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Retrospective Cross-Sectional Survey of Patients Diagnosed with Various Types of Gastro Intestinal Ulcers at Muhimbili National Hospital Gastroenterology Unit: A Call for Strategic *H. pylori* Screening

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Abstract

Background
Peptic ulcer is one of gastrointestinal (GI) disease presenting with dyspeptic symptoms whose cause often overlaps making the etiological diagnosis difficult. Endoscopy remains to be the ideal for identifying organic disease of foregut. *Helicobacter pylori* (*H. pylori*) infection has commonly been associated with most and various upper gastrointestinal pathologies.

Broad Objective
This scholarly cross-sectional study was conducted to determine the association between *H. pylori* infection and peptic ulcer disease in 116 dyspeptic patients who visited Gastroenterology Unit at Muhimbili National Hospital (MNH) in Dar es Salaam located in the eastern coast of Tanzania. The study aimed at obtaining data that could be used as benchmark for future *H. pylori* screening as a preventive measure to control peptic ulcer disease (PUD) in Tanzania.

Methods
The study included all patients with dyspeptic symptoms visiting and/or referred to Gastroenterology Unit from 1st to 30th August 2015. Dyspepsia was defined as persistent or recurrent pain or discomfort in the upper abdomen. Patients diagnosed with PUD within the observation period were verified through medical records. Information on psychosocial factors, medication and symptoms was obtained from a questionnaire completed at study entry. In this study *H. pylori* infection status was determined serologically.

Results
The most commonly identified endoscopic findings were gastritis, which accounted for 44 (37.9%) patients, gastro esophageal disease accounting for 35 (30.2%) patients and peptic ulcer disease in 30 (25.9%) patients. Among patients with peptic ulcer disease, 17 (56.7%) *had H. pylori* infections. The association between peptic ulcer disease and *H. pylori* infection was statistically significant (p-value < 0.001). Neither gastritis nor gastroesophageal reflux disease (GERD) was found to be associated with *H. pylori* infection.

Conclusion
There is a statistically significant association between *H. pylori* and PUD (gastric and duodenal ulcers), a signature to previous reports out of our settings. Our study benchmarks the need for further studies focusing on screening, for early diagnosis and predictions to establish the existing relationships and possible cofounders in these proposed relationships. The increasing number of reported PUD at MNH and presence of *H. pylori* infection warrant studies targeting to investigate the co-existence of these two closely linked GIT conditions for future effective interventions.

Key words: *Peptic Ulcer Disease, GI ulcer types, H. pylori, screening.*

Introduction

Various types of upper gastrointestinal disorders such as gastroduodenitis, PUD, malignancies, esophangitis, parasites infestations and functional dyspepsia can result into upper abdomen discomfort. Despite rarity, Bazaldua and Shneider (1) proposed inclusion of gastric and pancreatic cancers as serious causes of dyspepsia to be necessary.

Peptic ulcer disease (PUD) accounts for 4% of the population globally and about 10% of people develop peptic ulcers at some point in their life (2). Peptic ulcers cause tremendous morbidity and mortality if left un-attended with mortality increasing by age. Despite rarity, perforated peptic ulcer (PPU) for example can be quite life threatening disease with mortality varying from 10%-40% (3). Most patients with PUD die from comorbid illness with these underlying diseases considered to increase the short-term and long-term mortality compared with the standard population (4).

In Africa, perioperative mortality rates from complicated PUD are substantially high, regional and increasing over time despite potential regional differences (5). Infection by *H. pylori* has been ascribed to be the major cause of peptic ulcers with 50 - 80% of gastric (6) and up to 90 -100% of duodenal ulcers resulting from this infection though not the primary cause (7). The pathogen has a characteristic spiral shape, gram-negative bacteria that cause peptic ulcers by damaging the mucosa coating. By doing so, it reduces protection to the lining of stomach and duodenum from corrosive gastric acid and an enzyme pepsin, consequently exacerbating the damage to the lining of gastric mucosa causing ulcerations (8). Prolonged gastritis results due to chronic inflammation (9). Non-steroidal anti-inflammatory drugs (NSAIDs), tobacco smoking, stress due to serious illness, Behcet disease, Zollinger-Ellison syndrome, Crohn disease and liver cirrhosis are among other causes of ulcerations to GIT mucosa (10) although Kim et al (11) suggest differently the link between *H. pylori* and cirrhosis in pathogenesis of PUD. For example, patients with *H. pylori*-negative peptic ulcers who continuously take aspirin or antiplatelet agents are subject to high peptic ulcer bleeding risk than those who do not take any NSAIDS (12).

H. pylori infection can either be diagnosed by invasive test or non-invasive test. The sensitivity, specificity, and predictive values of the available tests for *H. pylori* detection from clinical samples has shown the accuracy order of histology > Rapid Urease Test RUT > serology > stool antigen test (13) which, may vary depending upon the laboratory settings and study population. The choice of test is dependent on the user and expertise.

Invasive test is commonly done using gastroenterological endoscopy. The non-invasive tests include; rapid urease test in which urease enzyme is detected using commercial assay Kits and is said to be the gold standard test. Other tests include histological tests in which the infecting *H. pylori* are identified by staining biopsy specimen. Identification of *H. pylori* can also be achieved through cultures from biopsy specimen in the laboratory. These non-invasive tests, do not involve discomfort that may be experienced during endoscopy. Serology is an immunological test that is also used to detect serum IgG antibodies against *H. pylori* indicative of infection whose importance arise from its potential use in pre-PUD screening as preventive approach (14). Other tests include Breath test that can detect isotopically labeled carbon dioxide in the breath of *H. pylori* positive individual after ingestion of 13C or C14 labeled urea. Stool antigen test is another immunological assay for *H. pylori* infection which is non-invasive, user friendly and quick to obtain results.

In Tanzania Mbulaiteye et al (15) reported a variable prevalence in *H. pylori* with children in their earlier age (0 – 4 years) reporting relatively lower prevalence (76%) compared to the rising to 99% for those relatively older (near eighteen and above years). This is because of increased exposure to various infection sources with increase in age hence the ultimate rate of infection. Aitila et al. (16) reported the rate of infection to be higher in school going children becoming even higher in children who attend schools in crowding environment with no or poor sanitary facilities associated with lack of clean drinking waters. In relatively younger ages (1 – 4 years), the major source of infection is person to person from parents, other family members or care givers whose infection might be limited while control of hygiene is also more stringent.

Seroprevalence as a screening tool might play a great role in surveillance and identification of infected but asymptomatic patients who remains reservoirs worldwide. Although Logan et al (17) proposed a set of medications in an attempt to eradicate Helicobacter infection in endemic areas, the high prevalence of *H. pylori* among dyspeptic patients in Tanzania (18), can be controlled through community-focused education on the safe use of drinking water which is potential source of infection (18). Our study aimed at evaluating the overall magnitude of the problem in the country with a focus on reported cases at Gastroenterology unit at MNH as a startup case. The idea is to propose for a proper and best approach in intervention strategy that might include countrywide regular *H. pylori* screening programs.

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Methods

Study area

This descriptive retrospective cross-sectional study was conducted at the Department of Internal Medicine, Gastroenterology Unit of the Muhimbili National hospital (MNH). The hospital is a renowned referral, research and medical teaching hospital, located in Dar es Salaam in the eastern coast of Tanzania. The hospital caters for referral cases from eastern zone and other parts of Tanzania attending 1,000 to 1,200 outpatients per week and admitting 1,000 to 1,200 inpatients per day. It has 29 departments and an official capacity of 1500 beds of which 210 beds are committed to the Department of Internal Medicine. There is an endoscopy unit within the department where this study was particularly done. The study included all patients with dyspeptic symptoms visiting and/or referred to Gastro Unit from 1st to 30th August 2015.

Sampling Strategy and Data Collection

All patients with dyspeptic symptoms were purposively included into the study. Data were collected from register book in gastro unit until when sufficient number of patients' data was obtained based on the calculated sample size of 116 patients. These included all patients with dyspeptic symptoms visiting and or referred to Gastroenterology Unit from 1st to 30th August 2015. Data collection forms were pre-tested first before were used for data collection.

Ethical Consideration

Ethical approval to undertake this study was granted by the MUHAS Senate Research and Publications Committee. Permission to conduct the study was obtained from the head of Gastroenterology Unit under MNH Guidelines for conducting research. Patient's confidentiality was observed as patients' coded numbers were used and not names.

Data processing and analysis

The data were entered and analyzed using computer based Statistical Package for Social Sciences (SPSS version 20.0. SPSS Inc., Chicago, IL, USA). Cross-tabulation was used to establish association of different variables. Categorical variables were compared using Chi-Square (χ^2) where differences with *p*-values <0.05 were considered statistically significant.

Results

This study was carried in a population that included patients with presenting symptoms and signs of peptic ulcer disease visiting the Gatroenterology Unit at MNH, the oldest and major referral hospital in the country that handles majority of complicated cases all over the country. During the study period, 116 patients underwent endoscopy due to dyspepsia. The female to male ratio was nearly 1 to 1 with the age ranging from 17 (minimum) to 81 years (maximum). The mean age was 45.89 years and the median age was 43 years. Most of the study subjects clustered in the age between 26 and 60 years with the mode of 31 years with the age of recruited patients normally distributed.

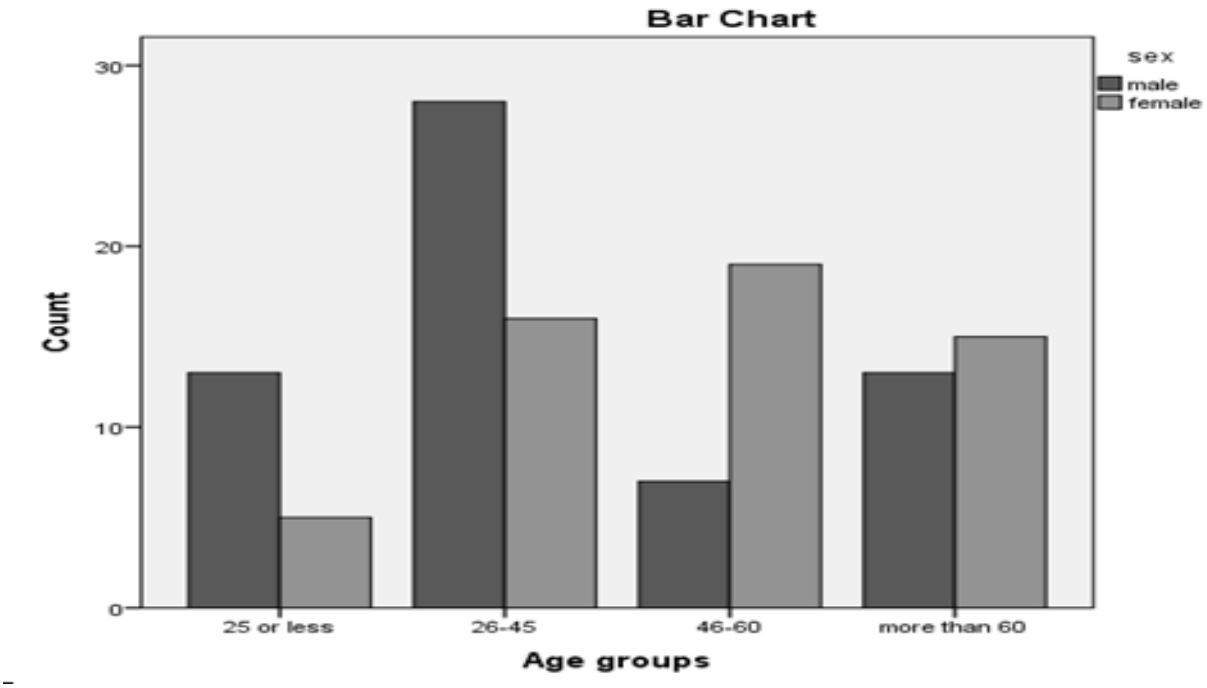

Figure 1: Age and sex distribution of patients with dyspepsia

The results (Figure 1) above show that most of patients with dyspeptic symptoms were males in the age group ≤ 25 and age group 26-45 while more females with the disease condition were found in the relatively older age group of 46-60 years and above. The difference in dyspeptic symptoms by sex seems to be statistically significant in all age ranges upto and including 60 years old patients ($p \leq 0.05$) with insignificant differences in patients older than 60 years of age ($p \geq 0.05$).

Presenting symptoms and signs

The clinical symptoms and signs in patients from this study are summarized in Table 1. Epigastric pain was reported by 82 (70.7%) of patients with dyspepsia with other presenting symptoms such as nausea which accounted for 60.3% of the reported cases. Heartburn accounted for 45.7% of cases while belching and early satiety accounted for 31.0% and 12.1%, respectively. Constipation was reported in among 5.2% cases. Patients reported duration of symptom to range from 3 months to 62 months.

Table 1: Various presenting symptoms and clinical manifestation of patients with dyspepsia

Symptoms	Number	Percent
Epigastric pain	82	70.7
Nausea	70	60.3
Heartburn	53	45.7
Belching	36	31.0
Early satiety	14	12.1
Constipation	6	5.2

Endoscopic findings

Endoscopic examination by a team of gastroenterologists revealed that all 116 subjects to have abnormal endoscopic findings. The most commonly identified endoscopic finding were gastritis seen in 44 (37.9%) patients, gastro esophageal disease in 35 (30.2%) patient and peptic ulcer (duodenal and gastric ulcer) disease in 30 (25.9%) patients (Table 2).

Table 2: Distribution of endoscopic finding in patients with dyspepsia

Endoscopic diagnosis	Number	Percent
Gastritis	44	37.9
GERD	35	30.2
Gastric ulcer	16	13.8
Duodenal ulcer	14	12.7
Others	7	6

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Distribution of dyspeptic symptoms in peptic ulcer disease H. pylori-infected patients

The distribution of dyspeptic symptoms in peptic ulcer patients who also had *H. pylori* infection is shown in Table 3. Among patients with peptic ulcer disease 17 (43.6%) of the 39 subjects had *H. pylori* infections. Majority of patients presented with more than one symptom and the most commonly identified symptoms in these patients were epigastric pain 16 (41.1%) patients, nausea in 10 (25.6%), heartburn 8 (20.5%) and belching in 5 (12.8%) of patients.

Table 3: Distribution of dyspeptic symptoms in peptic ulcer patients with positive H. pylori serology

Symptoms	**Number**	**Percent %)**
Epigastric pain	16	41.1
Nausea	10	25.6
Heartburn	8	20.5
Belching	5	12.8
Total	**39**	**100**

Association between H. pylori infection and peptic ulcer disease (PUD)

The association between *H. pylori* and PUD is presented in **Table 4.** Endoscopic results revealed a strong association between *H. pylori* infection with gastric ulcers and duodenal ulcers ($p < 0.001$). Gastritis and GERD results from endoscopy showed lack of association with *H. pylori* infection, a reflection that other factors than infection in association with this conditions in which *H. pylori* infection was determined serologically.

Table 4: Association between *H. pylori* exposure and peptic ulcer disease (PUD)

		Endoscopic Findings						
		Gastric Ulcers	GERD	Gastritis	Duodenal Ulcers	Others	Total	
H. pylori status	+ve	16	0	0	14	0	30	$p < 0.001$
	-ve	0	35	44	0	7	86	
Total		**16**	**35**	**44**	**14**	**7**	**116**	

Discussion

The present elective study assessed the various dyspeptic symptoms in association with PUD. In this study which considered, among other factors, age and sex, it was found that patients with dyspeptic symptoms were mostly males in the age group ≤ 25 and age group 26-45 years while most females with the disease condition were in the relatively older age group (46-60 years and above). The results, further showed the difference in dyspeptic symptoms by sex to be statistically significant in all age ranges upto and including 60 years old patients ($p \leq 0.05$) with insignificant differences in respect of disease in patients older than 60 years of age ($p \geq 0.05$). This implies that males aged 45 years or younger are more prone to PUD with the shift in susceptibility starting from the age beyond 45 years where females become more prone to the disease condition. The high prevalence of *H. pylorii* in relatively younger populations than older ones (19) may explain for more dyspeptic symptoms reported in young males aged < 25 years. A study by Kim et al (20) further explains the increased risk for PUD in older females than men ascribed to nutritional component. The findings also reveal that PUD might be more a disease of young males and old females for similar reasons! Our observation and experience may also support the higher prevalence in young males, particularly unmarried due to habitual long day stay without eating compared to females. Gastrointestinal ulcers are said to be associated with potentially lengthy empty stomach that trigger secretion of acidic gatric juice that correde the gastric mucosa to cause ulcers. Anand (21) however, proposed a contrverse in prevalence of PUD with a shift from predominance in males to similar occurrences in males and females with age trends. In their reports, the ulcer occurrence revealed a decline in rates of PUD for younger men, particularly for duodenal ulcer, and increasing rates in older women. This is more ulcer-type specific inclined than general (22, 23).

Different studies have shown that duodenal ulcers are most common in the age group of 45 and above and are twice as common in men as in women, while gastric ulcers become more common with age and affect women more or less equally (24). The trends have reflected a complex change in the risk factors for PUD, including age-cohort phenomena with the prevalence of *H. pylori* infection and the use of nonsteroidal anti-inflammatory drugs (NSAIDs) in older populations (21). The most attractive explanation could however be that men exhibit higher parietal cell mass and consequently greater level of acid secretion in comparison to women regardless to the proposed shift. The hypothesis as to the etiology for

the increasing occurrence of disease in women has been raised that includes psychological factors (25-28).

Evaluation of dyspepsia in this study found that gastritis (37.1%), gastro esophageal reflux disease (30.1%) and peptic ulcer (25.9%) were the commonest cause of dyspepsia. Similarly, Mbulaiteye et al. (15) reported gastritis, gastro esophageal reflux disease and peptic ulcer to be common causes of dyspepsia in northern Tanzania. The corresponding results could explain similarity in factors leading to dyspepsia in a given population, which could be ascribed to similar sociodemographic characteristics in similar populations. In such situations it is no uncommon that people will have similar lifestyles, feeding and feeding habits, types of food and common environment in general. The common causes of dyspepsia in most population include acid reflux, gastroesophageal reflux (GER), or gastroesophageal reflux disease (GERD), irritable bowel syndrome, infection (*H. pylori*) gastroparesis, gastrointestinal ulcers, stomach cancer and gastritis. These all condition are common in our population and can singly or in combination cause and influence the course of dyspepsia. Evaluation and management of dyspepsia has been largely achieved through focusing into identification and treatment these potential underlying causes (29). However, special attention should be taken with elderly due to potentially increased risk of drug interactions and poor compliance (30).

In this study most of the cases of PUD were clustered around mean age of 45 years. Similar results were reported by Tijjani and Umar (31) who reported a mean age of 37.9 years, the age that is close to the age range obtained in our study. This study found a male to female ratio of nearly 1:1 in proportion of PUD indicative of equitable susceptibility, with skewedness dependent on ulcer type. According to reports, duodenal ulcers are twice as common in men as in women and 1.5 times as common as gastric ulcers (32). A collection of etiological theories, characteristics, and observations of peptic ulcers has been established from existing data (33). Despite moderate genetic influence for liability to peptic ulcer disease (34), variable predisposition in PUD between males and female is reported with peak incidence is in the 40s for men and in the 50s to 60s for women (19, 32). We found similar trend in our present study (Figure 1). The magnitude of male preponderance in 40s could probably be explained by the fact that males are more aggressive and predisposed to the risk behavior for PUD than females. The variability fades as the age goes beyond 60s where the susceptibility nears each other (21).

The risk for *H. pylori* infection may vary between rural and urban areas depending on exposure and exposure patterns. Our study, showed that despite the majority of patients (75%) resided in urban areas compared to referred cases from upland (25%), there was no statistically significant difference between the area of residence and *H. pylori* infections (p=0.293). Different findings were reported by Contreras et al (35) ascribing low hygienic standards rural areas to be important factor for the higher prevalence of *H. pylori* infection than is for urban dwellers. Jaka and colleagues (18) insisted on drinking of safe water in order to minimize *H. pylori* infections as a measure of control in their study in Tanzanian population. Studies in children (36), adolescents and adults (16, 37, 38)) and breast feeding (39) have detailed on the epidemiology and risk factors to further emphasize on higher education (38) to be protective against *H. pylori* infection. Despite commonality the risk factors have however varied regionally (40-42) more so with prevailing socioeconomic differences in amongst communities (43).

In this study majority of patients with PUD experienced epigastric pain (70.7%), 60.3% had nausea, 45.7% had heart burn 31% had frequent belching, 12.1% had early satiety and 5.2% constipation (Table 1). It was also noted that 4.3% of patients had used eradication therapy with duration of symptom ranging from 3 months to 62 months. These findings are comparable to study done by Mbulaiteye et al (15), who reported nearly similar findings but slightly lower than what was reported for epigastric pain of 86.1%. Studies have also revealed, although not specific (44), epigastric discomfort (specifically, pain relieved by food intake or antacids and pain more frequently awakening at night or that occurs between meals) to be critical symptom in PUD (45-48). This pain has been described as a gnawing pain, and it may come and go (45-47, 51). Other associated symptoms and including warning symptoms for prompt urgent referral are also well documented (47). The duration of symptoms reported in our study is over two-folds compared to what was reported by Mbulaiteye et al (15) of 2 months to 2 years. The difference and similarities can probably be explained by lack of enough education, difference in income and access to clinic for early and perfect medical attention. Santos et al (43) emphasized on socioeconomic differences, despite ethnicity to significantly influence *H. pylori* infection which is consequently, a part and parcel of peptic ulcer disease.

The distribution of dyspeptic symptoms in peptic ulcers patients (Table 3) revealed that among patients with peptic ulcer (n= 30), 17 (56.7%) of the subjects had *H. pylori* infection.

The most commonly identified symptoms in these patients is epigastric pain 16 (94.1%) patients, nausea in 10 (58.8%), heartburn 8 (47.1%) and belching in 5 (29.4%). Most people with *H. pylori* predominantly do not have any symptoms or have tolerable symptoms (49, 50).

Serological detection of PUD in 30 patients (Table 4) revealed 16 (53.3%) to be serologically positive for *H. pylori* infection with gastric ulcers and 14 (46.7%) with duodenal ulcers. Despite insignificant association between *H. pylori* infection and GERD, gastritis and other conditions associated with PUD, the infection was significantly associated with gastric and duodenal ulcers ($p < 0.001$). These results are concordant with results from other studies that revealed existence of association between *H. pylori* and PUD (52-56). Reports also show strain specificity in virulence and causation of the disease (55-57). Together with non-steroidal anti-inflammatory drugs (NSAIDs), *H. pylori* infection are said to be the most common causes of PUD (58) through disruption of mucosal lining in the stomach and duodenum is due to gastric secretions and infection by *H. pylori* (59).

Limitations of the study

From our study we can highlight two main limitations: This study was hospital-based encompassing a single hospital of Muhimbili, therefore the results from this study may not show a complete diversification of PUD which may be present in the whole or at least most parts of the country as most of the cases at MNH are referral. In this study, only patients with peptic ulcer were tested for *H. pylori.* A clear picture could be obtained from anonymous screening of larger groups of diverse populations and destiny to real reflect the general population, potential ethnic difference and strain variations in virulence and severity of consequences.

Conclusion

This study has shown that gastritis, gastro-oesophangeal reflux disease and peptic ulcer are the common etiologies for dyspepsia. *H. pylori* infection is mostly associated with gastric ulcer and duodenal ulcers with unlikeliness for association with other conditions such as GERD and gastritis. A community-based survey that involves screening for *H. pylori* can be useful to limit the impact on PUD and thus create awareness to the community on the importance of early screening for this disturbing but otherwise preventable disease.

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Authors' Contributions

AHM conceived of the study and participated in revising the draft manuscript critically for important intellectual content prior to submission. EVM conception of the study; designing the study and drafting of this manuscript, revising it critically for important intellectual content before submission. AGM conceived of the study, participated in its design, conducted the research; entered the collected relevant data in SPSS for analysis and interpretation for its scientific meaning. OVN participated in revising the draft manuscript critically for important intellectual content prior to submission. All authors read and approved the final draft manuscript for submission.

Conflict of Interest

Authors declare no conflict of interest.

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