions stated below by considering p value of 0.5 .

$$n = \frac{Z^2 p (1-p)}{d^2}$$

Where,

- ❖ n = the number of endoscopically proven PUD patients to be assessed.
- ❖ Z = standardized normal distribution value for the 95% CI, which is 1.96.
- ❖ P = (0.5)
- ❖ d = the margin of error is taken as 5%.

- ❖ Using the above formula and substituting the values of parameters, the calculated sample size was 384.

Since N ~ less than 10,000 (N= 500) (source population).

Using correction formula $n_f = \frac{n}{1 + \frac{n}{N}}$

$n_f = 217$.

Sample size calculation was also done by calculating the sample size for major factors and taking the largest one. The sample size calculation using the associated factor of H pylori infection (OR-6.3)(23) Was done using EPINFO and the sample size was found to be 88.

NSAID usage was also associated with developing PUD (OR-6.2)(23). Using this, the sample size was found to be 143.

Table 1: sample size calculation

S.N	variable	95% CI	power	P	1-P	Calculated sample	Total sample size
1	H.pylori	1.96	80%	83.8	0.162	88	88
2	NSAID use	1.96	80%	83.5%	0.165	143	143

As the largest sample size from the above is 217, sample size of 217 is taken.

With the addition of 5% non-response rate, the size was 227.

4.6.2 Sampling procedure

The participants were selected using a convenience sampling method.

All patients of endoscopically proven PUD were included. Checklist was used for eligible cases.

4.7 Operational definition

- ❖ Helicobacter Pylori Diagnosis-Diagnosis which is made by visualization

the bacteria by both non-invasive and invasive (endoscopic) testing.

- ❖ PUD – Endoscopic proven digastric tract mucosal break of 3mm or more(1).
- ❖ Cigarette smoker refers to someone who has smoked more than 100 cigarettes in their lifetime and has smoked in the last 28 days (71)
- ❖ NSAID/ASA use- NSAID/ASA use of 30 or more pills/doses in the last one month (72)
- ❖ Alcohol consumption is defined as alcohol intake more than two drinks for men and one drink for women in a day (73)
- ❖ Khat chewing is defined as chewing khat 3 or more times per week (74)
- ❖ Psychological stress- those with documented psychiatric disorder.
- ❖ Danger sign- alarming symptoms and signs that denote the presence of complications.
- ❖ Complications defined by endoscopic finding of Ulcer bleeding, perforation, GOO, penetration and fistula

4.8 Data collection tools and procedure

Data collection involved reviewing the participants' medical charts using a structured checklist. The collected data included demographic information, risk factors, comorbidities, complications, and other variables. In cases where data was incomplete, phone calls were made, and outpatient visits were conducted over a period of four months. Data collection was conducted using Kobo Toolbox version 4.4. Data was collected by GI Unit attaching Internal Medicine Residents at SPHMMC after 1 hour long for 2 days intensive training on the procedure of data collection and objectives. Document review was done by data collectors and principal investigator. Then Data was submitted to EPI- info software and analyzed using SPSS 27.

4.9 Data Quality Assurance

The quality of data was assured by proper designing of the checklist. Pre-testing

of the questionnaires was performed using 5% of the sample size at Black Lion Hospital Addis Ababa, Ethiopia. Based on the pre-test some modifications were made to the questionnaire.

An hour long training was given to 3 data collectors and 2 supervisors (Internal Medicine Residents) by the principal Investigator for two days. The training included discussion on the objectives of the study and on the contents of the checklist one by one, on procedures, and data collection techniques and on the issues of confidentiality.

Every day after data collection, data was reviewed and checked for completeness by the supervisors and principal investigator and the necessary feedback was given to data collectors the next morning.

4.10 Data analysis and presentation

Data was collected using Kobo Toolbox version 4.4 and after that data was checked, coded and was exported to SPSS (Statistical Package for Social science) version 27 for analysis. Descriptive statistics were summarized using frequencies, tables, and figures. Bivariate logistic regression analysis was used to check variables association with dependent variable individually. In Bivariable, in dependent variable of $p\text{-value} < 0.25$ were entered in to multiple logistic regression models for further analysis and variables having $P\text{-value} < 0.05$ were considered as significantly associated with the dependent variable.

4.11 Ethical consideration

Ethical clearance was obtained from Institutional review board of St Paul's Hospital Millennium Medical College and SPHMMC research office prior to conducting the research. Permission was sought from the school administration to carry out the research. Each patient's name and other Identification revealing information was kept confidential.

4.12 Dissemination of result

The findings of the study will be submitted to the department of Internal Medicine, and it will be presented as one of the partial fulfillments of residency program in Internal Medicine Department. All efforts will be made to publish the results to the local and International Journals and to present it in national scientific conferences.

5. Result

5.1 Socio-demographic characteristics of study subjects

The study included a total of 227 patients, resulting in a response rate of 98.2%. Four subjects were excluded from statistical analysis due to incomplete data. The average age of the patients was 42 ± 14.8 years, with over half of the participants being above 40 years old. Males accounted for two-third (68.2%) of the study subjects, while nearly half (50.2%) of the participants lived in rural areas (Table 2).

Table 2: Socio-demographic characteristics of PUD patients who underwent upper gastrointestinal endoscopic evaluation at endoscopy unit, SPHMMC, from January 2018 to February 2023G.C

Variables	Category	Frequency	Percent
Mean Age		42 ± 14.8 years	
Age	18-28	44	19.7
	29-39	65	29.1
	40-50	56	25.1
	>50	58	26.0
Sex	Male	152	68.2
	female	71	31.8
Residence	Urban	111	49.8
	Rural	112	50.2

5.2 Exposure factors of PUD among participants

In terms of H. Pylori, 70 participants (31.4%) were tested positive for H. Pylori infection (Table 2). Among them, the majority (65.8%) were aged above 40 and lived in urban areas (55.7%). Among PUD patients with H. pylori infections, 84.3% had duodenal ulcers.

Only 10 participants (4.5%) had a history of NSAID use, and 6 of them took NSAIDs for more than 40 days. Among these participants, 80% presented with symptoms of PUD within 2 weeks of NSAID use (Table 3).

Twenty participants (9%) had a history of smoking, and among smokers, the majority (80%) had duodenal ulcers. Approximately one-third (27.4%) of the participants had a history of alcohol intake, and 26 (11.7%) had a history of khat use (table 3)

Eleven participants had psychological stress, and among them, 81.8% were diagnosed with major depressive disorder (MDD). Nearly one-third (34.5%) of the participants had a previous history of PUD, and among these, 38.1% were aged between 40 and 50. Furthermore, 93 participants (41.7%) had preexisting comorbid GI and hepatobiliary disorders, with the majority having hepatobiliary disease, including cirrhosis (80%). Thirty-one percent of those with cirrhosis were in the age group of 29-39, with a male to female ratio of 5.2:1 (Table 3).

Table 3: Risk factors among PUD patients who underwent upper gastrointestinal endoscopic evaluation at endoscopy unit, SPHMMC, from January 2018 to February 2023G.C

Variable	Category	Frequency	Percent
H.pylori	Negative	153	68.6
	positive	70	31.4
NSAIDs/ASA use	No	213	95.5
	Yes	10	4.5
Smoking	No	203	91.0
	Yes	20	9.0
Alcohol use	No	162	72.6
	Yes	61	27.4
Khat use	No	197	88.3
	Yes	26	11.7
Psychologic stress	No	212	95.1
	Yes	11	4.9
Previous history of	No	146	65.5
	Yes	77	34.5
PUD	yes	77	34.5
Preexisting GI disease	No	130	58.3
	Yes	93	41.7

5.3 Clinical manifestations of Participants

Majority of the cases (92.8%) reported experiencing abdominal pain, followed by nausea/vomiting (80.7%) and bloating (26%) respectively (Figure 2)

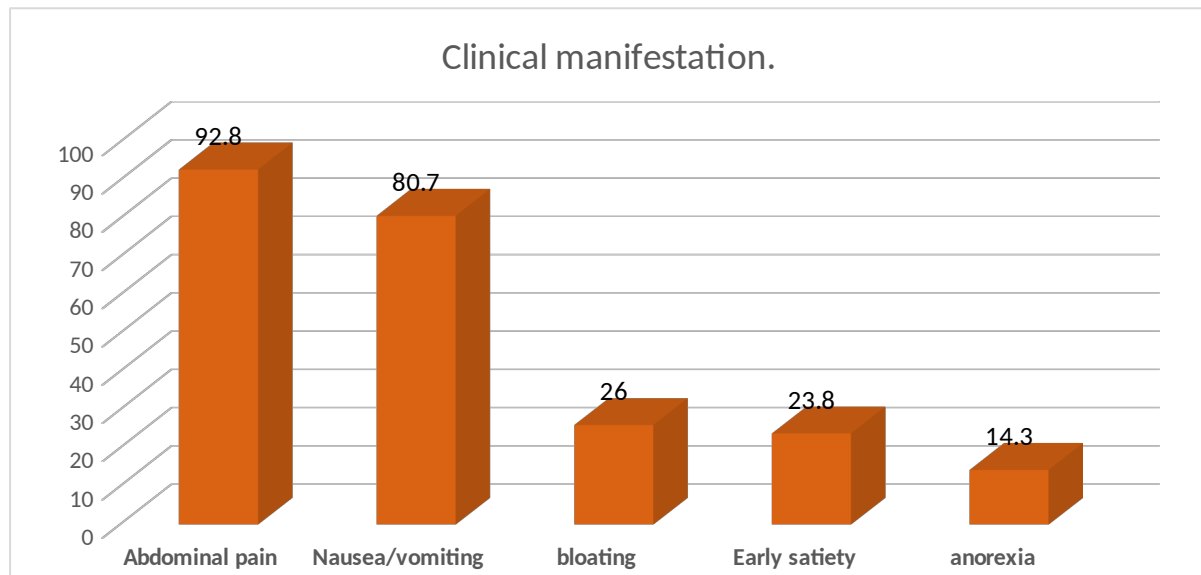


Figure 2: clinical presentation of PUD patients who underwent upper gastrointestinal endoscopic evaluation at endoscopy unit, SPHMMC, from January 2018 to February 2023G.C

Among the participants, most of them (76.7%) exhibited danger signs. Out of these participants, 105 (61.4%) had bleeding, 78 (45.6%) experienced weight loss, 61 (35.7%) had severe abdominal pain, and 32 (18.7%) had anorexia (Figure 3). It was observed that the majority (71.9%) of participants with danger signs were diagnosed with duodenal ulcers. The highest proportion of danger signs was seen in individuals aged above 50 (30.4%). Of those with danger signs, 70 out of 171 (40.9%) had been using PPI in the preceding 2 months. One quarter (27.4%) of the participants had PPI use in the preceding 2 months. More than half of them (50.6%) were urban residents.

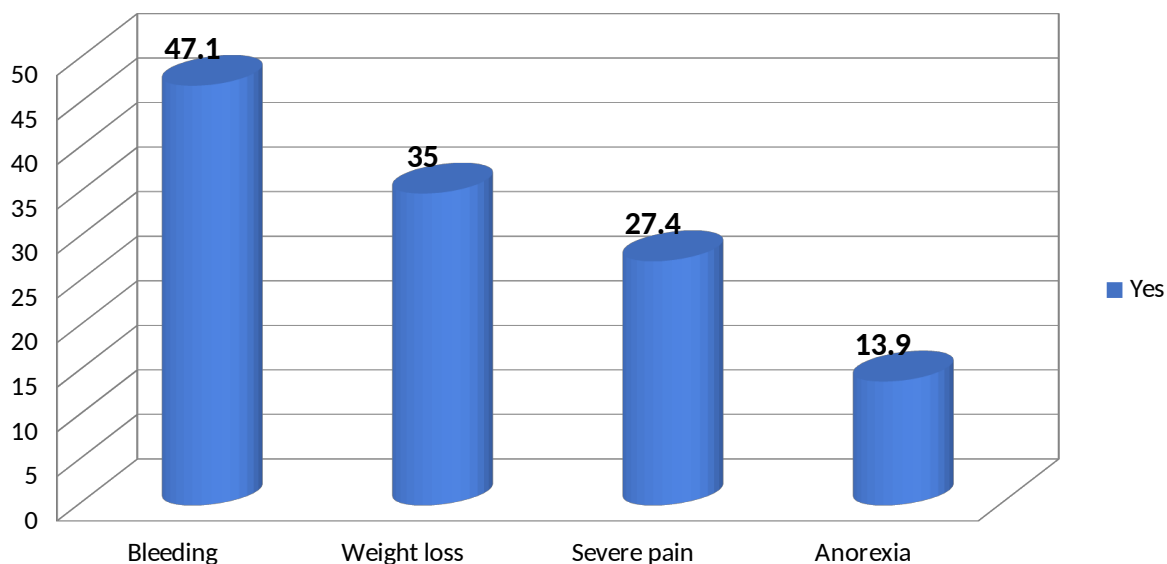


Figure 3: Danger signs among PUD patients who underwent upper gastrointestinal endoscopic evaluation at endoscopy unit, SPHMMC, from January 2018 to February 2023G.C

5.4 History of comorbidity among participants with endoscopic proven peptic ulcer disease

As shown in table 4, comorbidity was observed in 111 participants (50.2%). Among those subjects who had comorbidity, 111(40.5%) of them had Hepatobiliary diseases, excluding cirrhosis. Cirrhosis itself accounted for 44 participants (39.6%), followed by cardiovascular disorders 14(12.6%) and psychiatric disorders 11(9.9%). More than one third (36%) of those participants with comorbidity were categorized in the age group between 29 -39. Out of those with comorbidity, 85 out of 111 participants (76.5%) exhibited danger signs. Among those who had comorbidities the majority (78.4%) had duodenal ulcers. Additionally, among those with cirrhosis, 38.6% experienced complications related to PUD (table 4).

Table 4: Comorbidity among participants PUD patients who underwent upper gastrointestinal endoscopic evaluation at endoscopy unit, SPHMMC, from January 2018 to February 2023G.C

Variables	category	frequency	percent
Comorbidity (n=223)	No	112	50.2
	Yes	111	49.8
n=111			
Hepatobiliary Disease, except cirrhosis	No	66	59.5
	yes	45	40.5
Cirrhosis	No	67	60.4
	yes	44	39.6
Cardiovascular disease	No	97	87.4
	yes	14	12.6
Psychiatric disorder	No	100	90.1
	yes	11	9.9
DM	No	103	92.8
	yes	8	7.2
Malignancy	No	103	92.8
	yes	8	7.2
Respiratory	No	104	93.7
	yes	7	6.3
Genitourinary	No	115	94.8
	yes	6	5.2
Gastroenterology	no	115	94.8
	yes	6	5.2
others	no	108	97.2
	yes	3	2.8

others(RVI,Neurology)

5.5 Endoscopic Characteristics

The participants in the study were observed to have a higher prevalence of duodenal ulcers, which accounted for 74.4% of the cases. Stomach ulcers were the second most common, making up 20.6%. The remaining 5% of participants had both duodenal and stomach ulcers (figure 4).

Among those with duodenal ulcers, the highest number was found in the age group of 29-39 years, accounting for 29.5%. For gastric ulcers, the age group of 40-50 years had the highest prevalence at 30.4%.

Complications were more frequent in those with duodenal ulcers, with 50.6% experiencing complications related to PUD. Among gastric ulcer patients, 28.3% had complications.

Out of the participants who experienced endoscopic bleeding 79 (35.3%) , the majority fell into Forrest Class 3 (78.5%), followed by Class 2 (19%) and Class 1 (2.5%).

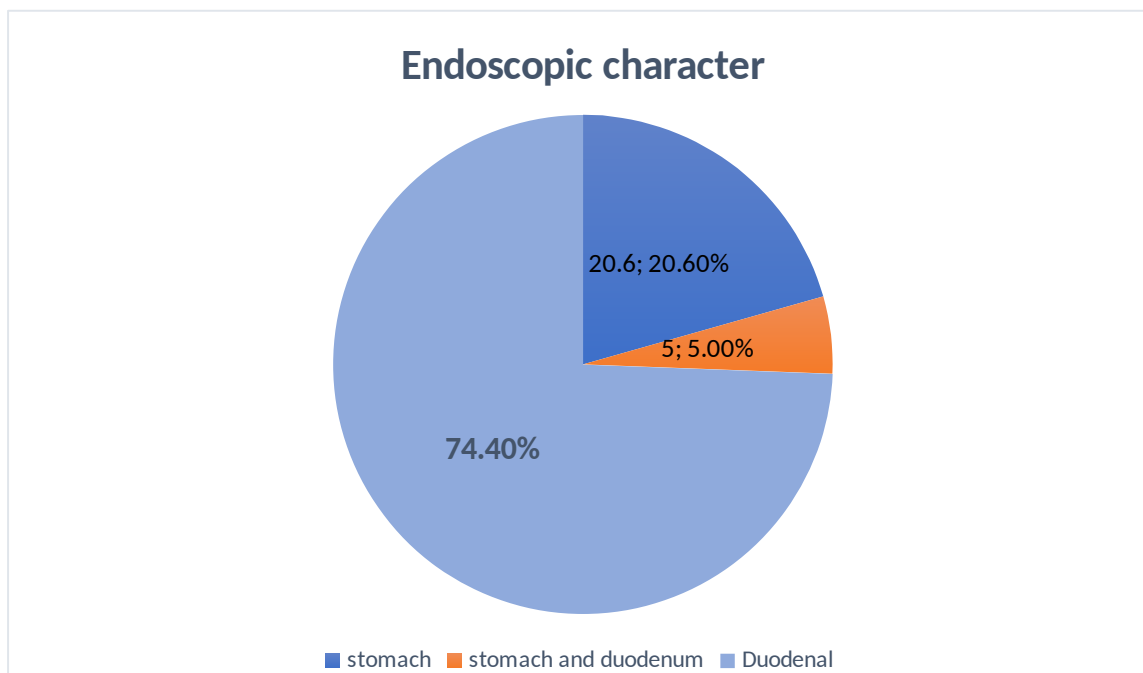


Figure 4: The site of ulcer among PUD patients who underwent upper gastrointestinal endoscopic evaluation at endoscopy unit, SPHMM, from January 2018 to February 2023G.C

More than one-third of the participants (35.3%) had other concomitant endoscopic findings, with the highest being esophageal varices (27 out of 223, accounting for 12.1%), followed by gastric cancer 17 (7.6%) (table 5).

Table 5: other endoscopic findings than PUD in PUD patients who underwent upper gastrointestinal endoscopic evaluation at endoscopy unit, SPHMMC, from January 2018 to February 2023G.C

n=79	frequency	Percentage
Esophageal varices	27	34.2
Gastric Cancer	17	21.5
GOO, stricture	14	17.7
GERD	13	16.5
Hiatal Hernia	6	7.6
Duodenal diverticuli	2	2.5

5.6 Complications

Out of a total of 223 subjects, complications were observed in 100(44.8%). The most common complication was bleeding, which was responsible for 79% of the participants. Other complications included gastric outlet obstruction (12%), stricture (10%), and perforation (2%) (Figure 5).

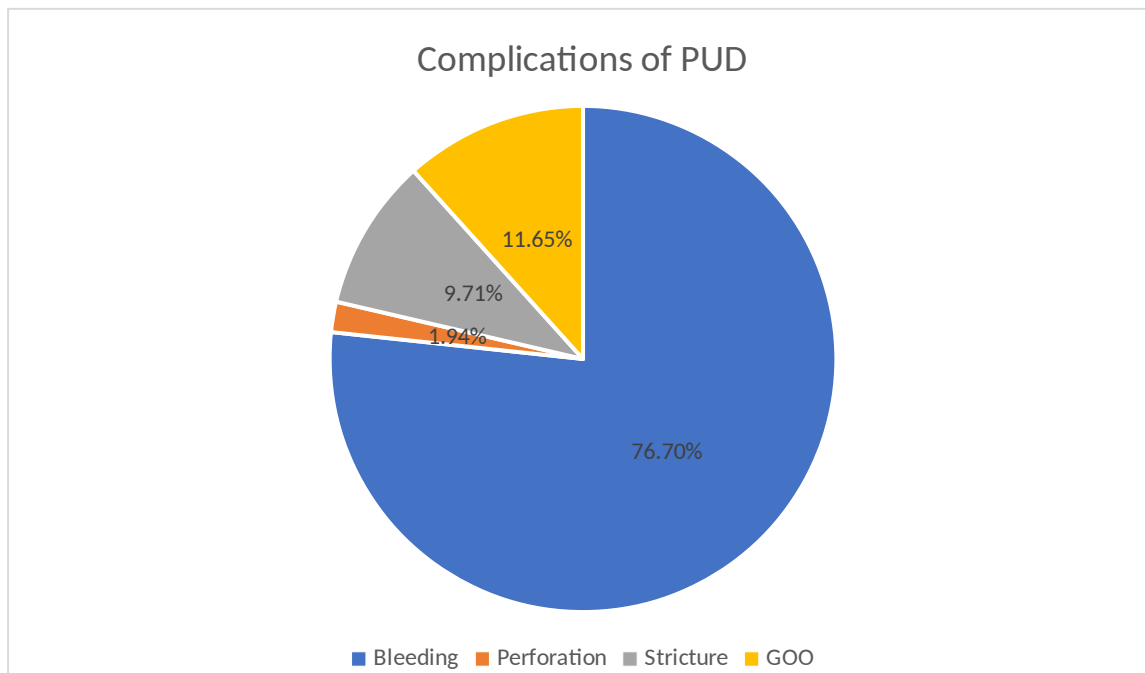


Figure 5: Complications of PUD patients who underwent upper gastrointestinal endoscopic evaluation at endoscopy unit, SPHMMC, from January 2018 to February 2023G.C

Among the subjects who experienced complications, those above the age of 50 had a higher percentage of complications (44%), and most of them were male (73%) and lived in rural areas (56%).

Regarding the site of the ulcer, the majority of complicated peptic ulcer disease were duodenal ulcers (84%). Of those with PUD complications, a majority (51%) tested positive for *H. pylori*, while none of them were found to be NSAID users. Additionally, 40% of them had preexisting gastrointestinal and hepatobiliary disorders.

Among those with complications, 23% had a history of alcohol intake, 14% were smokers, and 5% were khat chewers. Furthermore, among those who experienced complications, 39% had a history of preceding PPI use in the past 2 months, while the remaining individuals did not take PPI (table 6).

Table 6: Complication of PUD in respect of socio-demographic, risk factors, habits, ulcer site among endoscopically proven PUD participants.

NSAID use	no	100	100
Smokers	No	86	86.0
	yes	14	14.0
Alcohol	No	77	77.0
	yes	23	23.0
Khat	No	95	95.0
	Yes	5	5.0
Preceding PPI use	No	61	61.0
	yes	39	39.0
Ulcer site	Duodenum	84	94.0
	Stomach	13	13.0
	Stomach and duodenum	3	3.0
Bleeding	No	21	21.0
	Yes	79	79.0
Forrest class if bleeding (N=79)	1	2	2.50
	2	15	19.0
	3	62	78.5

5.7 Factors associated with risk of developing complications of PUD among participants with endoscopic proven peptic ulcer disease.

Odd ratio and 95% CI were used to measure the association between predictor variables and PUD complication. According to the binary logistic regression model age, sex, place of residency, H. pylori infection, previous history of PUD and smoking were selected for multivariate analysis. In the multivariable analysis, it was found that the odds of PUD complication in those aged 40-50 were three times higher than those aged 18-28 [AOR=3.004; 95%CI (1.098,8.2232)]. Furthermore, the odds of PUD complication in those aged over 50 years were twelve times higher than those aged 18-28[AOR=12.062; 95%CI (4.261,34.146)]. The odds of PUD complication in smokers were three times higher than non-smokers [AOR=3.907; 95%CI (1.224,12.472)]. Additionally, the odds of PUD complication in H. pylori infected participants were six times higher than those without the infection [AOR=5.914; 95%CI (2.878,12.151)] (Table 7).

Table 7: Factors associated with complications Of PUD among PUD patients who underwent endoscopic evaluation, at endoscopy unit, SPHMMC, from January 2018 to February 2023G.C

Variable	Catagory	PUD complication		COR	AOR(95% CI)
		Yes	NO		
Age group	18-28	9(9)	35(28.50		
	29-39	19(19)	46(37.4)	1.608(0.649,3.978)	2.68(0.611, 4.621
	40-50	28(28)	28(22.8)	3.889(1.58,9.57)	3.004(1.098,8.2232)*
	>50	44(44)	14(11.4)	12.222(4.737)	12.062(4.261,34.146)**
sex	Male	73(73)	79(64.2)	1.506(0.847,2.677)	O.963(0.482, 1.921)
	Female	27(27)	44(35.8)	1	1
Residence	Urban	44(44)	67(54.5)	1.523(0.895,2.589	1.782(0.912, 3.3519)
	rural	56(56)	56(45.5)	1	1
H. pylori	No	49(49.0)	104(84.6)	1	1
	yes	51(51)	19(15.4)	5.697(3.044,10.662)	5.914(2.878,12.151)**
Previous history	No	57(57)	89)72.4)	1	1
	Yes	43(43)	34(27.6)	1.975(1.128,3.455)	1.379(0.701,2.714)
Smoking	No	86(86)	117(95.1)	1	1
	yes	14(14)	6(4.9)	3.174(1.12.8.595	3.907(1.224,12.472*

Hosmer and Lemeshow Test=0.539; * significant; ** highly significant , previous history-previous history of PUD.

6. Discussion

The finding of our study showed that males were highly affected by PUD than females with a proportion of 2.1: 1. This is in line with other global and local studies (23). This study came up with (31.4%) H. pylori infection rate. Compared to a study conducted decades ago in southern Ethiopia, where 93 % PUD participants had Positive H.pylori result(33), our study has lower H.pylori infection rate. This may be explained using PPI, that may lead to false negative result and improvement in hygiene and sanitation. The other possible cause may be the difference in study area. As the current study was conducted in Addis Ababa, capital city of Ethiopia, the participants may have a better access for information on hygiene and sanitation. According to our study, the majority of those who are H. pylori positive were urban dwellers. Although this deviates from the thinking of Hygiene as a risk factor for H. pylori acquisition, the potential risk

of synergistic factors for acquisition of H.pylori increases with those smokers, who were majorly urban dwellers. According to this study most of those participants with H. pylori infection had duodenal ulcer and the odds of PUD complications were six times higher than their control counterparts. There are conflicting results with regard to this , though some studies suggest that H.pylori infection on top of NSAID use has association with Peptic ulcer bleeding, there are studies that showed H.Pylori's association with peptic ulcer bleeding(19).

Regarding NSAID use, this study didn't reveal any association to PUD complication. This contradiction to other studies that showed NSAID use was the strongest risk factor for PUD complication(19).With regard to smoking, according to our study,70% of the smokers had developed PUD complication and significant association had been observed between smoking and complication which is in line with a Danish study that reported an association between smoking and the risk of perforated peptic ulcer(19).The finding in our study revealed no association between Alcohol and PUD complication. Though there is one Danish study that found that peptic ulcer hemorrhage was significantly associated with alcohol consumption (RR: 2.8; 95% CI: 1.4 5.4) ,there are other studies that fails to show association between alcohol and PUD complication(19, 75, 76)

Psychological stress as seen from documented psychiatric disorder, our study revealed eleven of them had psychological stress, but no significant association with PUD complication. This contradict with few studies done elsewhere that have established that peptic ulcer complications become much more prevalent during periods of natural disaster or societal catastrophe(50, 77).This contradiction can be explained by the limited mental health seeking behavior of our society and lack of applicability of perceived stress scales in clinical practice.

Preceding PPI use in the past 2 months was not shown to be protective of PUD complication. Though there was evidence from other study that showed preceding use of PPI has protective effect against PUD complication, this was not seen in this study(19).the reason behind may be explained by the irregular and per needed use of PPI.

Preexisting Gastroenterology and hepatology disease was seen in 41.7% of participants, the highest percentage accounted for cirrhosis, followed by other hepatobiliary conditions,

cardiovascular disease, diabetes mellitus and malignancy. Among those with cirrhosis, it was observed that duodenal ulcer was the one highly encountered (80%). This contradicts other studies that showed Gastric ulcer as the majority. This needs further study to ascertain. As per this study less than half of those with cirrhosis had complication and no association was found with complications which contradicts with other studies that showed association between cirrhosis and PUD complication(52). This can be explained by the small number of cirrhosis patients in this study.

Though the majority(70%) of PUD patients were said to be asymptomatic, all of our participants in this study were symptomatic(13). This might be explained by the scarcity of endoscopy centers and the patient's presence to referral center after significant clinical complaint. The majority of the participants of our study had abdominal pain as the main clinical complaint. This is in line with other study(14).

Based on the Endoscopic finding, the majority of them had Duodenal ulcer, which is in line with other local and global studies (23, 36). Regarding other endoscopic findings, Esophageal varices were the one highly encountered. This contradicts with other recent local study which was done at Gondar where Gastritis/duodenitis was the one commonly seen. This can be explained by the difference in prevalence of liver disease within this country. This area needs further study and clarification(23).

The finding in our study revealed that 44.8% of them had PUD complication(15). This contradicts with other studies that had lower prevalence of PUD complication. This might be explained by the scarcity of endoscopic centers and medical professionals in nearby hospitals. For this reason patients present lately to referral hospital, where they access better investigation, imaging and management. The most common complication encountered was Bleeding. This goes in line with other studies(78). Age, H. pylori infection and smoking had shown significant association with PUD complications. But unlike other studies NSAID use, Alcohol, ulcer, PPI use and ulcer characteristics didn't show association with PUD complication(19).

7. Conclusion and recommendations

This study revealed that PUD complications are highly prevalent in St. Paul Millennium hospital. Age, smoking habit, and H. pylori infection are significantly associated with the complications of PUD. Much more effort should be undertaken to address PUD before it turns to be complicated. At a facility level effort should be made to make closer follow up and to provide education on lifestyle modification and sanitation of PUD patients at their outpatient visit. Ministry of health should organize Endoscopic centers at general hospital level and avail trainings for healthcare professionals. Further research should be conducted to investigate the association between comorbidity and PUD.

8. Limitations of the study

This is a hospital based Cross sectional study and secondary data were reviewed making generalizability difficult. Though this gap was tried to be filled by collecting missed data by phone and some patients were addressed at their Outpatient department visit, few of them were nonrespondent. There were also lost patient charts which decreased the total number of the study populations. Pertinent finding, ulcer size, was missing on some of the endoscopy report.

9. Strengths of the study

There was no study in Ethiopia which was done on PUD complication, but this study addressed the complications of PUD and its associated factors.

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11. Annex

11.1 Information sheet

Research title

CLINICAL CHARACTERISTICS OF ENDOSCOPICALLY PROVEN PEPTIC ULCER DISEASE AND ASSOCIATED FACTORS OF PUD COMPLICATIONS, A CROSS-SECTIONAL STUDY AT SPHMMC, ADDIS ABABA, ETHIOPIA

Principal investigator: Dr. Eden Muluneh (MD, Internal Medicine Resident)

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Mrs. Frehiwot Worku (BSc, MPH)

Sponsor: St. Paul's Hospital Millennium Medical Collage

11.2 Data collection check list

Card no _____

Date _____ phone no _____

Age(years)	
Sex	1. Male 2. female
Place of residency	1. Urban 2. Rural
H.Pylori	1. positive 2. negative
NSAID use	1. yes → if yes for how long? last use? 2. no
Previous History of PUD	1. yes 2. no
Psychologic stress	1. Yes 2. no
Preeexisting GI disease (cirrhosis, IBD)	1. Yes 2. no
Smoking history	1. yes 2. No
Khat	1. yes 2. No
Alcohol intake	1. Yes 2. no
Preceding PPI use in the past 2 month	1. Yes

	2. no
Presenting clinical symptoms.	1. Abdominal pain 2. Nausea/vomiting 3. Bloating 4. Early satiety provoked by eating 5. Anorexia
Danger sign	1. Bleeding 2. Weight loss 3. Severe pain 4. Anorexia
Comorbidity	1. Hepatobiliary disease,except cirrhosis 2. Cirrhosis 3. Diabetes Mellitus 4. Respiratory 5. HIV 6. cardiovascular 7. neurologic 8. psychiatry 9. malignancy 10. Rheumatologic disease (SLE,RA) 11. Other(specify)_____
Complications	1. Bleeding 2. Perforation 3. Stricture 4. GOO 5. Fistula formation 6. Other(specify)_____
Endoscopy(EGD) finding	1. Ulcer site 2. Ulcer size 3. Bleeding 4. Forrest class (if bleeding) Class 1 Class 2 Class 3 5. other(specify)_____

11.3 Assurance of the investigator

I the undersigned resident agree to accept all responsibilities for the scientific, ethical and technical conduct of the research project and for provision of required progress reports as per terms and conditions of the Research and Publication Directorate and /or Department of Public Health of St. Paul's Hospital Millennium Medical College.

Name of the Resident:_____

Signature:_____

Date: _____

Approval of Advisors

Name of Clinical Advisor:_____

Signature:_____

Date:_____

Name of Public Health Advisor: _____

Signature: _____

Date: _____