UPPER GASTROINTESTINAL FINDINGS IN DIABETIC OUTPATIENTS AT KENYATTA NATIONAL HOSPITAL, NAIROBI

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ABSTRACT

Objective: To determine the prevalence of *H. pylori* and the associated upper gastrointestinal endoscopic lesions in diabetic outpatients with dyspepsia.

Design: Cross-sectional study

Setting: Kenyatta National Hospital (KNH), Nairobi, Kenya.

Subjects: Adult diabetic outpatients with dyspepsia attending the KNH diabetic clinic.

Results: Of the 257 randomly selected diabetic outpatients screened, 137 (53.3%) had dyspepsia. Seventy one of these patients underwent an upper gastrointestinal endoscopy. Fifty five (77.5%) of the 71 patients had H. *pylori* infection identified by rapid urease test and histology. The prevalence of *H. pylori* increased with HbA1c level but there was no statistically significant association with poor glycaemic control (HbA1c >7.0%). Forty eight (67.6%) of the 71 had gastritis, 17 (25.7%) had duodenitis, eight (11.3%) had oesophageal candidiasis, seven (9.9%) had bile reflux, six (8.5%) had reflux oesophagitis, six (8.5%) had ulcers (five duodenal, one gastric) and one (1.4%) had gastric cancer. Fourteen (19%) had endoscopically normal mucosa. The prevalence of H. *pylori* was 82.3% (32/38) in patients with antral gastritis. All ulcers and the cancer lesion (adenocarcinoma) were associated with *H. pylori.* Histological gastritis was found in 57 (81.8%) and was significantly associated with *H. pylori.*

Conclusion: Although dyspepsia is common in diabetic outpatients at KNH, endoscopic findings and *H. pylori* status are not significantly different from those of non-diabetic population.

INTRODUCTION

Gastrointestinal tract (GIT) complications occur in up to 75% of diabetic patients(1). In the upper GIT, these manifest as dyspepsia, which is characterised by upper abdominal pain or discomfort. Other symptoms include early satiety, postprandial fullness or bloating, nausea, vomiting and anorexia. Dyspepsia interferes with food intake and absorption, contributes to poor glycaemic control, and may precipitate acute metabolic complications(2) and contributes to chronic complications of diabetes. Most studies have implicated diabetic autonomic neuropathy as the major aetiology leading to abnormalities such as diabetic gastropathy, oesophageal dysmotility and abnormal release of gastrointestinal regulatory peptides(3,4). As in the general population, dyspepsia may result from H. *pylori* or non-steroidal anti-inflammatory drug induced mucosal lesions especially peptic ulceration(5). Further, upto 70% of non-ulcer dyspepsia has been associated with H. *pylori* (6). H. *pylori* infection may ultimately cause gastric cancer which is a major cause of dyspepsia(7).

Diabetics are at increased risk of infection due to poor immunological function(8). Despite the knowledge that a diagnosis of dyspepsia due to H. *pylori* associated lesions in particular peptic ulceration is potentially curable, the contribution of H. *pylori* associated lesions to dyspepsia in diabetics remains unknown. Persico *et al.* (9). reported a prevalence of 79% in 29 Italian type II diabetics. In another European study, Gentile *et al.*(10) found 74% of 164 type II diabetics as compared to 50% controls with H. *pylori* infection. No local studies have so far addressed H. *pylori* in diabetics.

MATERIALS AND METHODS

Between June 2000 and March 2001, diabetes mellitus patients aged 18 years and above, were randomly selected during the weekly diabetic clinic every friday morning using a table of random numbers. This exercise continued until the target minimum sample size of 64 endoscopically examined diabetic dyspeptic patients was achieved. In total, 293 patients were randomly selected over the entire period; out of whom 36 were excluded: 12 were excluded due to history of use of H_2RA or PPI within four weeks, 10 due to use of NSAIDS including low dose aspirin within two weeks and seven due to use of antibiotics within two weeks of interview. Two were excluded due to previous H. *pylori* eradication therapy. Two patients with

congestive cardiac failure and one with hepatitis were also excluded.

The 257 diabetic patients who qualified for recruitment were screened for dyspepsia. Dyspepsia was defined as any combinations of the following symptoms:, upper abdominal pain or discomfort, anorexia, nausea, vomiting, early satiety, post-prandial fullness and flatulence (bloating); and such symptoms could be intermittent or persistent and should have been present for at least one month prior to the interview. Patients who consented to an upper GIT endoscopy were recruited into the study and allocated study numbers and details of their age, sex, weight, height, type of diabetes, duration since diagnosis and the type of glycaemic control were taken. History of other GIT symptoms, inter-current disease and use of medications was taken as well. Blood pressure and pulse rate was taken and a physical examination with emphasis on oral and abdominal findings was performed. The patients were then given appointment dates for the upper GIT endoscopy after fasting for at least six hours.

Two milliliters of blood was collected in EDTA bottles on the morning of the endoscopy. Total glycated haemoglobin and HbAlc were then determined using the Abbott IMx Glycated Haemoglobin test kit.

Standard upper gastrointestinal endoscopy procedure was performed. Two biopsy specimens from the antrum, the incisura and the body were taken. Biopsies of any lesions suggestive of malignancy were also taken for histopathological evaluation.

Urease test was immediately performed on one of the biopsy specimens from each site. A positive test was indicated by a colour change from yellow to red. Negative test was recorded if there was no colour change at 24 hours.

Biopsies for histology were preserved in formalin solution for at least six hours prior to processing and staining with Cold Ziehl-Neelsen staining method for *H. pylori* detection. Giemsa stain was used for quality control. Processed specimens stained with Haematoxylin-Eosin stain were used for histological evaluation. All the specimens were then examined by an experienced pathologist blinded to the urease test results. *H. pylori* was declared positive if both histological finding and urease test were positive and negative if both or either test were negative.

The data was collected using a standard questionnaire and analysed using the SPSS 10.0 software. Statistical significance was defined as p-value of less than 0.05.

RESULTS

One hundred and thirty seven (53.3%) of the 257 diabetic outpatients had dyspepsia. Most patients had multiple symptoms of dyspepsia. The commonest was upper abdominal pain (76.1%), followed by early satiety (53.5%), flatulence (bloating) (46.5%), postprandial fullness (45.1%), anorexia (38.2 %), nausea (25.4%) and vomiting (21.1%).

Endoscopic findings: Table 1 shows the endoscopic mucosal findings of the patients. Antral gastritis was the commonest form of gastritis (38 out of 48) while predominantly fundal gastritis was present in 10 out of the 48 patients with gastritis. None of the patients with history of alcohol intake and smoking had duodenal or gastric ulcers. However, eight of the 11 patients with history of alcohol intake had histological gastritis. Endoscopic diagnosis of gastritis correlated poorly with histological diagnosis of gastritis, (Kappa statistic= 0.285, P=0.015). Only one of the patients with oesophageal candidiasis had oral thrush. The candidiasis was significantly associated with poor glycaemic control (HbAlc >8.00%, P=0.009).

Table 1

Upper GIT endoscopic findings of the (n=71) diabetic outpatients with dyspepsia

Endoscopic finding$^\varphi$	Frequency (n=71)	% (n=71)
Gastritis*	48	67.6
Duodenitis	17	25.7
Duodenal ulcers	5	5.7
Gastric ulcers	1	1.4
Oesophageal candidiasis¥	8	11.3
Reflux oesophagitis	6	8.5
Bile reflux	7	9.9
Gastric nodules *	2	2.8
Deformed antrum†	2	2.8
Normal	14	19.7

n = Number of patients studied

φ= Some patients had more than one endoscopic lesion. 14 of the 17 patients with duodenitis also had endoscopic finding of gastritis. Three patients with esophageal candidiasis also had gastritis. Bile reflux occurred together with reflux oesophagitis in four patients. There were multiple other combinations of findings occurring together.

¥ = Only one had oral thrush but all had HbAlc above 7.0%

* = All were benign at histology

† = At histology, one patient had benign gastric cancer (adenocarcinoma)

At histology, the most common histological finding was gastritis which was found in 81.8% of the 71 patients. The commonest form of gastritis was chronic (61.6%), followed by active chronic gastritis (11.2%) and then atrophic gastritis (9.0%). Normal histology was found in 16.8%. Gastric malignancy (poorly differentiated adenocarcinoma) was present in one (1.4%) patient, which at endoscopy had appeared as a deformed antrum in a 60 year old female.

H. pylori prevalence: H pylori was detected in 55 (77.5%) of the 71 patients by both urease test and histology. The biopsy urease test correlated well with the histological detection of *H. pylori* (Phi statistic =0.779, P= 0.000). Four patients with a positive urease test but with negative histology and one with positive histology alone were considered negative for *H. pylori.*

Figure 1 shows the variation of *H. pylori* prevalence with the duration since diagnosis of diabetes. *H. pylori* prevalence increased with the duration of diabetes peaking at 6 to 10 years of diabetes.

Figure 1

Variation of H. pylori prevalence with duration (since diagnosis) of DM of the 71 diabetic outpatients with dyspepsia.
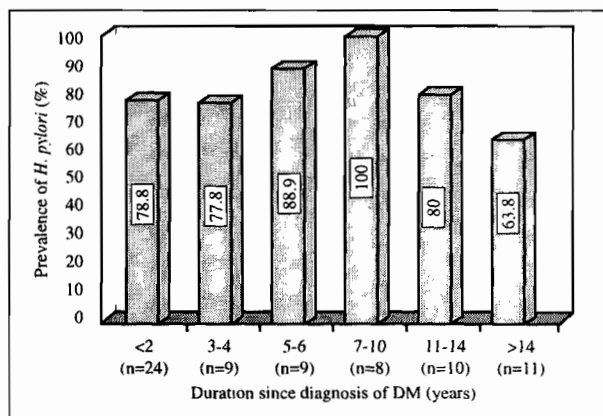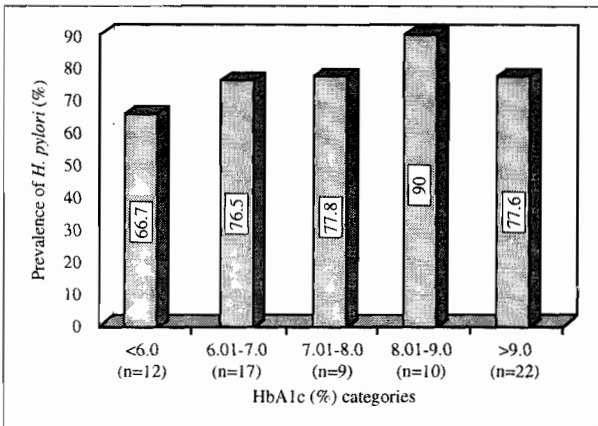

n = Number of patients per each duration category

Figure 2 shows the variation of *H pylori* with the level of glycaemic control (HbAlc), there was a general trend of increase in the prevalence of *H. pylori* with HbAlc. However, there was no statistically significant difference in the prevalence between patients who were well controlled (HbAlc <7.0%) and those who were poorly controlled (HbAlc >7.0%), (P= 0.428).
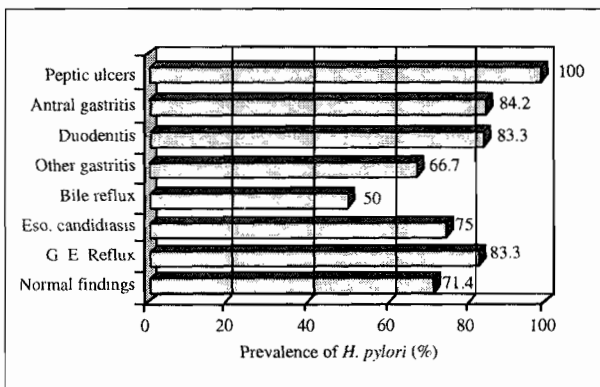
Figure 2

Variation of H. pylori prevalence with HbAlc of the 71 diabetic outpatients with dyspepsia

n = Number of patients per each duration category

Figure 3

Prevalence of H. pylori in association with endoscopic findings of the 71 diabetic outpatients with dyspepsia

G. E. Reflux = Gastroesopheagal reflux
Eso. Candidiasis = Oesophageal candidiasis

Figure 3 shows the prevalence of *H. pylori* in association with the endoscopic findings. *H. pylori* prevalence was high and was significantly associated with peptic ulcers (P= 0.021), histologically confirmed antral gastritis (P= 0.024), and duodenitis (P=0.050). In contrast, other endoscopic findings had lower prevalence of *H. pylori*.

DISCUSSION

The high prevalence of dyspepsia in diabetic outpatients at KNH (53.3%) in this study is in conformity with other studies showing high prevalence of GIT complications in diabetes mellitus patients(1,11).

Endoscopic findings: The commonest endoscopic finding was gastritis, which was found in 67.6% of the studied patients. As expected, the endoscopic diagnosis of gastritis correlated poorly with histological evaluation(12). At histology, there was chronic gastritis in 62.0%, chronic active gastritis in 8.5% and atrophic gastritis in 11.3% of the patients, with an overall prevalence of 81.8%. MaLecki *et al.*(13) found an overall prevalence of gastritis of 63% (chronic gastritis 41% and reactive gastritis 22%) of the 39 European diabetics with autonomic neuropathy(13). Most studies in predominantly non-diabetic patients with dyspepsia have shown less common finding of gastritis. For example, Lule *et. al.*(14)reported 16 out of 66 (24%) patients with gastritis while Ogutu *et al.*(15) found a prevalence of 31.7%. In these two studies, the commonest finding was normal mucosa (39.4% and 34.2%, respectively) as compared to only 19% of normal upper endoscopic finding we found in diabetes mellitus patients.

Unlike gastritis, peptic ulcers were found in only 8.2% as compared to other local studies that reported rates above 30%(14,15). The low prevalence of ulcers observed in this study may have been influenced by three possible factors. Peptic ulceration may be less symptomatic in diabetics due to associated autonomic neuropathy, and thus could have been missed out at the screening stage. Another possibility is 'crowding out' of peptic ulcers as a cause of dyspepsia by the high prevalence of other causes in diabetic subjects. Previous researchers studied highly selected patients (dyspeptic patients referred for upper GIT endoscopy) and thus could have had more severity of dyspepsia. Future comparative studies between diabetics and non-diabetics with dyspepsia and between dyspeptic diabetics and non-dyspeptic diabetics may help determine the contribution of these confounding factors. However, results of this study concur with previous studies that have shown very low ulcer prevalence in diabetics(16). Thus, non-ulcer dyspepsia associated with gastritis is the predominant finding in diabetes mellitus. This observation may be explained by the fact that mucosal damage is partly mediated by the hosts' immune response to H. *pylori* infection(17), and reduced immunity in diabetes mellitus may alter the mucosal outcome of *H. pylori* infection.

Oesophageal candidiasis was found in 11.3% of the studied patients and was significantly associated with poor glycaemic control. The fact that only one of these patients had oral thrush means that oesophageal candidiasis should always be considered as a contributing factor to dyspepsia especially if the patient has poor glycaemic control with HbAlc above 8%. Reflux oesophagitis and bile reflux found in this study may reflect the state of GIT

dysmototility associated with diabetic autonomic neuropathy(3).

Malignancy was found in one patient (1.4%) as compared to previous local studies that have found prevalence range of 2.7% to 9.1% in non-diabetics(14,15,18). This wide range may be explained by the different study populations and selection criteria of the studied patients. The ratio of duodenal to gastric ulcer in this study was 5:1, which is within the range of 7.5:1 and 3:1 observed from previous local studies in non-diabetics(3,15,18).

H. pylori prevalence: 77.5% of the diabetic dyspeptics had *H. pylori* infection which is comparable to 81.7% found in non diabetic dyspeptic patients by Ogutu *et al.*(15). Gentile *et al.*(10) found a prevalence of 74% in 29 Italian type II diabetics which is comparable to our finding. Some western European studies found similarly high prevalence(9,13) while others found rates as low as 30%(13). This wide range may partly be explained by the different selection criteria used by the different researchers and the different geographical settings of the studies.

The H. p*ylori* prevalence increased with age with a tendency to level off after the 6th decade. This compares with findings by Lule *et al.* in a study of non-diabetics with dyspepsia(14). On the contrary most other studies have demonstrated a cohort effect whereby the prevalence of *H. pylori* increases with age regardless of the geographical location or type of patients including diabetes. A possible reason is the fact that most epidemiological studies are serologically based such that once infected the persistence of antibodies gives positive tests regardless of the true *H. pylori* status(19). Another possible reason is the fact that the older Kenyan age groups (above 60 years) experienced better socio-economic conditions and lived in sparse populations during their childhood and thus accounting for lower H. *pylori* infections then and lower current prevalence at older ages.

The prevalence of *H. pylori* increased with duration of diabetes mellitus with a peak at 10 years after diagnosis where a prevalence of 100% was found and then lower rates thereafter. A possible explanation for this observation comes from a study by Ma Lecki *et al.*(13) who reported a lower prevalence of *H pylori* patients with diabetic gastropathy (a feature of autonomic neuropathy) as compared to diabetic controls without dyspepsia. We postulate that the initial increase in the *H. pylori* prevalence is due to low immunity in diabetes but later reduces as autonomic neuropathy sets in. This subsequent drop may be due to increased use of antibiotics arising from increased rates of infections as autonomic neuropathy develops. However a study large enough to allow statistical validation of this pattern is recommended.

Although there was a tendency for the prevalence to increase with HbAlc, no statistically significant difference was found between the poorly controlled and the well-controlled diabetics suggesting lack of association between glycaemic control and *H. pylori* infection. However, a single HbAlc reading is only a measure of the glycaemic control in the recent three months and does not reflect the quality of control over the entire duration of diabetes.

H. pylori was significantly associated with histologically confirmed diagnosis of gastritis (81.8%), P= 0.024. This is in conformity with both local studies in non-diabetics and studies from the developed countries in diabetic dyspeptics(9,10,14,15). This is in agreement with previous studies which have consistently demonstrated H. *pylori* association with type B (antral) gastritis(20). In contrast to antral gastritis, body gastritis and pangastritis had lower prevalence of H .*pylori.*

All the diabetics with peptic ulcers in this study had *H. pylori* infection, which is similar to reports from studies in non-diabetics in which 100% of duodenal ulcers are found associated with *H. pylori*(5,15). Similarly, *H. pylori* was identified in the gastric cancer lesion, not a surprise finding since *H. pylori* is an established carcinogen implicated in causation of gastric cancer(7).

From the foregoing discussion, it can be summarised that, dyspepsia occurs commonly (53.3%) in diabetic outpatients at KNH with H. *pylori* infection occurring in upto 77.5% of these dyspeptic diabetics. The *H. pylori* prevalence lies within the range observed from studies of non-diabetic local historical controls. Further, histologically confirmed gastritis, as in non-diabetics, occurs in close association with *H. pylori* infection. However, there are two outstanding differences arising from this study, the relatively fewer ulcers and more oesophageal candidiasis found in dyspeptic diabetics. Oesophageal candidiasis may thus be considered a possible contributing factor to dyspepsia in diabetics with poor glycaemic control. These differences need to be validated in subsequent studies designed to adequately control for the confounding factors.

In conclusion, although dyspepsia is common in diabetic outpatients at KNH, endoscopic findings and *H. pylori* status are not significantly different from those of non-diabetic population.

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