

## Upper gastrointestinal endoscopic findings and prevalence of *Helicobacter pylori* infection among adult patients with dyspepsia in northern Tanzania

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**Abstract:** Dyspepsia is a common presenting complaint of various upper gastrointestinal disorders. The symptoms of causes of dyspepsia often overlap and this makes etiological diagnosis difficult. Endoscopy is the ideal procedure for identifying organic diseases of the foregut. *Helicobacter pylori* infection is associated with various upper gastrointestinal pathologies. A cross-sectional study was conducted to determine endoscopic findings and *H. pylori* status in two hundred and eight consecutive dyspeptic adult patients between June 2009 and April 2010 at Kilimanjaro Christian medical Centre, a referral and teaching hospital in northern Tanzania. The most commonly identified endoscopic findings were gastritis (61.10%), Gastroesophageal reflux disease (GERD) (57%), and Peptic ulcer disease (PUD) (24.1%). Gastric cancer was identified in 6.7 % of patients and all of them were aged 40 years and above ( $p=0.00$ ). *H. pylori* infection was detected in 65% ( $n=130$ ) of patients. *H. pylori* infection was present in 57% ( $n=24$ ) of patients who were tested within six months after eradication therapy. Gastritis and duodenal ulcer were statistically significantly associated with *H. pylori* ( $p<0.001$ ). No association was found between GERD and *H. pylori* infection ( $p>0.05$ ). Gastritis, GERD, and PUD are the leading causes of dyspepsia. *H. pylori* infection is present in significant proportion of dyspeptic patients. Patients with Gastritis and PUD should undergo empirical eradication therapy if a confirmatory test is not available. Patients with dyspepsia who are over 40 years of age should undergo Endoscopy (EGD) for initial work up. Study on antimicrobial susceptibility pattern of *H. pylori* is recommended to guide choices for evidence based treatment option.

**Keywords:** endoscopy, dyspepsia, *Helicobacter pylori*, gastrointestinal tract, Tanzania

### Introduction

Dyspepsia is a common presenting complaint of various upper gastrointestinal disorders. The causes of dyspepsia are many and the major ones include gastroduodenitis, PUD, malignancies, esophagitis, parasitic infestations, and functional dyspepsia. The distribution of these upper gastrointestinal lesions varies significantly in different countries and within geographic locations in the same nation (Tytgat, 2002; Kibiki et al., 2006). Furthermore, symptoms of these causes often overlap and this makes etiological diagnosis difficult. Endoscopy is the ideal procedure for identifying organic diseases of the foregut, but this service is yet to be widely available in developing countries including Tanzania. *H. pylori* infection is known to be among the most common human infections worldwide; approximately 50% of the world's population is infected with *H. pylori* (Brown, 2000; Go, 2002). *H. pylori* infection is associated with various upper gastrointestinal pathologies such as gastritis, peptic ulcers and gastric cancer (Graham, 1994; Blaser, 1995; Go, 2002; Marshall & Winsdor, 2005). Because of the strong association between this gram negative bacterium infection and gastrointestinal diseases and its high prevalence rate in developing countries (Suerbaum & Michetti 2002; Frenck & Clemens, 2003; Kazuo et al., 2004; Xia et al., 2005; Tkachenko et al., 2007; Kate et al., 2009), *H. pylori* infection is among the leading gastroenterological public health problems in developing countries (Kate et al., 2009).

*H. pylori* infection can be diagnosed either by invasive tests which require endoscopy and gastric biopsy (e.g., rapid urease test) or by noninvasive tests (e.g. urea breathe test). The choice of

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test depends to a large extent on availability and cost. Other important factors are: clinical situation, population prevalence of infection, pretest probability of infection, differences in test performance, and factors that may influence the test results, such as the use of anti-secretory treatment and antibiotics. The gold standard (endoscopy with rapid urease testing) is not readily available in all parts of the world. In some regions where *H. pylori* prevalence is very high, diagnostic tests for the infection are not cost-effective and the decision to treat must then assume the presence of the infection. In low-resource communities, considerations of precision and sensitivity may sometimes be traded against costs and the availability of resources. Therefore, it is recommended to do empirical eradication therapy than do nothing (World Gastroenterology Organization Guidelines, 2010; Jemilohun *et al.*, 2013). Eradication therapy heals peptic ulcers, prevent relapses and thus cure the disease in most patients (Hopkins *et al.*, 1996; Gaby, 2001; Yi-Chia *et al.*, 2008). Some studies suggest eradication of the organism reverses some low-grade mucosal associated lymphoid tissue (MALT) lymphomas of the stomach (Stolte *et al.*, 2002; Fischbach *et al.*, 2004) and early treatment of *H. pylori* infection before the development of gastric atrophy or intestinal metaplasia prevents the development of gastric cancer (Yi-Chia *et al.*, 2008).

An optimal diagnostic approach to patients with dyspepsia continues to be debated and there is no single algorithm that would be applicable in all geographic settings. In resource limited settings, especially when access to endoscopy service and tests for *H. pylori* are limited, it is very important for clinicians to know common causes of dyspepsia and frequency of *H. pylori* infection. Thus, the aim of this study is to determine the common upper gastrointestinal lesions and the prevalence of *H. pylori* infection among dyspeptic patients. This study would assist clinicians in choosing an optimal diagnostic and management approach to dyspeptic patients in our setting and similar institutions. It will also contribute evidence for development of a guideline for the management of dyspepsia and provide valuable information for similar studies in the future.

## Materials and Methods

### Study area

This cross-sectional study was conducted at the Department of Internal Medicine of Kilimanjaro Christian Medical Centre (KCMC). KCMC is a referral, research and teaching hospital, located in Moshi in northern Tanzania. The hospital caters for northern and central zones of Tanzania and has the catchment population of over 15 million. The hospital has 25 clinical departments and an official capacity of 450 beds of which 88 beds are committed to the department of internal medicine. There is an endoscopy unit within the department.

### Study design and data collection

Consecutive 208 patients ( $\geq 13$  years) with dyspeptic symptoms who presented to out-patient medical clinic or admitted to hospital or referred for endoscopy between June 2009 and April 2010 were recruited to participate in the study. Only patients who signed informed written consent and who had at least one of the following three symptoms; epigastric pain or burning, early satiety and postprandial fullness and who had no contraindications to undergo EGD were included. The study was approved by the institution's research and ethics committee. Upper GI endoscopy was performed by experienced endoscopist using video endoscope Olympus-exera 160 series and findings were coded and documented on standardized data collection sheet. Antral biopsy was taken from the lesser or greater curvature of the stomach and rapid urease test (CLOTest®) was performed to test for *H. pylori* infection. In selected cases such as suspected malignancy, at least 4 biopsy specimens were preserved in 10% formalin, labeled appropriately and dispatched for histological examination by a histopathologist.

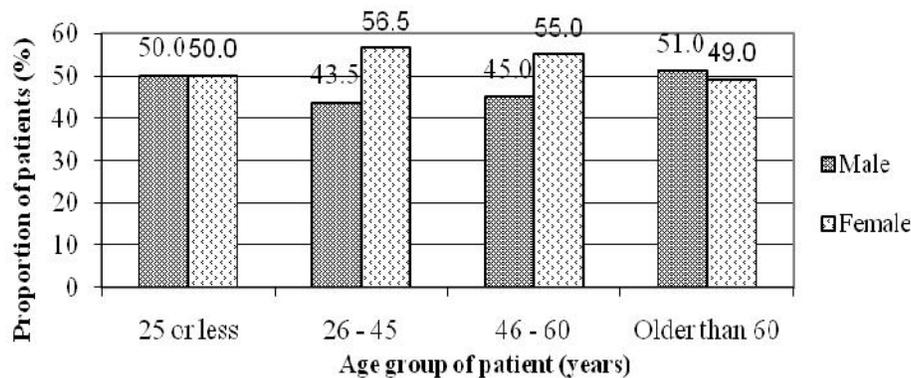
### Data analysis

Data was analyzed using SPSS version 15. Chi-square test was used to test the association between variables and a p value of  $\leq 0.05$  was considered indicative of statistically significant difference. The likelihood of occurrence of events was tested by odds ratio at 95% confidence level.

### Results

#### Characteristics of the study population and presenting symptoms and signs

During the study period, 208 patients underwent endoscopy due to dyspepsia. The female to male ratio was 1.1 to 1. The age range (median) was 13 to 95 (48) years.



**Figure 1: Age and sex distribution of patients with dyspepsia (n=208)**

Epigastric pain was reported by 179 (86.1%) of patients with dyspepsia. Other presenting symptoms were heart burn (58.2%), nausea (46.6%), and early satiety (41.3%). Duration of symptoms ranged from 2 days to 20 years. Epigastric tenderness was elicited in 57 (27.4%) patients.

**Table 1: Distribution of endoscopic findings in patients with dyspepsia (N=208) (Some patients had two or more endoscopic findings).**

Endoscopic diagnosis	Number	Percent
Gastritis	127	61.1
Gastroesophageal reflux disease	122	58.7
Duodenal ulcer	38	18.3
Duodenitis	32	15.4
Sliding Hiatus hernia	14	6.7
Gastric cancer	14	6.7
Gastric ulcer	12	5.8
Esophageal cancer	4	1.9
Other	9	4.3
Normal	12	5.8

#### Endoscopic findings

When examined by EGD, 196 (94.2%) of the 208 subjects had abnormal endoscopic findings. The most commonly identified endoscopic findings were gastritis seen in 127 (61.10 %) patients, Gastroesophageal reflux disease (GERD) in 122 (58.7%) patients, and peptic ulcer (duodenal and gastric

ulcer) disease in 50 (24.1%) patients. Histologically confirmed gastric cancer was diagnosed in 14 (6.7%) patients with dyspepsia and all patients with Gastric cancer were aged 40 years and above. The association of age above 40 years and gastric cancer was statistically significant ( $p < 0.0001$ ) (Table 1).

### Frequency of *H. pylori* Infection among Patients with Dyspepsia

Rapid Urease Test (RUT) was done to 205 patients but the test was inconclusive in 5 patients and therefore these were excluded from analysis. In three out of 208 patients, biopsy was contraindicated on medical grounds such as bleeding diathesis. Of the remaining 200 patients, 130 (65.0%) had positive RUT result indicating *H. pylori* infection. Among the 200 patients, 42 (21.0%) reported that they had undergone *H. pylori* eradication therapy (within the past 6 months from the date of examination) for a median duration of 10 days. The regimens used for eradication were combination of proton pump inhibitors with Nitroimidazole and Amoxicillin (43%), or Nitroimidazole and Macrolides (33%), or Macrolides and Amoxicillin (11%), or various combinations of the above with doxycycline (13%). Of these 42 patients, 24 (57.1%) had positive RUT results. There was no significant difference in RUT results of patients who underwent eradication therapy and who did not ( $p = 0.230$ ) (Figure 2).

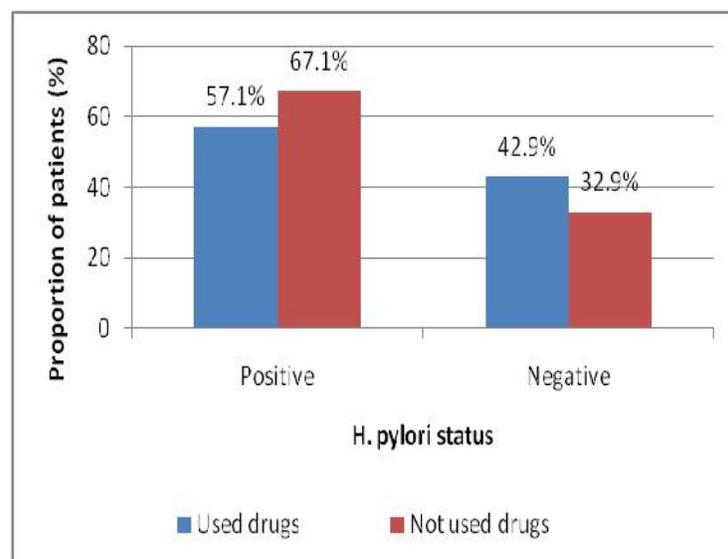


Figure 2: Relationship between use of eradication therapy and RUT results (n=200)

Out of 127 patients with Gastritis, 94 (72%) were positive for *H. pylori* infection. The presence of Gastritis was statistically significantly associated with diagnosis of *H. pylori* infection (OR, 2.9, 95% CI 1.6-5.4,  $p < 0.001$ ). Among 38 patients with duodenal ulcer, 34 (89.5%) were infected with *H. pylori* and the association between presence of duodenal ulcer and *H. pylori* infection was statistically significant (OR, 5.8; 95% CI, 1.98-17.25,  $p < 0.001$ ). However, *H. pylori* infection was not significantly associated with GERD, gastric ulcer and gastric cancer ( $p > 0.05$ ) (Table 2).

**Table 2: Relationship between upper gastro-intestinal lesions and *H. pylori* infection among patients with dyspepsia (N=200)**

Endoscopic findings	<i>H. pylori</i> status		Total N (%)	P-value	OR (95% CI)
	Positive (N=130) N (%)	Negative (N=70) N (%)			
Gastritis	94 (72)	33 (28)	127(63.5)	<0.001	2.9 (1.60-5.37)
Gastro-esophageal reflux disease	81 (66)	41 (44)	122(58.7)	0.605	1.2 (0.65-2.12)
Duodenal ulcer	34 (89)	4 (11)	38(19)	<0.001	5.8(1.98-17.25)
Duodenitis	22 (69)	10 (31)	32(16)	0.627	1.2 (0.54-2.75)
Gastric cancer	8 (58)	6 (42)	14(7)	0.523	0.7 (0.23-2.10)
Esophageal candidiasis	8 (62)	5 (48)	13(6.5)	0.787	0.9 (0.27-2.71)
Gastric ulcer	6 (50)	6 (50)	12(6)	0.261	0.5 (0.16-1.66)

## Discussion

In resource limited settings, especially when access to endoscopy service is limited, it is very important for clinicians to know common causes of dyspepsia and frequency of *H. pylori* infection. In our study, most of the dyspeptic patients had organic causes which were diagnosed with endoscopy. This is consistent with the findings of the studies done in Ethiopia (Asrat *et al.*, 2004) and Nigeria (Mustafa *et al.*, 2007) where organic causes of dyspepsia were documented in 96.4% and 82.1% of dyspeptic patients, respectively. However, our finding differs from that of (Tytgat *et al.* 2002) where meta-analysis of 22 studies from the developed countries showed abnormal endoscopic findings in only 51% of dyspeptic patients. The differences may be attributed to how patients were selected and in the inclusion and exclusion criteria used in different studies (Marshall & Winsdor, 2005), differences in socioeconomic status, and health care seeking behavior.

Gastritis and peptic ulcer diseases were found to be common causes of morbidity in Tanzanian patients. Moreover, this study also demonstrated the expected relationship between duodenal ulcer and *H. pylori* infection as reported in other studies from Africa and elsewhere (Ogotu *et al.*, 1998; Ndububa *et al.*, 2001; Suerbaum & Michetti, 2002; Asrat *et al.*, 2004; Mustafa *et al.*, 2007;). There is ample evidence regarding the beneficial role of *H. pylori* eradication therapy in patients with PUD and gastritis (Hopkins *et al.*, 1996; Gaby, 2001; Yi-Chia *et al.*, 2008). Thus, clinicians should test and treat for the infection if resources are available. In resource poor settings where confirmatory test is not available or may not be cost-effective, empirical therapy is recommended (World Gastroenterology Guidelines, 2010).

The association between *H. pylori* infection and gastric ulcer and gastric cancer was not statistically significant. This is likely due to small number of patients with gastric ulcer and cancer in this study. Slightly over half of the patients with dyspepsia had endoscopic evidence of GERD in our study. This is consistent with the findings of (Mustafa *et al.*, 2007) from Nigeria who reported esophagitis in two-thirds of dyspeptic patients. However, earlier studies from Ethiopia (Asrat *et al.*, 2004) and Kenya (Ogotu *et al.*, 1998) reported GERD in only 1% and 4.2% of dyspeptic patients respectively. An increase in prevalence of GERD has been reported from developed countries (Pandolifino *et al.*, 2004). Our findings could be an indicator of change in pattern of upper GI diseases in Tanzania which is similar to trends reported from Kenya (Hudson *et al.*, 2005) and Asian countries (Ho *et al.*, 2005; Lim *et al.*, 2005). Possible contributing factors for the increase in frequency of GERD include rising obesity rates, increasing life span, change of food habits, and consumption of medications affecting esophageal function and improving health seeking behavior.

Upper GI malignancies were identified in 8.6% of the dyspeptic patients. Of these, gastric cancer and distal esophageal cancer were identified in 6.7% and 1.9% patients respectively. Gastric

cancer was found only in patients aged 40 years and above and this difference was statistically significant. The frequency of Gastric cancer in the present study is consistent with the findings of Ogotu *et al.*, 1998, from Kenya but higher than other reported from other studies in Africa (Asrat *et al.*, 2004; Mustafa *et al.*, 2007) and other studies from developed countries (Tytgat, 2002). This may be attributed to mountainous nature of the study site where risk of gastric cancer was reported to be high due to lack of trace minerals in volcanic soils (Bourdenx *et al.*, 1983). It may also be due to differences in genotypes of *H. pylori* which are more carcinogenic (Axon, 1999).

In this study about two-thirds of the dyspeptic patients had *H. pylori* infection. This is lower compared to findings of a previous study in Tanzania (Kazuo *et al.*, 2004) and other studies from elsewhere in Africa (Ogotu *et al.*, 1998; Ndububa *et al.*, 2001; Asrat *et al.*, 2004; Oladejo *et al.*, 2004; Mustafa *et al.*, 2007). This lower prevalence of the infection is probably due to improvements in sanitation and water supply over the past decades as well as increased awareness and the widespread use of antibiotic therapy. Despite several reports suggesting decreasing prevalence of the infection (Rothenbacher & Brenner, 2003; Xia *et al.*, 2005; Tkachenko *et al.*, 2007; Kate *et al.*, 2009) clinicians working in developing countries should still consider *H. pylori* as important etiologic agent.

We found that more than half of patients who underwent RUT after receiving the commonly used eradication regimen ('Triple therapy') still had the infection. Interpretation of this finding is limited by the small number of patients, lack of sensitivity testing and difficult of assessing medication compliance. Conversely, this observation would be of immense concern as resistance of *H. pylori* to antibiotics is increasingly being reported worldwide. For instance, Metronidazole (the most frequently used drug by our patients), is also used to treat common parasitic and anaerobic bacterial infections; often empirically. Accordingly, studies from India and Senegal documented *H. pylori* resistance to metronidazole (Datta *et al.*, 2005; Seck *et al.*, 2009). Thus, the concern and uncertainty about our observation requires elaboration by further studies to evaluate the prevalence of *H. pylori* resistance to commonly used antimicrobial agents.

In conclusion, the present study confirms that gastro-duodenitis, peptic ulcer disease, GERD, and gastric cancer are the most common aetiologies of dyspepsia. *H. pylori* infection is still present in significant proportion of dyspeptic patients. It is also important to note the high prevalence of GERD. In view of the high frequency of gastric cancer we recommend EGD for initial work up of dyspeptic patients over 40 years of age. Due to presence of *H. pylori* infection in significant number of patients who completed eradication therapy, further studies on susceptibility pattern of *H. pylori* are needed to guide clinicians' choice for evidence based eradication regimens.

### Competing interests

The authors declare that they have no competing interests.

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