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ORIGINAL ARTICLE

Prevalence of *Helicobacter pylori* infection and the incidence of the associated malignant and peptic ulcer disease (PUD) at Nelson Mandela Academic Hospital: a retrospective analysis

Stephen Z. Molaoa

Walter Sisulu University and Nelson Mandela Academic Hospital, Department of Surgery, and Department of Health Studies, University of South Africa, Mthatha, South Africa

ABSTRACT

Background: *H. pylori* infection is associated with both benign and malignant gastrointestinal diseases. However, no studies have been conducted locally describing the prevalence of *H. pylori* and its associated GIT diseases. The objectives of this study are to determine the prevalence of *H. pylori*, and the incidence of PUD and gastric malignancies among patients who are infected with *H. pylori* or who have the stigmata of previous exposure to *H. pylori*.

Material and methods: Data was collected retrospectively from files of adult patients with upper gastro-intestinal symptoms from January to December, 2012. The gastric mucosal biopsy specimens were analyzed for the presence of *H. pylori*, chronic gastritis, PUD, and gastric malignancies.

Results: Of 156 records there were 70 (45%) males and 86 (55%) females, with a median age of 56.5. The prevalence of *H. pylori* was 54.5%; 95% of 156 had chronic gastritis (CG). Ninety-sever percent of the 85 *H. pylori* positive and 93% of the 71 *H. pylori* negative patients had CG. However, the difference was not statistically significant (97% vs 93%, $p = 0.322$). The incidence of PUD was 16% and 10 (6.4%) had gastric malignancies, of which four (2.7%) and three (2%) were antral intestinal-type and proximal diffuse types, respectively. Three (2%) had gastric MALT lymphoma. The risk of both gastric malignancies and PUD was demonstrated to increase with advancing age.

Discussion and conclusion: The prevalence of *H. pylori* was equivalent to the global prevalence; however, high prevalence of CG may be indicative of high local infection rate. The incidence of *H. pylori* and/or chronic gastritis-associated intestinal-type gastric adenocarcinoma, MALT lymphoma, and PUD is equivalent to that reported globally. Advancing age and active *H. pylori* infection or stigmata of past exposure thereto are associated with increased risk of peptic ulcers and malignant gastric diseases.

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H. pylori; peptic ulcer disease; gastric cancer; MALT lymphoma; chronic atrophic gastritis

Background

It is estimated that more than 50% of the world population is infected with *H. pylori,* with a remarkable variation in the prevalence among countries, and within different regions of the same country[1–3]. Africa, a third world continent, has the highest number of people harboring *H. pylori*, ranging from 87% prevalence in South Africa[4], to 91% in Nigeria[5]. This contrasts with the prevalence of 30–50% among affluent Western European adults, and 23% among a Canadian 50–80-years age group[3,6].

Interest in *H. pylori* resulted from its association with a variety of gastrointestinal conditions, ranging from benign to malignant diseases. Peptic ulcer disease is strongly related to chronic *H. pylori* infection[3,7]. Data from the developed world has shown that in the first decade of the discovery of *H. pylori*, 95% of duodenal ulcers, and 85% of gastric ulcers were associated with *H. pylori* infection and that lifetime risk of developing peptic ulcer disease (PUD) was 3–10-times higher in *H. pylori* positive subjects than in their *H. pylori* negative counterparts[8]. A decline in the incidence of peptic ulcer in the western countries during the last two decades has been attributed to the decrease in the prevalence of *H. pylori* in the population[8].

It has been observed that Mucosal Associated Lymphoid Tissue lymphoma (MALT lymphoma) occurs in less than 1% of patients infected with *H. pylori*, and that nearly all these patients are *H. pylori* positive[8]. Depending on the degree of gastric atrophy (GA), the lifetime risk of developing gastric cancer (GC) in *H. pylori* infected people is 1–2% in the Western World[6].

It has further been observed that, though East Asia, West Asia, and Africa have a high prevalence of *H. pylori*, the incidence of gastric carcinoma (GC) and peptic ulcer disease (PUD) is disproportionately low in Africa and East Asia

CONTACT Stephen Z. Molaoa steve.molaoa@gmail.com Walter Sisulu University and Nelson Mandela Academic Hospital, Department of Surgery and Department of Health Studies, Walter Sisulu University and Nelson Mandela Academic Hospital University of South Africa, Mthatha 5100, South Africa

compared to West Asia – the so-called "African and Asian enigma"[9,10]. This has been attributed to the variation in bacterial strains, the host genetic makeup, nutritional status of the host, duration of infection, and environmental factors[10]. However, Agha and Graham[11] and Hooi et al.[9] refuted the concept of "African and Asian enigma" and contend that the incidence of *H. pylori*-associated gastric malignancy is similar in Africa as in other regions; the apparent lower incidence is due to under-counting and premature death from infectious diseases.

At Nelson Mandela Academic Hospital, which is the main referral hospital for the Eastern part of the Eastern Cape, the prevalence and the role of *H. pylori* in the causation of PUD and gastric malignancies has not been determined.

The objectives of this study, therefore, are to determine the prevalence of *H. pylori*, and the incidence of PUD and gastric malignancies among patients who are infected with *H. pylori* or who have stigmata of previous *H. pylori* exposure.

Materials and methods

The data was collected retrospectively from files of consecutive adult patients with upper gastro-intestinal symptoms who presented at the endoscopy unit for gastro-duodenoscopy over a 1-year period, from January to December, 2012. The gastric mucosal biopsy specimens were analyzed for the presence of *H. pylori* after staining with modified Giemsa stain. Hematoxyline & Eosin stain was used for identification of chronic gastritis which was defined as infiltration of lamina propria with mononuclear cells with or without plasma cells. Patients with carcinoma of the esophagus and those who presented for follow-up endoscopy were excluded. Data on patients' characteristics, presentation, endoscopic findings and histopathology reports were collected and analyzed for *H. pylori* prevalence, the prevalence of chronic gastritis, incidence of PUD, and gastric malignancies. The proportions of patients with PUD, MALT lymphoma, and *H. pylori* associated gastric cancer in the background of chronic gastritis (CG) and or *H. pylori* infection were determined.

Descriptive statistics were used to summarize patients' demographic data, and Z-test for proportions to determine gender deference in *H. pylori* prevalence and prevalence of CG between *H. pylori* positive and negative patients. A *p*-value of ≤ 0.05 was considered as statistically significant.

The ethical clearance for the study was granted by the Research Ethics Committee of the University of South Africa (UNISA), HSHDC/424/2015; and the permission to conduct the study was granted by Nelson Mandela Academic Hospital.

Results

Files of 156 patients were collected and analyzed. There were 70 (45%) males and 86 (55%) females, with a median age of 56.5 years (inter-quartile range = 43–66 years, and range = 18–90 years).

The prevalence of *H. pylori* was 54.5% (85 patients). There was no statistical difference in the prevalence of *H. pylori* in males and females (56% vs 54%), $p = 0.781$.

Of the 156 records, 148 (95%) had histologically proven chronic gastritis (CG). Of the 85 *H. pylori* positive patients, 82 (97%); and 66 (93%) of 71 *H. pylori* negative ones had CG. There was, therefore, no statistically significant difference in the prevalence of CG between *H. pylori* positive and negative patients (97% vs 93%, $p = 0.322$).

Table 1 illustrates of *H. pylori*-associated gastric diseases in relation to age and chronic gastritis status.

PUD was diagnosed in 24 (15.4%) of 156 patients analyzed; and in 16% of patients with current or prior exposure to *H. pylori*; 20 (84%) of which were gastric and four (16%) were a combination of isolated duodenal and type 2 (prepyloric and duodenal) ulcers. Fifteen (62.5%) of the 24 patients with PUD were *H. pylori* positive. *H. pylori* was positive in 12 (60%) patients with gastric ulcer (GU) and three (75%) with duodenal ulcers (DU) and type 2 GU. CG was

Table 1. Proportion of benign and malignant gastric diseases by age, *H. pylori* status, and presence of chronic gastritis.

Pathology	Age range (years)	No. of cases	Proportion of cases in relation to stigma of Hp infection ($n = 148$)	Hp Status	CG
Malignances :10 (6.4%)					
Intestinal GC: 4	<30 30–49 ≥50	0 1 (25%) 3 (75%)	2.7%	75% Pos.	100%
Diffuse: 3	<30 30–49 ≥50	1 (33%) 2 (66%) 0	2%	All Negative	33%
MALT-Lymphoma: 3	<30 30–49 ≥50	0 0 3 (100%)	2%	All Negative	100%
PUD: 24 (15.4%)					
GU: 20 (84%)	<30 30–49 ≥50	2 (10%) 5 (25%) 13 (65%)	13.5%	12/20 (60%)	20 (100%)
DU+ [a]Type 2: 4 (16%)	<30 30–49 ≥50	1 1 2 (50%)	2.7%	¾ (75%)	4 (100%)

[a]Type 2 Gastric ulcer: Gastric ulcer co-existing with duodenal ulcer, usually associated with high acid output.[12]

histologically confirmed in all patients with PUD irrespective of *H. pylori* status.

The incidence of PUD seems to increase with advancing age: 10% of patients with PUD were seen in the <30 years of age category; whereas 25% and 65% were diagnosed in the 30–49 and 50 years and above categories, respectively.

Of 156 patients, 10 (6.4%) had gastric malignancies, of which four (2.7%) and three (2%) were antral intestinal type and proximal diffuse types, respectively. Three (2%) had gastric MALT lymphoma. All patients with antral adenocarcinoma had CG, three (75%) of whom were *H. pylori* positive at diagnosis.

In contrast, two (66%) patients with diffuse proximal gastric cancer were both *H. pylori* and CG negative. Though all three patients with MALT lymphoma were *H. pylori* negative, CG was described in all.

As for benign ulcers, the risk of gastric malignancy in this study increases with increasing age. All (three) MALT lymphomas and three (75%) of the antral adenocarcinomas were seen in the >50 year age and CG positive category. However, 66% of proximal diffuse gastric cancer was reported in the <40 years of age, *H. pylori*, and CG negative patients.

Table 2 depicts counts and ages of patients with GA and IM. Of the 156 records analyzed, GA and IM were reported in only 59 (36%) of the records, and there was no reporting of this data in the 31–59-year age categories. Of the 10 patients with GA, seven (70%) had IM. When stratifying by age, 40% of GA was seen in the 20–30 year age group and 75% (three of four) had IM.

Discussion

The purpose of this study was to describe the prevalence of *H. pylori* and the incidence of *H. pylori*-associated gastric malignancies and PUD among symptomatic patients undergoing upper gastrointestinal endoscopy at Nelson Mandela Academic Hospital. We found that the prevalence of *H. pylori* among the symptomatic patients was 54.5%, but chronic gastritis, which is a stigma of current or past exposure to *H. pylori*, was seen in 95% of the patients. As reported in other studies[13,14], the current study demonstrated no statistically significant gender difference in the prevalence of the infection.

Regarding the prevalence of GA and IM which are the necessary changes in the progression of pathological transformation from CG to GC according to Correa's multi-step theory of the evolution of GC[15], collected data for this study demonstrated inconsistent reporting of these pathological changes (GA and IM). Despite the small number of subjects with GA and IM reported in our data, our results demonstrated that the incidence of GA and IM increases with advancing age; and that subject between the ages of 20–30 are not spared of the step-wise progression of the mucosal pathological changes from chronic gastritis, GA to IM.

In the younger patients (20–30 year age group) GA was reported in 40% of the patients and in 60% of those 60 years of age and above. IM was reported in 43% of those 20–30 years of age and in 57% of those 60 years of age and above. This observation is in keeping with the reports of other studies that reported the increasing of incidence of GA and IM with increasing age[16–18].

The current study demonstrated 50% prevalence of *H. pylori* in patients with GA and IM. This may be attributed to eradication prior to testing, and false negative results associated with gastric biopsy testing method. This may also be explained by what Zhang et al.[17] attributes to unfavorable environment for *H. pylori* survival caused by GA and IM.

The incidence of *H. pylori*-associated antral intestinal type gastric adenocarcinoma was 2.7% and MALT lymphoma was 2% in patients who either tested positive for *H. pylori* and/or who had histologically proven chronic gastritis. All patients with intestinal type gastric adeno-carcinoma had CG. Sixty percent of patients with GU and 75% of those with DU were *H. pylori* positive, and all had chronic gastritis.

Figures 1(a,b), 2(a,b) and 3 are endoscopic and histology images illustrating low grade MALT lymphoma, mucinous variant of intestinal type adenocarcinoma, signet ring cell variant of diffuse gastric adenocarcinoma, and benign gastric ulcer, respectively[19–21].

This study demonstrates that advancing age coupled with active *H. pylori* infection or stigmata of past exposure thereto are associated with increased risk of both benign peptic ulcers and malignant gastric diseases as demonstrated by 65% of GU, 50% of DU; all MALT lymphomas (100%) and

Table 2. Prevalence of GA and IM in patients with CG ($n = 10$).

Age (years)	*n*	Hp +	CG	GA	IM
20–30	4	1	4	4 (40%)	3 (43%)
60–90	6	4	6	6 (60%)	4 (57%)
Total	10	5 (50%)	10	10	7 (70%)

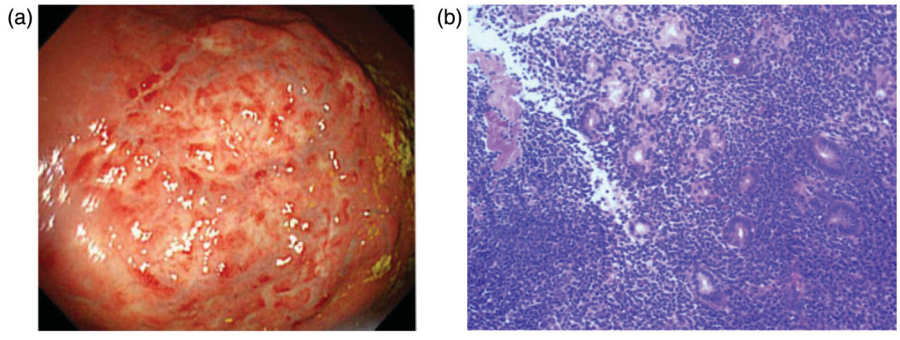

Figure 1. (a) Endoscopic image of MALT lymphoma. (b) Histology of MALT lymphoma.

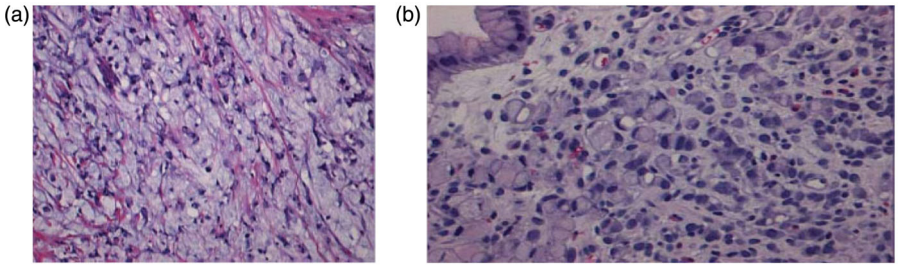

Figure 2. (a) Histology of mucinous variant. (b) Histology of signet ring variant of intestinal type GC diffuse GC.

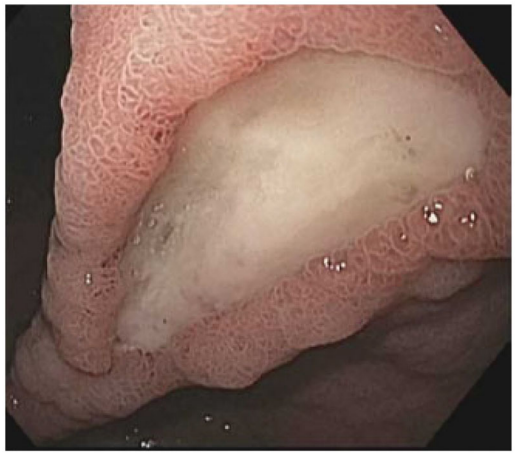

Figure 3. Large ulcer of incisura.

75% of intestinal type gastric adeno-carcinomas occurring in the ≥50 year age category, *H. pylori* positive and all with histologically proven chronic gastritis. In contrast, diffuse type gastric adenocarcinoma occurred in younger (≤50 years), *H. pylori* negative patients, and 2/3 (66%) without chronic gastritis. All patients with MALT lymphoma tested negative for *H. pylori*, though they all had chronic gastritis. The negative *H. pylori* status may be attributed to eradication before referral for endoscopy or false negative results as a result of reliance on small numbers of biopsies used for testing.

Though the local prevalence of *H. pylori* of approximately 55% reported in this study is slightly higher than the 50% global prevalence[1], the high prevalence (95%) of chronic gastritis may be indicative of high exposure of the local population to *H. pylori*, which is comparative to the prevalence of 87–91% reported in the Eastern Cape, South Africa, and in Nigeria[4,5].

The 2.7% incidence of *H. pylori* associated gastric cancer and 2% incidence of MALT lymphoma reported in this study is higher than that reported elsewhere. In the Western series, the incidence of gastric carcinoma of the intestinal type is 1–2%, and that of MALT lymphoma is <1%[8]. Our results compare favorably with the 2.4% incidence of GC in an *H. pylori* infected African population reported in a systematic review by Agha and Graham[11].

After identification of *H. pylori* as a causal agent for PUD, 95% of duodenal ulcers and 85% of gastric ulcers were attributed to *H. pylori*[7]; and that life time risk of developing PUD was 3–10 times higher in *H. pylori* infected individuals than in their uninfected counterparts[8]. This contrasts with the current study, where 60% of GU and 75% of DU were associated with current or prior exposure to *H. pylori*. Of note is that there was a 16% risk of PUD among patients exposed to *H. pylori*.

Due to the retrospective nature of this study, it is not known whether patients who had PUD during the procedure had just received eradication therapy that resulted in other patients testing negative for *H. pylori* though they had stigmata of exposure.

The results of this study corroborate the systematic review by Hooi et al.[9] and Agha and Graham[11] that refuted the concept of the African enigma, as the incidence of *H. pylori*-associated malignant and benign gastrointestinal diseases reported in this study does not differ from that reported by other studies.

The current study demonstrated that the *H. pylori*-associated gastric cancer was seen in the older age group. This supports the multi-stage theory of the evolution of gastric cancer from infection with *H. pylori* to chronic gastritis, gastric glandular atrophy, and gastric intestinal metaplasia to dysplasia culminating in invasive cancer[15]. A long lag time is required for all the stages to take place before invasive carcinoma occurs; hence the older age of presentation which may under-estimate the incidence of distal adenocarcinoma in the regions characterized by shorter life expectancy[9,11].

The limitation of this study was its retrospective nature. This may have led to under-estimation of *H. pylori* prevalence as some patients might had received antibiotics before presentation; and the information in this regard was not available. However, the presence of chronic gastritis might be indicative of past *H. pylori* infection. It can therefore be inferred that patients who were chronic gastritis positive were exposed to *H. pylori*. The possibility of an inadequate biopsy taking technique also might have resulted to under-reporting of *H. pylori* prevalence. This could have been improved by more sensitive tests, such as the Rapid Urease Test (RUT) or Urea Breath Test (UBT) which were not done during the data collection. A minimum of three biopsy specimens and the maximum of five were taken, which fall short of the 10 recommended biopsy specimens. This, therefore, falls short of the number of specimens and sites from which specimens should had been taken. This may account for the spuriously low prevalence of *H. pylori* reported in this study.

Due to the small numbers of records with GA, IM, gastric malignancies, and PUD, further analysis beyond descriptive analysis of these pathological conditions could not be done.

Despite the limitation imposed by the retrospective nature of this study, it has demonstrated that the incidence of both *H. pylori*-associated PUD and gastric malignancies in our population is not different from that reported in the Western and Asian literature.

In view of the non-negligible risk of *H. pylori* associated gastric cancer among our patients, a prospective study to define the group of *H. pylori* positive patients or with stigmata thereof who may be at increased risk of *H. pylori*-related adeno-carcinoma may need to be conducted in order to devise follow-up strategies aimed at early detection of gastric cancer, and therefore timely curative treatment.

Transparency

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Ethical information

The authors confirm the manuscript has all the necessary ethical approval and the authors have informed consent for its publication.

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