Hiv And *Helicobacter Pylori* Co-Infection In Dyspeptic Patients In Abeokuta, Nigeria.

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Abstract: Synergistic severity of *H. pylori* and HIV co-infection in dyspeptic patients and its seroprevalence by socio-economic and environmental factors in this locality was studied. 109 confirmed seropositive HIV patients suffering from dyspepsia were tested for the presence of *H. pylori* IgG antibodies from 230 patients, attending out-patient clinics of Sacred Heart Hospital, Abeokuta, Nigeria. 47.4% has *H. pylori* and HIV antibodies with significant *H. pylori* IgG titre more than 1:40. 29.4% was recorded in age group 26-35 while 3.5% was recorded in 66-75. Female subjects were more predisposed having 52.7% to the disease while 27.5% have malaria as associated disease. Unemployed individuals are 17.4% with a significant titre of 1:60 compare to artisan with 36.7% prevalence rate but with low titre of 1:20. Low CD4 count of 213cell/mm3 among 17.4% unemployed and 405 cell/mm3 among 36.7% artisan was observed. Prevalence of *H. pylori* in HIV is correlated to poor socio-economic condition (that is low daily income), associated low-level of education and overcrowding which could predispose many HIV seropositive individuals to severe dyspepsia and other severe disease conditions.

[Ejilude O., Akinduti P.A, Idowu M, Ogunbileje J.O , Akinbo J.A. **Hiv And *Helicobacter Pylori* Co-Infection In Dyspeptic Patients In Abeokuta, Nigeria.** New York Science Journal 2011;4(9):1-5]. (ISSN: 1554-0200). http://www.sciencepub.net/newyork.

Keywords: Dyspepsia, HIV, *Helicobacter pylori*

INTRODUCTION

Until 1980s, peptic ulcer was seen as a disease of excessive gastric acid production with non-malignant duodenal and gastric ulcer resulting in considerable mortality and morbidity (Megraud, 1993). In recent past, induction of gastric infection in a host usually causes mucosa damage and chronic active gastritis which could progress to active non-ulcerated dyspepsia. This has been strongly associated with gastroduodenal peptic ulcer and gastric adenocarcinoma (Ananthakinshman *et al*, 1998). Host immune response in HIV and *H. pylori* co-infection reduces CD4 count when helper T-cells are involved (Newell, 1991; Barua *et al*, 1997). Patients living with HIV usually have low *H. pylori* prevalence and peptic ulcer than HIV negative individuals with similar symptoms (Hida et al, 1999; Smythies et al, 2000). The mechanism of chronic active gastritis in HIV seropositive may be different from HIV negative with various opportunistic infection of upper GIT which is likely to occur in HIV seropositive with CD4 lymphocyte count less than 200/mm^3 (Andersen et al, 1992; Forman , 1992). In an Italian study, prevalence of both *H. pylori* colonization and peptic ulcer disease were noted, and these both correlated with CD4 count (Dubois, 2000; Cacciarelli et al, 2006). Increasing dyspepsia caused by *H. pylori* in HIV seropositive individuals in this locality was observed to be linked to the socio-economic factor and their life-style. Therefore, this study was conducted to evaluate synergistic severity of *H. pylori* and HIV co-infection in dyspeptic patients and its seroprevalence in poor socio-economic and environmental condition that persist in this locality.

MATERIAL AND METHODS

Study area: the patients recruited for this study were among the outpatients visiting the Sacred Heart Hospital, Abeokuta which serves as referral centre for endoscopy and HIV infection and it is located at Latitude 7^0 15N and Longitude 3^0 25E, 106km North of Lagos and 81 km from Ibadan which were among the most populated towns in South Western Nigeria (NPC, 2007).

Study population: Total of 109 confirmed seropositive HIV patients suffering from dyspepsia were tested for the presence of *H. pylori* IgG antibodies from 230 patients having various symptomatic gastritis, peptic ulcer and gasrtric adenocarcinomal. The study was conducted between June, 2005 to July 2007 at Sacred Heart Hospital, Abeokuta; which is one of the hospitals that manage largest populace of peptic ulcer patients in South-western Nigeria ethical permission.

***H. pylori* IgG Detection**:

Each serum obtained from the patients were analysed for *Helicobacter pylori* IgG antibodies using enzyme immunosorbent assay technique (EIA) to quantify the titre of IgG in each respective sera using Immunocomb (R)II Helicobacter pylori IgG test kit having excellent sensitivity of 92.1% and specificity of 80.75%. 25ul of diluted serum was reacted with commercially prepared inactivated Helicobacter pylori antigen and after 30 minutes reacted with goat anti-human IgG antibodies labelled with alkaline phosphatase. Newly formed conjugated anti-human complex was reacted after washing with chromogenic substrate solution containing 5-bromo-4-chloro-3-indolylphophate (BCIP) and indicator nitro blue tetrazolium (NBT). The test was performed at room temperature. Titre of IgG was determined according to manufacturer's description taking significant titre at $\leq$1:40.

HIV Antibody detection:

Sera from the blood samples were screened for HIV-1/2 antibodies using Determine™ test kit based on qualitative immunochromogenic assay detection of antibodies to HIV-1 & 2 (Immunocomb(R)II Helicobacter pylori, Orgenics Limited, Yavne, Israel) and CHEMBIO Diagnostic system, Inc; HIV-1/2 stat-pack dipstick assay which is a single immunochromatographic screening to detect antibodies to HIV 1 and 2, according to manufacturer description with sensitivity of 99.91% and excellent specificity of 98.16% to HIV antibodies . These two HIV test kits were recommended as national algorithm standard for HIV diagnosis (Badaru et al, 2004). Screened positive samples were further confirmed for HIV antibodies using Genscreen HIV enzyme immunoassay which its p24 HIV monoclonal antigen and gp160 recombinant antigenic protein containing artificial functional consensus polypeptide composed of variable sequences of HIV 1 & 2.

Western blotting: Each screened positive sera was further confirmed using Western blotting (New LAVBLOT1; Sanofi Diagnostics).

CD4 Count: Peripheral blood CD4 counts were carried out using a PARTEC easy count kit (Partec GmbH, Germany) flow cytometric analysis according to the manufacturer's instructions.

Statistical analysis: Proportions were compared using a descriptive student t-test and χ^2 test at 95% confidence intervals (95% CI). It was observed to be statistically fit.

RESULTS:

Out of 230 dyspepsia patients examined, 109 (47.4%) were HIV positive and with clinical co-infection with H. pylori. Table 1 shows titre of 1:40 with high prevalence rate of 29.4% in age group 26-35 while a low rate of 3.5% was recorded in 66-75 age group. Peptic ulcer, as associated disease shows 10.1% rate with high significant titre of 1:120 while malaria which has become pandemic in West Africa shows prevalence rate of 27.5% in Table 2. From Table 3; female subjects were more predisposed having 52.7% to the diseases than male individuals showing 47.4%. Socio-economic status of the subjects tested show that unemployed are the high risk group to H. pylori infection and HIV showing 17.4% with a significant titre of 1:60 compare to artisan with 36.7% prevalence rate but low titre of 1:20. Low CD4 count of 213cell/mm3 among 17.4% unemployed and 405 cell/mm3 among 36.7% artisan was observed.

TABLE 1: **Age distribution of *Helicobacter pylori* IgG antibody titres in HIV patients**

Age group	*Seropositive Subjects n(%)*	*Seropositive Mean IgG titre (ul/ml)*	*Seronegative subjects n(%)*	*Seronegative Mean IgG titre (ul/ml)*	*Control subjects n(%)*	*Control Mean IgG titre (ul/ml)*
15-25	21/31(19.3)	1:20	10/31(38.7)	<1:20	1/21(4.76)	1:20
26-35	32/39(29.4)	1:40	7/39(17.9)	<1:20	2/11(18.18)	1:20
36-45	28/60(25.7)	1:20	32/60(3.3)	<1:20	0/20(0.0)	1:20
46-55	19/52(17.4)	1:60	33/52(3.8)	<1:20	2/22(9.09)	1:20
56-65	5/34(4.6)	1:60	29/34(11.8)	<1:20	2/14(14.29)	1:20
66-75	4/14(3.5)	1:40	10/14(28.6)	<1:20	1/12(8.33)	1:20
TOTAL	**109/230(47.7)**		**21/230(8.3)**		**8(0.08)**	

N=109 Mean=18.2 SD=11.58 p<0.05

TABLE 2: **Associated disease conditions in HIV+ patients with *H. pylori* IgG antibody.**

Disease condition	Seropositive N(%)	MEAN TITRE (U/ml)
Anaemia	19(17.4)	1:20
Malaria	30(27.5)	1:40
Sepsis	3(2.8)	1:20
Diarrhoea	21(19.3)	1:40
Burns	1(0.9)	1:20
Gastritis	14(12.8)	1:90
Pneumonia	10(9.2)	1:20
Peptic ulcer	11(10.1)	1:120

N=109 mean=13.6 SD=9.59 p=0.005

TABLE 3: Seropositive prevalence of *H. pylori* IgG in HIV patients by sex distribution.

Sex	Rate N(%)	Mean IgG Titre U/ml
MALE	52/105 (47.7)	1:40
FEMALE	57/125 (52.3)	1:40

TABLE 4: Socio-economic determinant of HIV patients with *H. pylori* IgG antibody.

Occupation	Seropositive n(%)	Mean IgG U/ml	CD4 Count Cell/mm^3
Artisan	40(36.7)	1:20	405
Civil servant	20(18.3)	1:40	325
Student	30(27.5)	1:40	236
Unemployed	19(17.4)	1:60	213

N=109 mean=27.25 SD=9.84 P>0.005

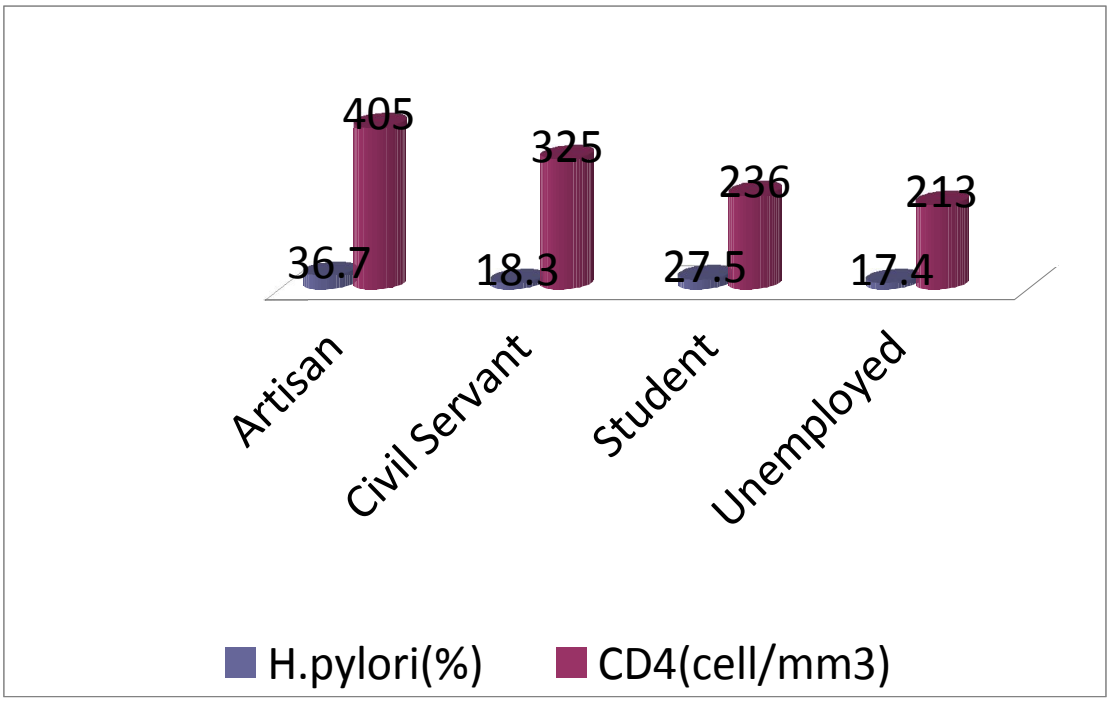

Figure 1; H.pylori IgG antibody and CD4 cell count distribution

DISCUSSION

This study is in agreement with Vaira *et al* (1995) showing that serology is a reliable marker for *H. pylori* infection in HIV seropositive patients, including those with advanced diseases (Enroth *et al,* 2001). The prevalence rate of *H. pylori* in HIV subjects was 47.4%, indicating a very high prevalence HIV and *H. pylori* co-infection in apparent dyspepsia patients. This does not correlate with a study by Fernando, (2001) who suggested a discordance of HIV and *H. pylori* with 35% prevalence among impoverished people in urban area (Vaira, 1995). High seroprevalence of *H. pylori* IgG in HIV patients according to their age group indicate 29.4% in 26-35 age group while 25.7% was recorded in 36-45 age group with an average significant IgG titre of 1:60U/ml. The significant IgG titre recorded by age group was contrary to a report that in developing countries where IgG seropositivity is low in childhood and rises slowly at age approximately 0.5% per year while in developed world the infection is acquired in early childhood with prevalence of 70% by age of 5 (Dubois, 1995).

Peptic ulcer as an associated disease in HIV subject with *H. pylori* IgG has 10.1% rate with a very high significant *H. pylori* IgG titre of 1:120U/ml while less IgG titre of 1:20U/ml is observed in malaria with high rate of 27.5%. Female subjects are more predisposed, having high rate of 52.3%. gender inequality cannot be outright yardstick for

demographic distribution of H. pylori in this settings. Socio-economic determinant of HIV seropositive patient with *H. pylori* IgG antibodies is high among the artisans which were primarily carpenter, trader, shoe cobbler and petty traders showing 86.7%. Surprisingly, a very high IgG titre of 1:60U/ml was observed among unemployed individuals with 17.4% rate. This high prevalence of dyspepsia in HIV seropositive unemployed subjects reflect severe *H. pylori* infection among a populace with poor socio-economic support for living where many of them would live with hunger and prone to unprotected sex to make a living for themselves and their immediate family. Thereby contracting HIV/AIDS. A very low CD4 cell count of 213cell/mm3 recorded among the unemployed indicate a significant association of poor socio-economic conditions and poor daily income with prevalence of *H. pylori* and compromised immunity (Olmos *et al*, 2004). The co-infection of HIV and *H. pylori* can debilitate the defence humoral immune mechanism of these patients and increase morbidity and mortality over a short period of time.

Adults with HIV infection and/or a low CD4 count would loose the tropic mechanism by which *H. pylori* colonization is sustained, and infection intensity which would diminish with adequate antibiotic therapy with effective reduction of gastric acidity. Gross gastroduodenal pathology may sometimes be related to opportunistic infections in AIDS patients with low CD4 counts rather than to *H. pylori* (Dempsey *et al*, 2005) which could induce a vigorous humoral antibody response. Despite humoral antibody induced by the infections, only adequate antiretroviral therapy administered regularly could improve the patient's health status (Johnson, 2000). Genetic immune polymorphism in the host, would favours pro-inflammatory factors like interleukin IL-1, the most potent inhibitor of gastric acid secretion but could increase the risk of gastric cancer by the host and bacteria factors (Okodua *et al*, 2003). A low CD4 cell count of 213 cell/mm3 in 17.3% unemployed being positive with HIV and *H.pylori* antibody of 1:60 suggest that CD4 cells play a specific role in inducing gastritis, by which *H. pylori* colonization is enhanced by increasing transexudation of serum components. During this specific immune response, immature T helper (Th) cells expressing CD4 can differentiate into two functional subtypes: Th1 cells, secreting interleukin- 2 and interferon, and Th2 cells, secreting interleukin- 4, interleukin-5, and interleukin-10. Whereas Th2 cells stimulate B cells in response to extracellular pathogens, to inactivate *H. pylori which* is non-invasive and induces a strong humoral responses (Smythies *et al*, 2000; Harris *et al*, 200). Therefore, this co-infection of HIV and *H. pylori* compromises the defence humoral immune mechanism of patients making them vulnerable to other opportunistic infections. Public health awareness on HIV spread should be encouraged while risk factors to *H. pylori* infection such as smoking, alcoholism and abuse of drug mostly among the unemployed or poor socio-economic individuals must be emphasized with adequate HIV management.

Management and Recommendation

For effective therapeutic management of dyspepsia in HIV patients, smoking, alcoholism and use of NSAIDs should be avoided. Surgery may still be considered as the mainstay for complicated peptic ulcer disease in HIV seropositive patients but slow healing of surgical wound on gastric mucosa could as well pose a deadly threat due to septicemia, poor immune compensation and long term sequelae (Malaty *et al*, 1992).

In conclusion, public health awareness on HIV spread should be encouraged while risk factors to *H. pylori* infection must be emphasized with adequate HIV management.

Acknowledgement:

The authors acknowledge the support of the management and specially Medical Director of Sacred Heart Hospital, Lantoro, Abeokuta and all laboratory staff for their effort.

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3/22/2011