ORIGINAL ARTICLE

Influence of *Helicobacter pylori* infection on the prevalence and patterns of upper gastrointestinal symptoms in Nigerians with diabetes mellitus

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Abstract

Background: Infection with *Helicobacter pylori* infection is widespread in our environment. However, whether this fact has any bearing on the prevalence and pattern of symptoms referable to the upper gastrointestinal (GI) system in our population of diabetes mellitus (DM) patients has not been much studied.

Aim: We embarked on this study to evaluate if *H. pylori* infection played any significant role in the prevalence and patterns of upper GI symptoms in type 2 DM patients in Lagos, Nigeria.

Materials and Methods: A case–control design was employed. One hundred consecutive, consenting, and ambulant type 2 DM patients were recruited from the Lagos University Teaching Hospital and 100 age- and sex-matched nondiabetic controls were drawn from medical outpatient clinics of the same hospital. All subjects were investigated for a marker of active infection with *H. pylori* via stool antigen testing, had anthropometric measurements taken, and completed a structured questionnaire administered to elicit for the presence of various upper GI symptoms over the preceding 3 months prior to the time of the study. The controls were further tested for DM. For analysis, the symptoms were divided into dyspepsia, gastroesophageal reflux (GER), and others.

Results: *H. pylori* infection status was neither significantly associated with dyspepsia in either cases or controls (χ^2 [1] = 2.198, P = 0.138) nor significantly associated with the symptomatic suggestion of GER in either cases or controls (χ^2 [1] = 3.742, P = 0.053). Moreover, the same held for the other upper GI symptoms in cases or controls (χ^2 [1] = 0.157, P = 0.203). *H. pylori* infection was detected in 18% of DM patients and 13% of controls, but there was no statistical significance in this difference (χ^2 [1] = 0.954, P = 0.329).

Conclusion: Infection with *H. pylori* does not appear, from the results of this study, to influence the prevalence and patterns of upper GI symptoms in patients with DM in Nigeria.

Key words: Diabetes mellitus, gastrointestinal symptoms, *Helicobacter pylori,* Nigeria

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Introduction

Some researchers consider that gastrointestinal (GI) symptoms are more prevalent in diabetes mellitus (DM)

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patients than in the general population.[1-3] Furthermore, others have noted that *Helicobacter pylori* infection might contribute significantly to this relationship. The latter notion has been put to the test by various researchers.

Gasbarrini *et al.*[4] reported a higher prevalence of several dyspeptic symptoms in type 1 DM patients with *H. pylori* infection as compared with the *H. pylori*-negative group. The study, however, did not correct for confounding factors such as age, gender, and socioeconomic factors with multivariate analyses. The same investigators also suggested that the upper GI symptoms observed previously were improved with *H. pylori* eradication.[5] The second report was also flawed in that there was no placebo control group. Their results were supported by similar earlier findings among type 2 diabetics.[6] In addition, a local study from Lagos showed a higher prevalence of GI symptoms in DM patients than in nondiabetics.[7]

On the other hand, later studies have strengthened arguments against the notion that *H. pylori* infection influences GI symptoms in DM. Xia *et al.*[8] found that *H. pylori* infection was not associated with any upper GI symptom, either before or after adjustments for potential risk factors. Similarly, findings were reported in a population of young people with type 1 DM.[9]

Again, other workers in the Iasi region of Romania reported that the prevalence of *H. pylori* infection was neither associated with the known duration of diabetes nor any significant difference in the upper GI symptoms score between *H. pylori*-positive and *H. pylori*-negative diabetic patients.[10] In fact, the endoscopic findings in patients with DM (whatever their *H. pylori* infection status) were in the same range with those found in dyspeptic subjects from the same region.

In 2008, a Turkish publication reported that even within a type 2 DM population, there was no significant increase in *H. pylori* prevalence between those who complained of dyspeptic symptoms and those who did not.[11] Such results were mirrored a study from Abakaliki where it was found that prevalence and patterns of dyspeptic symptoms were not significantly different between *H. pylori* seropositive diabetics and similarly, infected nondiabetic controls.[12]

Aim

The objective of this study was to investigate if *H. pylori* had any significant role to play in the pattern of upper GI symptoms in Nigerians with DM.

Materials and Methods

Study location

Lagos University Teaching Hospital (LUTH), the location for this study, is situated in Idi-Araba, Surulere Local Government Area of Lagos State, Nigeria. The catchment area of the hospital referral base is statewide (and even beyond) and embraces a diverse array of patients with differing tribal, socioeconomic, and lineage backgrounds.

Study design

The study employed a case–control design. Here, measurement of cause and outcome variables among both cases and controls was carried out at the same point in time.

Subjects

The subjects for this study were drawn from adults with type 2 DM patients of LUTH. They were all ambulant patients attending the DM outpatient clinics.

The age of the patients was from 31 to 82 years, and they agreed to sign the consent forms as an indication of willingness to participate in the study.

Selection criteria for cases

Inclusion criteria for cases

(1) Patients with objective evidence of DM as demonstrated by the World Health Organization (WHO) criteria for diagnosis of diabetes,[13] i.e., fasting plasma glucose is ≥7.1 mmol/l (126 mg/dl) or a 2-h postprandial plasma glucose of ≥11.1 mmol/l (200 mg/dl) or those with classical symptoms and random blood glucose >11 mmol/l. Those who had been previously diagnosed with DM by this criterion but whose blood glucose had now been controlled with diet, drugs ± insulin were included in the study. (2) All recruited subjects agreed to sign the informed consent form for permission to be included in the study.

Exclusion criteria for cases

Presumed type 2 DM patients whose blood glucose estimations at diagnosis do not meet the minimum requirements as dictated by the WHO were excluded from this study along with those that declined the offer to sign the informed consent form.

As diarrheic stools are not appropriate for testing with the immunoassay-based Rapid Strip HpSA™ kit,[14] cases (and controls) whose submitted loose, watery stools were excluded.

Selection criteria for controls

Inclusion criteria for controls

Age- and sex-matched controls were drawn from the other patients attending the other nondiabetic medical outpatient clinics.

All were required to show consent to participate in the study by agreeing to sign the informed consent form in the presence of a witness before being enrolled in the study and before samples are taken for relevant tests.

Exclusion criteria for controls

Controls whose blood glucose estimations met the WHO criteria for diagnosis of DM were excluded from inclusion as controls. Prospective controls with diarrhea and those who declined the offer to sign the informed consent form were also excluded from the study.

The possibility of bias was excluded by ensuring that patients with dyspepsia complaints attending the gastroenterology clinics were excluded from the study. Further, all controls who had had eradication therapy for *H. pylori* in the past were excluded from the study.

Data collection

Questionnaire

After obtaining informed consent, 100 consecutive consenting patients and 100 consenting controls satisfying the inclusion criteria were recruited from among only ambulant outpatients of LUTH.

A well-structured pretested questionnaire was administered by a medical doctor to each participant. The first page of the questionnaire included biodata, anthropometry, socioeconomic variables such as occupation and level of education, and if the participant had prior knowledge of whether he or she was diabetic.

The already validated diabetes bowel symptom questionnaire was modified and administered to determine GI symptoms.[15] All questionnaires were administered by a medical doctor.

The patients were then required to submit stool samples which were tested for evidence of *H. pylori* infection with the immunoassay-based Rapid Strip HpSA™ (Meridian Bioscience, Europe- a division of Meridian Bioscience, Incorporated, Cincinnati, U.S.A) (sensitivity 96.1%, specificity 90.6%).[14]

Age- and gender-matched controls were then selected from the pool of nondiabetics attending the other outpatient clinics in LUTH. After signing informed consent forms, they had the questionnaires administered to them.

However, each one of the controls had blood drawn for fasting blood glucose and those who met the minimum WHO requirements were excluded from being controls in this study. They were also required to provide stool samples for *H. pylori* testing. However, they were encouraged to submit their own stool samples early on a working day morning as they would simultaneously have fasting blood glucose analysis.

Sample analysis

The two analyses run in this study were those of determining if all participants were positive or not for *H. pylori* stool antigen and if the controls had blood glucose ranges that were diabetic or not. A glucometer was used to determine the latter in the fasted state according to the WHO guidelines. The former parameter was determined as stated in the manual of the immunoassay-based Rapid Strip HpSA™.[14]

Ethical considerations

Ethical approval was obtained from the Ethics Committee of LUTH prior to the commencement of the study.

Statistical analysis

For analysis, the upper GI symptoms were divided into three groups:

a. Dyspepsia (defined as pain or discomfort centered around the upper abdomen)
b. Gastroesophageal reflux (GER; indicated in the questionnaire as persistent heartburn and/or regurgitation)
c. Overall (defined as any of the above symptoms put together).

The body mass index (BMI) was used to determine obesity by the formula; weight/height^2 - a value of ≥30 kg/m^2 being the threshold for obesity.[15]

The data obtained were analyzed using the IBM SPSS Statistics for Windows, Version 20.0. IBM Corp. Released 2011. Armonk, NY: IBM Corp. Data were expressed as means ± standard deviation and frequencies.

Statistical analysis was done using Student's *t*-test for continuous variables and Chi-square for categorical data. Multivariate analysis was included in view of possible confounding factors.

Results

Helicobacter pylori and dyspepsia

Of the 100 recruited type 2 DM patients, 30% ($n = 30$) had symptoms of pain and/or discomfort in the upper half of the

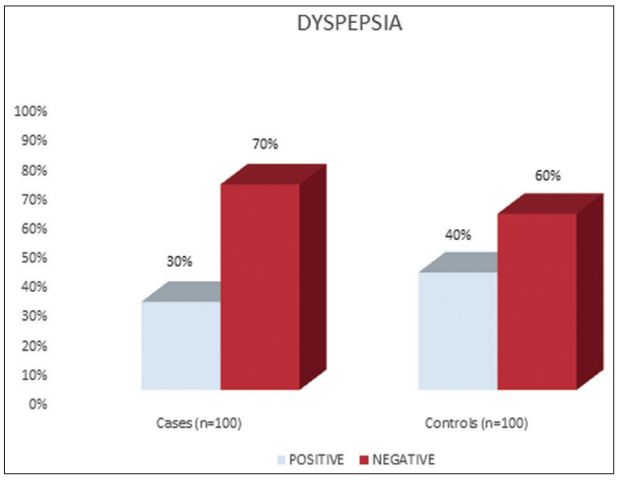

Figure 1: Proportion of participants with dyspepsia

abdomen (dyspepsia) over the preceding 3 months to time of questionnaire administration. A similar high percentage of controls, 40% ($n = 40$), also had these complaints [Figure 1]. Infection with *H. pylori* was not significantly associated with the difference in the prevalence of dyspepsia across the two groups (χ^2 [1] = 2.198, $P = 0.138$).

Helicobacter pylori and gastroesophageal reflux-suggestive symptoms

The predominant complaints in GER are typically heartburn and acid regurgitation[16] – these two symptoms were itemized in the administered questionnaire.

Results show that a high proportion of respondents (20% of diabetics and 32% of controls) had, within a 3-month period, symptoms suggestive of GER. There was no significant relationship between groups (χ^2 [1] =3.742, $P = 0.053$) [Figure 2].

Again, *H. pylori* infection status was not significantly associated with the symptomatic suggestion of GER in either cases or controls (χ^2 [1] = 3.742, $P = 0.053$). The association between sex and likelihood of having GER symptoms was not statistically significant in either set-controls (χ^2 [1] = 2.804 $P = 0.094$) and diabetics (χ^2 [1] = 0.500, $P = 0.480$).

A noteworthy fact from the data in this study is that it did not reveal significant relationship between BMI and the presence of symptoms suggestive of GER (case: [χ^2 [1] = 1.667 $P = 0.435$]; control: [χ^2 [1] = 3.236 $P = 0.357$]). Further, smoking appeared not to be significantly associated with GER symptoms both in cases (χ^2 [1] = 0.336 $P = 0.845$) and in controls (χ^2 [1] = 0.064 $P = 0.969$).

Helicobacter pylori and other upper gastrointestinal symptoms

Table 1 summarizes the pattern of upper GI symptoms among respondents.

Among control subjects, a high percentage (56%) had experienced one or more upper GI symptoms within 3 months of symptoms questionnaire administration – the list of symptoms is presented in Figure 3. In the nondiabetic controls, the prevalence of individual symptoms ranged from 40% (for abdominal pain or discomfort) to 2% (for dysphagia).

The overall prevalence of upper GI symptoms was 51% in men and 61% in women which was not significantly different across the sexes for controls (χ^2 [1] = 2.029, $P = 0.154$). Age was similar in those with or without symptoms (means 53.8 ± 10.85 vs. 55.8 ± 9.86 years), t (198) = −1.364, $P > 0.05$.

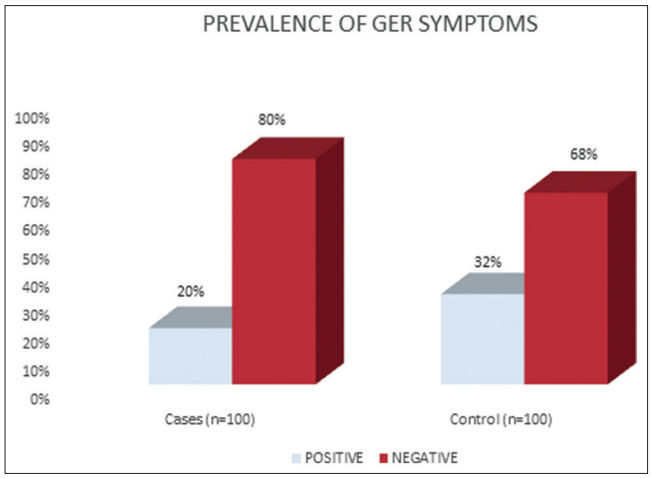

Figure 2: Prevalence of gastroesophageal reflux symptoms among study participants

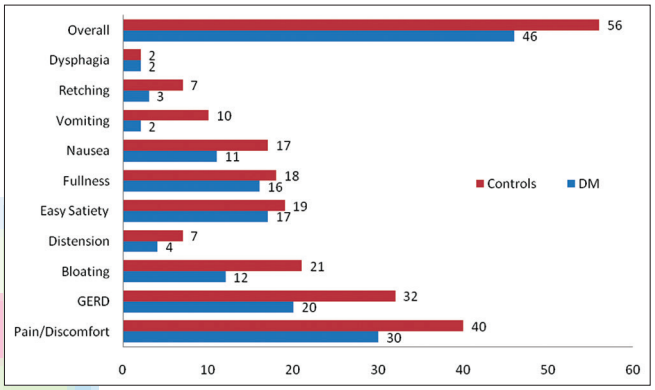

Figure 3: Prevalence of upper gastrointestinal symptoms in cases ($n = 100$) and controls ($n = 100$)

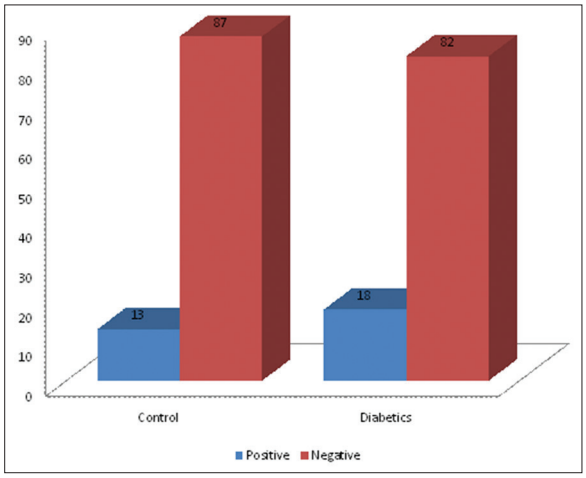

Figure 4: Prevalence of *Helicobacter pylori* infection among study participants

Overall, symptoms were not associated with *H. pylori* status in controls 53.9% in *H. pylori*-negative subjects and 55.2% in *H. pylori*-positive subjects, (χ^2 [1] = 0.020, $P = 0.887$)

Table 1: Prevalence of *Helicobacter pylori* infection and gastrointestinal symptoms in diabetics and nondiabetic controls

	Cases (n=100)	Control (n=100)	P value
Abdominal pain/discomfort only (n=%)			χ^2 (1)=2.198;
Positive	30	40	P=0.138
Negative	70	60	
GERD symptoms only (n=%)			χ^2 (1)=3.742;
Positive	20	32	P=0.053
Negative	80	68	
Overall upper GI symptoms (n=%)			χ^2 (1)=0.157;
Positive	46	56	P=0.203
Negative	54	44	

neither BMI (χ^2 [1] = 1.376, P = 0.241) nor smoking history (χ^2 [1] = 0.064, P = 0.469).

A similar high proportion of type 2 DM cases (47%) had experienced one or more upper GI symptoms. On comparison with controls, upper GI symptoms were not significantly associated with the presence or otherwise of type 2 diabetes among the study population (χ^2 [1] = 3.742, P = 0.053).

However, analysis of relationship between DM status and dyspepsia in obese participants revealed that female sex in this subgroup was significantly associated with this particular symptom (χ^2 [1] = 5.000, P = 0.025, odds ratio = 0.143, 95% confidence interval = 0.023–0.877). The same did not hold true for male sex in this subgroup (χ^2 [1] = 0.117, P = 0.733).

H. pylori infection as detected by the presence of the stool antigen marker was positive in 18% of DM patients and 13% of controls; however, there was no statistical significance in this difference (χ^2 [1] = 0.954, P = 0.329) [Figure 4].

Discussion

The objective of this study was to assess whether *H. pylori* infection is associated with prevalence and patterns of upper GI symptoms in the study population. From the findings in this study, *H. pylori* infection does not appear to significantly influence the prevalence in both cases and controls or pattern of GI symptomatology. The results are in keeping with findings in a local study where it was found that *H. pylori* infection prevalence did not have any relationship with dyspeptic symptoms between diabetics and nondiabetics.[12] Although another study reported a higher prevalence of GI symptoms in Lagos DM patients versus nondiabetics, the difference failed to reach statistical significance.[7]

There are also various reports that support this finding.[8,11] While the former[8] was a report from a community-based, seroprevalence study, the latter[11] is a 2008 Turkish study on histology findings from the gastric mucosa of dyspeptic diabetics and controls.

An Italian study reported a higher prevalence of several upper GI symptoms in *H. pylori*-positive compared with *H. pylori*-negative patients with type 1 DM.[4] The need for correction for potential confounding variables such as age and socioeconomic factors by multivariate analysis has been noted above. Unfortunately, it seems that this was not done by the Italian team before reaching conclusions about the differences observed.[8]

Female sex in the subgroup of obese DM patients was shown to be significantly associated with dyspeptic symptoms. This might have not been previous documented in our locality, but it is not a novel concept. Previous studies had identified female gender as an independent risk factor for upper GI symptoms.[8,17-19] Xia *et al.*[8] summarized the proposed underlying mechanisms that are speculated to account for this association:

- Estrogen and progesterone secretion may modulate GI motility[20,21]
- Psychological factors play a significant role in this difference as Talley *et al.*[22] had reported that emotional and psychological distress was independently associated with upper GI symptoms in diabetes while Wredling *et al.*[23] have reported that women with DM experienced more anxiety and depression than men.

In addition, obesity has been established to have a significant association with several key GI symptoms.[24] Increasing BMI has long been significantly related to increases in prevalence and differences in pattern of GI symptoms.[24-26]

The sample size was small, and thus, the study is rather underpowered to decisively answer the scientific question of whether *H. pylori* has any influence at all on the prevalence and pattern of upper GI symptomatology in DM patients. However, it represents an initial step to this. Another possible confounding factor could be control of diabetes in the study subjects. Hence, the interpretation of the results of this study will be limited as this was not accounted for. All in all the study results, however, still merit consideration as a springboard for further discuss inquiries and larger more empowered studies on the subject matter.

Conclusion

Colonization of the GI tract with *H. pylori* did not have a significant association with the prevalence and patterns of upper GI symptoms in patients with DM in Lagos, Nigeria. The study shows that female sex in the subgroup of obese

DM patients was significantly associated with symptoms of dyspepsia.

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Conflicts of interest
There are no conflicts of interest.

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