Prevalence of Helicobacter pylori-related dyspepsia using a near-patient testing method in Port Harcourt, Nigeria

Andrew A. Bock-Oruma[1], Paul O. Dienye[2], Alex B. Akani[3], Nnenna O. Nnadi[4], Rachel A. Idika[5]

[1]Shawsand Medical Centre, P. O. Box 6082, Port Harcourt, Nigeria
[2]University of Port Harcourt Teaching Hospital, P. M. B. 6183, Port Harcourt, Nigeria
[3]University of Port Harcourt Teaching Hospital, P. M. B. 6183, Port Harcourt, Nigeria
[4]University of Port Harcourt Teaching Hospital, P. M. B. 6183, Port Harcourt, Nigeria
[5]University of Port Harcourt Teaching Hospital, P. M. B. 6183, Port Harcourt, Nigeria

ABSTRACT

Background: The association between *Helicobacter pylori* (HP) infection and dyspeptic symptoms has long been established with HP infection having a 5% population attributable risk for dyspepsia. **Aim:** Using a near- patient testing method, this study determined the prevalence of *Helicobacter pylori* infection, assessed sociodemographic influence on *Helicobacter pylori* infection and determined the treatment outcome of the subjects.**Design:** A prospective study **Setting:** The study was carried out at the family medicine clinic of the University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria. **Methods:** Consenting and eligible dyspeptic patients were tested for *Helicobacter pylori* using ^{14}Carbon Urea Breath Test (CUBT). CUBT-positive patients had eradication therapy for *Helicobacter pylori*, while CUBT-negative patients had empirical therapy. Follow –up period was 8 to 12 weeks. **Result:** The prevalence of dyspepsia at the University of Port Harcourt Teaching Hospital Family Medicine Clinic was 6%. The mean age of respondents was 38.7±14.5 years. The prevalence of *Helicobacter pylori* infection in this study was 44.7% with a cure rate of 81.1% using recommended eradication regime. This study also showed a statistically significant relationship between the social class and age of the subjects and *Helicobacter pylori* infection, with lower socioeconomic class and increasing age being more infected with HP. **Conclusion:** Primary care management of Helicobacter pylori infection using the near- patient testing approach with good patient outcome can reduce burden on specialist consultation and secondary care facilities.

Keywords: Dyspepsia, *Helicobacter pylori*, Primary care, Near-patient testing, ^{14}Carbon Urea Breath Test.

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Introduction

Dyspepsia is generally defined by most clinicians as the presence of upper abdominal pain or discomfort with or without other upper gastrointestinal symptoms, such as nausea, belching, vomiting, etc.[1] Dyspepsia is a common problem in the general population that frequently induces visits to the primary care physician (PCP) and most of these dyspeptic patients are managed by their PCP, with only a minority being referred for endoscopic diagnosis.[2] The prevalence of dyspepsia ranges from 7% in Singapore, 23% in Spain to 45% in Nigeria.[1]

Contact:
Andrew A. Bock-Oruma
Shawsand Medical Centre, P. O. Box 6082, Port Harcourt, Nigeria.
e-mail : bockuroma@yahoo.com
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Dyspepsia could be due to several causes such as peptic ulcer disease (PUD), reflux disease, drugs (especially non-steroidal anti-inflammatory drugs, NSAIDs), and idiopathic; with overlap of symptoms, making diagnosis difficult.[3]

The association between *Helicobacter pylori* (HP) infection and dyspeptic symptoms has long been established with HP infection having a 5% population attributable risk for dyspepsia.[1,4] HP is an important pathogen for gastroduodenal diseases and more than 50% of the world's population and nearly 73% of Nigeria's population are infected by this bacteria.[5,6] Its prevalence is highly variable in relation to age, ethnicity, gender, geography, socioeconomic status as well as the different strains of HP that appear to be associated with differences in virulence,[7] the virulence factor also affecting the clinical outcome of the disease.[8]

Helicobacter pylori infection produces a local mucosal and systemic antibody response, which

allows potential diagnosis of the infection through detection of anti- *Helicobacter pylori* IgG antibodies in the patient's serum, saliva or urine. Also, *Helicobacter pylori* antigens may be detected in the patient's stool. Another form of testing relies on the ability of *Helicobacter pylori* to produce urease, an enzyme that catalyses the hydrolysis of urea to form carbon dioxide and ammonia.[9] Its diagnosis therefore relies on the detection of its antigen or antibody in a patient's sample, with the detection of antigen giving a more precise result, considering the waning nature of antibodies especially after an infection.[10]

Various diagnostic tests for *Helicobacter pylori* have therefore been developed and they can be broadly classified into invasive and non-invasive tests. The invasive tests utilize endoscopic biopsy samples for histology, culture, rapid urease test (RUT) and polymerase chain reaction (PCR), all with sensitivity and specificity that are well above 90%. The non-invasive tests, however, do not require endoscopy. These include urea breath test (UBT), immunoglobulin G and M serology, stool antigen test, saliva antibody test and urinary antibody test.[6]

In primary care, the preferred ways of testing for *Helicobacter pylori* are serology, urea breath test, and faecal antigen test.[9, 11] The accuracy of these tests, however, has put urea breath test and faecal antigen test using monoclonal antibody test above serology test because of their higher sensitivities and specificities (C-urea breath tests were more accurate than serological tests with median sensitivity and specificity of 96.5% and 96%; vs. 91% and 90%, respectively, for laboratory-based serological tests; vs. 86% and 75.5% for near-patient serological tests; Stool antigen tests using monoclonal antibodies have sensitivity and specificity of 96% and 97%). However, the predictive value of a test also depends on the prevalence of the infection in the population, since with decreasing prevalence; there is increasing risk that a positive test result will be a false-positive result.[9]

Importantly, these tests can be performed on near-patient (or point-of-care) testing basis, affording the PCP the opportunity to perform the test at or near the location of patient care.[3, 12] Near-patient testing has the clinical and organizational advantages of decreased turnaround time, shorter therapeutic response interval or prompt therapy control and operator's level of competence is not important as a trained laboratory technician may not be required. A minor advantage is of course**,** the substantially improved convenience for the patient, the PCP and the staff performing the test. A disadvantage that can easily be tackled is the criticism from laboratory physicians and clinical scientists on the lack of analytical performance and quality control of near-patient testing.[12]

For patients with dyspepsia, the National Institute for Health and Clinical Excellence (NICE) advises primary care practitioners to adopt a 'test and treat' policy before considering a referral for gastroscopy.[11] This approach is also supported by the Maastricht 2–2000 guidelines and primary care guidelines for the management of *Helicobacter pylori* infection which recommend a test-and-treat approach without endoscopy for adult patients under 45 years presenting in primary care with persistent dyspepsia.[3] However, there is much more limited evidence on the test and treat approach in primary care facilities in Nigeria.

The management of dyspepsia is an important issue for both primary care physicians and specialists as the initial approach may dictate both patient outcome and future consumption of health care resources.

The study will provide relevant data on the near-patient testing for *Helicobacter pylori* infection in a primary care setting in Rivers State. It will provide information on prevalence of *Helicobacter pylori* infection using CUBT in the area. The study will provide information on the "test-and-treat'' approach recommended by relevant bodies. This study will go a long way in curtailing irrational use of antibiotics because of the high level of sensitivity and specificity of the test kit, since only patients with positive test result will require eradication therapy with antibiotics. It will also provide information on the family physician being the "gatekeeper'' of healthcare delivery in the country; in differentiating patients who will need primary or secondary care, manage the uncomplicated conditions, thus reduce burden on secondary care facilities.

The objectives of this study are to determine the prevalence of *Helicobacter pylori* infection, assess sociodemographic influence on *Helicobacter pylori* infection and to determine the treatment outcome of the subjects.

Methods

A prospective study of eligible and consenting dyspeptic patients that presented to the Family Medicine Clinic of the University of Port Harcourt Teaching Hospital, and a teaching primary care centre in Port Harcourt, South-South Nigeria. The study was from April to September, 2011. Follow up period was 8 to 12 weeks. Patients studied were aged 15_years and above, with dyspeptic symptoms, defined as epigastric pain, bloating,

belching or heartburn of at least two weeks' duration, attending the Family Medicine clinic, UPTH, Port Harcourt. The exclusion criteria were dyspeptic symptoms with alarm symptoms such as weight loss, bleeding, anaemia, dysphagia, jaundice and palpable mass; regular NSAIDs use; antibiotics use of two weeks or less on presentation; proton pump inhibitors and H_2-receptor blockers use and Pregnancy.

Social class definition: The Registrar-General's Social Classes based on Occupation was used in assigning individuals to classes, described as follows:

I Professional occupations
II Managerial and technical occupations
IIIN Skilled non-manual occupations
IIIM Skilled manual occupations
IV Partly-skilled occupations
V Unskilled occupations

Individuals are assigned to the classes first by being allocated to an occupational group according to the kind of work they do, then each occupational group is assigned as a whole to one of the Social Classes. [13]

Sample size estimation: The study was designed to detect a 5% difference in prevalence of *Helicobacter pylori*-related dyspepsia, with an alpha error of 5%, acceptable beta error of 20%, and a statistical power of 80%; while the estimated prevalence will be taken as 45%.[1]

Using the usual formula for sample size determination for studying proportions in populations of more than 10,000, the minimum required sample size was thus determined to be 420 (10% attrition rate inclusive).[14] A computer-generated table of random numbers was used in selecting the eligible subjects.

Ethical approval for this study was sought and obtained from the Ethics and Research Committee of the University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria.

The patients were then subjected to urea breath test (Heliprobe breath card and Analyser, Kibion AB, Uppsala, Sweden) using ^{14}carbon urea following the method described in the UBT protocol. Patients were reviewed with their results; those with positive UBT result had eradication therapy with either of three regimes available while those with negative UBT had empirical therapy with proton pump inhibitors (PPI). Adjuncts that were added to either treatment group were antacids and domperidone. The treatment regimens used were omeprazole, esomeprazole or rabeprazole 20 milligrams plus amoxicillin one gram plus clarithromycin 500 or 250 milligrams twice daily for fourteen days, with a proven efficacy of 80-95%.[15]

^{14} Carbon Urea Breath Test (CUBT): The CUBT was done for the patients using the heliprobe test kit (Heliprobe breath card and Analyser, Kibion AB, Uppsala, Sweden). It is a validated tool that can be used in a clinical setting, allowing the preparation of test results on-site in less than one hour.[16, 17] In order to carry out the UBT, after an overnight fast, the patient will swallow a ^{14}C-labeled urea-containing capsule (Helicap^{TM}) with water. The overall activity of this capsule is as small as 1 μCi (37KBq). After 15 minutes, the patient will breathe out into a dry cartridge (Heliprobe breath card, Kibion AB, Uppsala, Sweden) through its mouthpiece until the color of the card indicator changes from orange to yellow, which will take about 1min to 2min. Thereafter, the breath card will be inserted into a small desktop Geiger Muller counter (Heliprobe Analyser, Kibion AB, Uppsala, Sweden), and the radioactivity of the breath samples will be read after 250 seconds of an automated process. Finally, the test results are expressed on the liquid crystal display (LCD) of the analyzer in a numeric fashion (0: patient not infected, 1: borderline result, 2: patient infected), which corresponded to radioactivity as count per minute (CPM) : <25 CPM: patient not infected, 25–50 CPM: borderline result, >50 CPM: patient infected. UBT positive indicates HP-related dyspepsia while UBT negative indicates Non-HP-related dyspepsia.

Data analysis: The data was analyzed using SPSS™ (Statistical Program for Social Sciences) software program version 16.0. Pearson's Chi square was used for detection of differences in categorical variables between the two groups (*Helicobacter pylori* - positive and *Helicobacter pylori*- negative). All tests were done using a priori level of significance of 0.05.

Results

Three hundred and ninety-one subjects, representing 93.1% of the estimated sample size did the pre-treatment urea breath test (UBT). The mean age of the subjects was 38.7±14.5 years. The age range was 15 to 75 years. Two hundred and forty-one representing 61.8% of the subjects were female.

Majority of the subjects, 58.2% were of the lower socioeconomic class while only 21.2% were of the upper socioeconomic class (Table 1).

Table 1. Social class of the subjects

Social class	Frequency	Percentage
I	9	2.4
II	73	18.8
III	80	20.6
IV	80	20.6
V	149	37.6
Total	**391**	**100.0**

One hundred and seventy-five of the respondents representing 44.7% tested positive to the urea breath test, 3.5% were indeterminate and 51.8% were negative. This gave a prevalence of 44.7% for HPI in the family medicine clinic of the University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria (Table 2). The sex of the respondents showed that majority of them, 61.6% were females, giving a male: female ratio of 2:3. However, this did not reflect on the infectivity with *Helicobacter pylori,* since about the same proportion from both sexes tested positive to *Helicobacter pylori,* p value = 0.950 (Table 2).

Table 2. Sex prevalence of *Helicobacter pylori* infection using ^{14} Carbon Urea Breath Test (CUBT)

Sex	Heliprobe test result			Total (%)
	Negative (%)	***Borderline (%)***	***Positive (%)***	
Female	124 (51.4)	9(3.8)	108(44.8)	241 (61.6)
Male	78 (52.3)	5 (3.1)	67 (44.6)	150 (38.4)
Total	**202 (51.8)**	**14 (3.5)**	**175(44.7)**	**391(100.0)**

Pearson's Chi square = 0.004; p =0.950 (CI= 1.000-1.000).

Only thirty-seven of the one hundred and seventy-five of the subjects who tested positive representing 21%, had post treatment UBT. Thirty of the subjects, representing 81.1% had negative test results giving a cure rate of 81.1%, while 13.5% had a positive test result (Table 3).

Table 3. Post treatment ^{14} Carbon Urea Breath Test (CUBT)

urea breath test result	Frequency	Percent
Negative	30	81.1
Borderline	2	5.4
Positive	5	13.5
Total	**37**	**100.0**

There was statistically significant association between *Helicobacter pylori* infection and those within the age group of 40 - 49, 50-59 and 70-79 years. This suggests a relationship between increasing age and *Helicobacter pylori* infection (Table 4).

The result of *Helicobacter pylori* infection and social class showed a statistically significant association between *Helicobacter pylori* infection and those in social classes II and IV and V. This suggests a significant association between low socio economic class and *Helicobacter pylori* infection (Table 5).

Discussion

In general *Helicobacter pylori* infection is more frequent in developing countries than in developed countries. In developed countries, *Helicobacter pylori* infection is acquired at fairly constant rate of 2–6% per year with prevalence 20–40% in adults.[3] Nigerian data shows that the prevalence of HP infection varies widely from 26.3 to 94.5%.[4, 6] The highest rates were from seroprevalence conducted studies. In this study *Helicobacter pylori* was diagnosed in 44.8% of the patients. This is higher than result gotten from a seroprevalence study in South Eastern Nigeria,[4] but lower than results from studies done in the western and northern parts of Nigeria.[6, 18]The seemingly low prevalence of *Helicobacter pylori* -related dyspepsia from this study could be due to several reasons. Firstly, the use of over the counter medications- antibiotics, proton pump inhibitors and H_2-receptor blockers by the patients before presentation to clinic could have reduced the sensitivity of the test.[19] Secondly, the decline in the prevalence of *Helicobacter pylori* infection seen in this study may reflect the steady improvement in the hygienic state of the study population, since the setting for this study was an urban based primary care clinic.[4] Thirdly, previous studies in Nigeria and other parts of West Africa using the ^{14}CUBT (Heliprobe^{TM}) were unavailable to compare this study with. The age related prevalence of *Helicobacter pylori*- dyspepsia from this study has shown a predominance in the third and sixth decade of life. This study agrees with earler studies where it has been shown that *Helicobacter pylori* –related dyspepsia is higher in adults than in teenagers even though the infection is acquired early in life especially in the developing nations.[5, 20] However, the double-peaked prevalence could be due to earlier findings where prevalence of *Helicobacter pylori* infection increases by 2-6% per year after adolescence, reaching a plateau of approximately 50% ± 20% by the seventh decade in the developed nations,[4, 21] and this could be higher in the devloping nations.

Our study showed no significant relationship between sex prevalence of the subjects in contrast to a study done in the United Kingdom, where the

male sex was found to be associated with an increased prevalence of helicobacter pylori infection.[22]

Our study also showed that those in the lower social economic class V have a higher prevalence of *Helicobacter pylori*- related dyspepsia as compared to the upper social class I. The study also showed that *Helicobacter pylori*- related dyspepsia is associated with the lower socieconomic class as compared to the upper socioeconomic class, which is consistent with findings from other studies.[7]

The eradication rate of *Helicobacter pylori* from this study is consistent with findings from other studies where it has been shown that anti-*Helicobacter pylori* treatments using recommended regimens achieves eradication rates of 60-95%.[3, 15, 16.] This study however, recorded a low follow-up rate which is a common problem in the study setting.

Our study had several limitations. The study was conducted in an urban primary care setting which may not reflect the overall population of primary care attendees which are largely based in suburban and rural settings. The low follow up rate recorded in our study may have led to an overestimation of some of our findings. A population based study or multicentred studies is recommended to look into the cost effectiveness of the ^{14}CUBT in testing for *Helicobacter pylori* in the developing countries.

Conclusion

The prevalence of *Helicobacter pylori* infection in this study was 44.7% with a cure rate of 81.1% using recommended eradication regime. This study also showed a statistically significant relationship between the social class and age of the subjects and *Helicobacter pylori* infection, subjects with lower socioeconomic class and increasing age being more increasingly infected.

Conflict of interest: We declare that we have no financial or personal relationship(s) which may have inappropriately influenced us in writing this paper.

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Table 4. Age specific prevalence of *Helicobacter pylori* infection

Age group (years)	Heliprobe test result			Total (%)	X^2	P value
	Negative (%)	*Borderline (%)*	*Positive (%)*			
<20	7(60.0)	0 (0)	5 (40.0)	12 (2.9)	0.333	0.564
20-29	38 (41.5)	0 (0)	56 (58.5)	94 (24.1)	3.447	0.063
30-39	71 (57.4)	2 (1.9)	52 (40.7)	125(31.8)	2.935	0.867
40-49	46 (64.5)	5 (6.5)	20 (29.0)	71 (18.2)	10.242	0.001
50-59	16 (30.4)	5 (8.7)	32 (60.9)	53 (13.5)	5.333	0.021
60-69	12 (50.0)	2 (10.0)	9 (40.0)	23 (5.9)	0.429	0.512
70-79	12 (83.3)	0 (0)	1 (16.7)	13 (3.5)	9.308	0.002
Total	**202 (51.8)**	**14 (3.5)**	**175(44.7)**	**391 (100.0)**		

Table 5. Prevalence rates of *Helicobacter pylori* infection in relation to social class

Social class	Heliprobe test result			Total (%)	X^2	P value
	Negative (%)	*Borderline (%)*	*Positive (%)*			
I	2 (25.0)	2 (25.0)	5 (50.0)	9 (2.4)	1.286	0.257
II	48 (65.6)	2 (3.1)	23 (31.1)	73 (18.8)	8.803	0.003
III	46 (57.1)	0 (0)	34 (42.9)	80 (20.6)	1.800	0.180
IV	53 (65.7)	3 (2.9)	24 (30.4)	80 (20.6)	10.922	0.001
V	53 (36.0)	7 (4.8)	89 (59.2)	149 (37.6)	9.127	0.003
Total	**202 (51.8)**	**14 (3.5)**	**175(44.7)**	**391 (100.0)**		