African Journal of Basic & Applied Sciences 1 (5-6): 123-128, 2009
ISSN 2079-2034

Seroprevalence of *Helicobacter pylori* Infection in Patients with Gastritis and Peptic Ulcer Disease in Kaduna, Kaduna State, Nigeria

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Abstract: This study was carried out to determine the seroprevalence of *Helicobacter pylori* infection among patients with gastritis and peptic ulcer disease (PUD) in Kaduna state and to assess the frequency and association of the ABO blood group factor with *H. pylori* infection. A total of two hundred and twenty five (225) blood samples were collected from patients attending the Out Patient Department of three government hospitals in Kaduna State, diagnosed for gastritis and PUD. Enzyme linked immunosorbent assay (ELISA) technique was used to test for the IgM and IgG *H. pylori* antibodies in patients' serum samples. Chi square test (x^2) and odd's ratio (OR) were used to test for the association of blood group and sex with *H. pylori* infection. $P \leq 0.05$ was considered significant at 95% confidence interval. Seroprevalence for *H. pylori* was 80.4%(181). Only 22.2%(50) were positive for IgM. There was a female predominance (81.1%) over males (78.8%) but this did not reach statistical significance, $x^2 = 0.027$, p value 0.686 and OR=0.86 (0.40<OR<1.87). Although there was a high frequency of O blood group among patients (109/225), there was no association with patient's blood group and infection, $x^2 = 0.005$, p value 0.391 (P>0.05). The result showed that *H. pylori* infection is high in gastritis and PUD patients in Kaduna State and no association between infection and patient's blood group.

Key words: Seroprevalence · *Helicobacter pylori* Patients · Gastritis · Peptic ulcer

INTRODUCTION

Gastric ulcers were originally thought to be caused by excess acid in the stomach and was related to stress and dietary factors. The therapeutic measures taken however did not resolve the issue of disease recurrence [1]. Evidence of spiral-shaped Gram negative bacteria in the stomach of animals and humans was first known at the end of the 19th century but was dismissed as incidental [2]. Steer and Colin-Jones [3] observed the presence of Gram negative bacteria in 80% of patient with gastric ulcer. It was in 1983 however that two Australian physicians, Robin Warren and Barry Marshal isolated spiral-shaped Gram negative bacteria from the stomach of patients with gastritis and peptic ulceration. They made an association between their colonization and gastro-duodenal inflammation by Koch's postulates [4]. The organism was originally named *Campylobacter pyloridis* but was later given a new genus, *Helicobacter* and was named *Helicobacter pylori* [5].

Infection by *H. pylori* produces hyper gastrinaemia and gastric acid hyper secretion. The increase in gastrin is what causes an increase in acid secretion in the duodenum thereby resulting in ulceration. Local acid production in response to gastrin determines the location and severity of inflammation and the clinical outcome of the bacterial infection in individuals. This response to gastrin maybe due to variations in bacterial strains, differences between host immune responses, the pre morbid acid secretory status or interactions with dietary constituents [6, 7].

The genetics of ABO blood group, secretor and non-secretor phenotypes interact to alter an individual's risk for infection and disease by *H. pylori*. Association of this factor in relation to susceptibility towards infection by the organism has been presented [8]. Epidemiological studies have demonstrated high frequencies of the O blood group and the non-secretor phenotypes of ABH antigens among peptic ulcer patients.

H. pylori infection may lead to acute gastritis (abdominal pain, nausea and vomiting) within two weeks following infection. Many patients infected with the organism have recurrent abdominal symptoms (non ulcer dyspepsia) without ulcer disease. Duodenal inflammation

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(duodenitis) also often occurs, as well as peptic ulcer (PU). Long standing infection results in persistent inflammation which can lead to an inflammatory response of the stomach known as type B atrophic gastritis, a precursor for gastric ulcer (GU) disease and gastric cancer. Chronic infection also causes gastric mucosa associated lymphoid tissue (MALT) lymphomas. In the absence of ulcer-inducing medication of non steroid anti inflammatory drugs (NSAID) such as aspirin and ibuprofen, *H. pylori* is present in 90% of duodenal ulcer (DU) patients and 70% gastric ulcer (GU) patients [9, 10]. There is a high prevalence of *H. pylori* infection in dyspeptics and peptic ulcer disease (PUD) patients in African countries. Between 70-100% of the patients are said to be positive [11, 12]. Seropositivity of 85-88% in gastritis and PUD patients in South Western Nigeria has been reported by different authors [13-15].

Since the discovery of *H. pylori* as the important etiological agent in gastritis and PUD, investigation for this bacterium during endoscopy has become a standard clinical practice [16]. Some authors have suggested that all PUD patients should be tested for *H. pylori*. However, endoscopy is invasive, less well accepted and costly. Others recommended that all dyspeptic patients with serological evidence of *H. pylori* infection should be treated empirically with antibiotics to eradicate the infection, even before endoscopic evaluation. But some authors insist that there is still a need to endoscope in order to establish active *H.pylori* infection [13, 15]. Others claim that those in whom *H. pylori* cannot be detected by other methods have a low false positive rate by serology and that "false-positive" serology may well, in fact, reflect false-negative biopsy [12, 17].

The rationale for non-invasive *H. pylori* testing is the identification and cure of underlying disease without the need for expensive investigation [18, 19]. This "Test and treat "strategy for the management of *H. pylori* infection in patients with dyspepsia not evaluated via endoscopy or upper gastrointestinal (UGI) tract imaging is increasingly being adopted by primary care physicians in several countries of the world. In Africa there are varying opinions to the test-and-treat' strategy due to the disparity between the high prevalence of *H. pylori* infection and occurrence of clinically important disease, "the African Enigma". Between 45%-100% of Africans by the age of ten years are infected without showing any clinical symptoms [20]. This has led researchers to postulate that *H. pylori does* not play a major role in the etiologic findings of UGI system pathology, apart from gastritis [21]. Toveh and Tunstall [22] have shown that DU forms the major part of all abdominal surgery in Sub Sahara Africa in Eastern West coast comprising West African countries. A number of major cities in Africa have also been reported to have a high incidence of DU and PUD is said to be relatively common in Uganda and Nigeria [23, 24].

In Nigeria, there is considerable confusion over the management of *H. pylori* infection. There is no national or regional consensus guidelines and very few documented pathological role of the bacterium [25].

MATERIALS AND METHODS

A total of 225 patients attending the out patient department (OPD) from July to December, 2005 at three (3) hospitals in Kaduna metropolis, Kaduna State, were recruited into the study. The hospitals are attended by patients from all over Kaduna state. The patients were diagnosed for gastritis and or peptic ulcer disease by different primary care physicians in the various hospitals. Approval for the blood specimen collection was given by the various hospitals' Medical Directors and Heads of Department. Subjects gave informed consent to their participation in the study.

Subjects included in the study were aged from thirteen years, having persistent or recurrent abdominal pain or discomfort and with at least two of the symptoms of the epigastric pain and associated symptoms such as bloating, nausea, flatulence and anorexia, for up to six months in the year or years preceding the study. All subjects with recent on set dyspepsia,' alarm' symptoms of haematemesis and meleana and who have had previous case of major abdominal surgery or blood transfusion were all excluded [25, 12].

Questionnaire on the socio demographic features, medication on NSAID and antibiotic and the characteristics of the epigastric pain and symptoms were administered. The abdominal history was patterned on the basis of previously validated instrument, the Bowel Disease Questionnaire [26].

Three (3) milliliters of venous blood was drawn from the patients, using 5mls syringe. The blood was tested for group type before serum was separated. ABO blood group typing was by the slide agglutination technique, using anti-A, - B and -D sera for slide and tube agglutination, by Laboratory Diagnostic Product, Middlesex, UK.

Assay for *H. pylori* IgG and IgM antibodies in patients serum samples was according to the manufacturers of the test kits, using the principle and

technique of Enzyme Linked Immunosorbent Assay (ELISA). The test kits were manufactured by Clinotech Diagnostic and Pharmaceutical Inc., Richmond, Canada and Diagnostic Systems Laboratories Inc. Texas, U.S.A, for the IgM and IgG antibodies tests respectively. The microtitration wells in which the diluted patient's serum and control samples were incubated and previously coated with purified and inactivated *H. pylori* antigens including CagA and VacA. At the end of the reactions each well's optical density (OD) was read with a microplate reader, EIA multi-well reader II by sigma Diagnostics, U.S.A. The absorbance measured is directly proportional to the concentration of anti-*H. pylori* antibodies present in the serum samples.

RESULTS

From the serology, of the 225 gastritis and peptic ulcer disease patients tested, 181(80.4%) were positive for *H. pylori* and 44 (19.6%) were negative. Majority (159) of the patients were females with 129 (81.1%) of them being positive whereas 30 (18.9%) were negative. Of the 66 males tested, 52 (78.8%) were positive and 14 (21.2%) were negative. The test of association between sex and infection performed showed that the x^2 value was 0.027 and 0.686 was the observed level of significance ($p>0.05$). The computed odd's ratio for the test was 0.86 ($0.40<OR<1.87$) [Table 1].

The pattern of infection among age group of patients from the IgM and IgG antibodies test results was also considered.. The IgM showed a slight rise from the 10-20-years age group to almost a uniform spread among the rest age groups. The IgG however showed an increasing infection rate with age, reaching a peak at the 31-40-years age bracket and began to decline with age above 40 years (Fig 1).

Table 2 shows the frequency of patients' blood groups and infection rate of the pathogen. The O blood group had the highest frequency of the patients with 109 tested, infectivity rate was highest in blood group B with 48 out of 58 (82.8%) being positive and 10 (17.2%) negative. The next highest infectivity rate was the group O with 89 (81.7%) of the 109 tested being positive and 20 (18.3%) negative. The A group were 48 tested, 38 (79.2%) were positive and 10 (20.8%) negative. The AB blood group had the least frequency of 10 patients as well as the least infectivity rate. Only 6 (60%) of the total were positive and 4 (40%) negative. The x^2 test showed a value of 0.005 (3df), with an observed significant level of 0.391 ($p>0.05$).

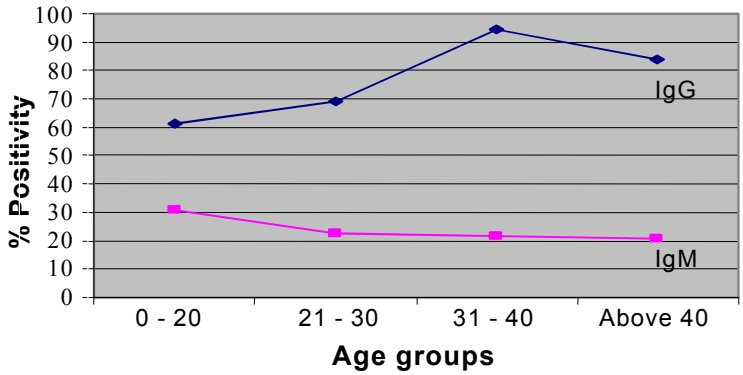

Fig. 1: Distribution of *H. pylori* IgG, IgM antibodies among age groups

Table 1: Prevalence of *H. pylori* infection in gastritis and peptic ulcer disease patients.

Sex	Number Tested	H. pylori positive (%)	H. pylori negative
Males	66	52(78.8)	14(21.2)
Females	159	129(81.1)	30(18.9)
Total	225	181(80.4)	44(19.6)

Table 2: Distribution of *H. pylori* infection by blood group

Blood group	Total number tested	*H. pylori* positive (%)	*H. pylori* negative (%)
A	48	38(79.2)	10(20.8)
B	58	48(82.8)	10(17.2)
AB	10	6(60)	4(40)
O	109	89(81.7)	20(18.3)
Total	225	181(80.4)	44(19.6)

DISCUSSION

Three patients admitted to having used non steroid anti inflammatory drugs (NSAID) for a period of time, for accident and migraine cases. These patients were negative for *H.pylori* infection. Studies have shown that idiopathic DU disease and an exaggerated meal stimulated gastrin response may be responsible for *H. pylori*-negative DU patients [6, 27]. A 69 years old woman who had no evidence of UGI tract abnormality from an ultra sound result, despite having dyspeptic symptoms was *H. pylori* positive. A number of non ulcer dyspeptic (NUD) patients are said to have the same abnormality of acid secretion as DU patients. *H. pylori* positive NUD patients, however have lower acid out put than DU patients [28]. It has been suggested that *H. pylori* may be responsible for the symptoms in a small proportion of patients with NUD. In some of these cases anti-*H. pylori* therapy may be beneficial, but this suggestion remains to be established [29].

The test of association between sex and infection rate showed that *H. pylori* infection has no significant association with sex ($P>0.05$). There are varying reports of higher prevalence of *H. pylori* infection in either males or female, but with no significant association between the infectivity rate and sex [13, 15].

The peak of infection in this study was 31-40 age brackets with 94.5% seropositivity (Fig. 1). [30] reported that the fifth decade of age was the peak of infection among dyspeptic patients in Ghana. Peak incidence of peptic ulcer is between 55 and 65 years of age and this in part is said to be explained by the fact that older people are at highest risk of *H. pylori* infection. It has been suggested that a non-invasive *H. pylori* test and treat policy may be as appropriate as early endoscopy for the initial investigation and management of patients more than fifty five years presenting with uncomplicated dyspepsia [31, 32].

The low percentage of IgM incident rate of 22.2% as recorded in the serology is a further indication of the chronic condition of the subjects studied. Studies have shown that adult responses are very transient since most would have been colonized by *H. pylori* for decades. However, IgM antibody detection may reflect whether or not an acute infection exists [33, 34]. Association of blood group has been implicated as a risk factor for *H. pylori* infection. The people with blood group O especially, were earlier observed to be 1.5 to 2 times more likely to develop ulcer than people with type A and B. This frequency was observed in this study (Table 2) as 109 out of 225 patients recruited in the study were of blood group O. However, there was no statistical association between the infection rate and patients blood group in the study. The fact that other blood groups still get ulcers, as recorded in the study may be explained by the possession of other adhesins for attachment and colonization of hosts by *H. pylori* [35, 36]. It has been demonstrated that mucin-binding properties of *H. pylori* to gastric mucous can be affected by pH. At acidic pH all *H. pylori* strains can bind to the MUC5AC mucin molecule irrespective of host blood group [37].

CONCLUSION

The findings in this study show that there is a high prevalence of *H. pylori* infection in gastritis and peptic ulcer disease patients in Kaduna State. None of the patients recruited for the study was previously recommended for *H. pylori* infection test by the various primary care physicians. The patients were treated either by use of acid suppressing drugs and/or by empiric anti-*H. pylori* therapy. There was no association between *H. pylori* infection and patient's blood group.

Recommendations: There is a need to improve our understanding of the modes of transmission, immuno pathogenesis of the associated UGI tract diseases, diagnosis and treatment regimen of *H. pylori* infection in our region. Diagnosis for *H. pylori* infection in our region is very difficult. Endoscopic procedure is invasive and very costly and would not be affordable by the majority of patients. Serology has been used for initial pre endoscopy or pre-treatment screening in dyspeptic patients [38]. The presence of serum IgG antibody is closely associated with infection found in microbiological and histological methods [39, 40]. Serological kits should be specially manufactured for local use and antigens in such kits should be from local *H. pylori* strains [41].

Doctors would not automatically check for *H. pylori* because changing medical belief and practice takes time. There is a need therefore to establish national and regional consensus guidelines on the management of *H. pylori* infection in gastritis and peptic ulcer disease patients.

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