



High Prevalence of *Helicobacter pylori* Infection, Atrophic Gastritis and Hypochlorhydria in HIV-Positive Cameroonians Tested by Serological Stomach-Specific Biomarkers (GastroPanel®)

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Authors' contributions

This work was carried out in collaboration among all authors. Author AIE conceptualized and together with author VNN, designed the study. Authors AIE, VNN, NKT, LBM, MNI and SPA carried out sample collection, analysis, interpreted the data and drafted the manuscript. Authors LAN, NND, PL and KS provided technical advice and corrected the manuscript. Author KS is the director of this work and responsible for the general supervision of the study. All authors read and approved the final manuscript.

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ABSTRACT

Background: The human immunodeficiency virus (HIV) and *Helicobacter pylori* (*H. pylori*) are associated with significant chronic inflammation of the gastric mucosa. Gastric inflammation is a precursor to many gastrointestinal disorders including, peptic ulcer disease, atrophic gastritis (AG) and gastric cancer (GC). AG is usually accompanied by low hydrochloric acid (hypochlorhydria), low pepsinogens (PG) and high gastrin (G) levels and is the most significant risk condition for GC. Acid-free stomach is a risk factor for impaired drug absorption including anti-retroviral therapy and antibiotics. The role of *H. pylori* infection in HIV-infected subjects has been conflicting.

Objectives: We assessed the prevalence of *H. pylori* infection, AG and acid-free stomach (hypochlorhydria) amongst HIV/AIDS subjects in Yaounde Cameroon.

Methods: HIV/AIDS subjects were recruited during January-May 2018. Clinical and socio-demographic data of the subjects were recorded. An aliquot of 5 ml of blood was aseptically collected for analysis by GastroPanel® biomarker test for PGI, PGII, G-17 and *H.pylori* IgG antibodies. GastroPanel results were interpreted using the software application GastroSoft®. Statistical analyses were run by Epiinfo7.0. Ethical clearance was obtained from the National Ethics Committee.

Results: A total of 84 subjects were recruited, aged between 17-63 years (mean 37.6 ± 8.9 years). *H. pylori* seropositivity (IgG ≥30 EIU) was detected in 68(81.0%) of the subjects. *H. pylori* seropositivity was closely associated with low CD4 counts (p=0.01). Altogether, 26(31.0%) of the subjects presented with AG of the corpus while, hypochlorhydria was detected in 32(38.1%) of the patients. AG and hypochlorhydria were associated with low CD4 counts <200µl/l (p=0.01) and (p=0.005), respectively.

Conclusion: *H. pylori* infection, AG and acid-free stomach were common among HIV/AIDS patients, associated with an increased risk for GC and impaired absorption of micronutrients and some medicines.

Keywords: *Helicobacter pylori*; atrophic gastritis; hypochlorhydria; HIV; serological biomarkers.

1. INTRODUCTION

Human immunodeficiency virus (HIV) infection is common in Cameroon. It is estimated that over 600,000 persons live with HIV, with a population prevalence of 4.8%. Dyspepsia-like symptoms are very frequent amongst HIV/AIDS subjects during the course of their disease [1]. *Helicobacter pylori* (*H. pylori*) remains one of the most common infectious agents worldwide, with an estimated prevalence of >80% in certain underprivileged populations in Africa [2]. *H. pylori*-associated chronic active gastritis usually progresses into atrophic gastritis (AG) and acid-free or hypochlorhydric stomach, both being well established risk factors of gastric cancer (GC) [3].

HIV and *H. pylori* are associated with marked chronic inflammation of the gastric mucosa. Once progressed to AG, this chronic inflammation leads to hypochlorhydria and finally acid-free stomach, characterized by low serum levels of pepsinogen I and II (PG I and PGII), and refractory elevation of serum gastrin levels. Apart from GC, acid-free stomach is a risk factor for enteric infections and impaired

absorption of drugs, including those used in anti-retroviral therapy and antibiotics [4].

Gastrins are peptide hormones that stimulate gastric acid (HCl) output by gastric parietal cells, the biologically most active being gastrin-17 (G-17). G-17 release by G-cells in the gastric antrum is stimulated by the presence of food in the stomach [5-8]. G-17 release is also regulated by feedback inhibition via somatostatin from the adjacent D-cells in the presence of a low gastric pH [9]. High fasting blood levels of G-17 are typical to patients with chronic gastritis (caused by *H. Pylori* infection or autoimmune disease) [9,10]. Chronic AG leads to the loss of parietal cells in the corpus, with hypochlorhydria, acid-free stomach and high G-17 levels as end results.

H. pylori infection itself can also cause mild increase of G-17, triggered by the inflammatory process in the mucosa [4]. Several studies have reported higher serum G-17 concentrations among HIV-positive patients [11,12] while one study failed to demonstrate any effect of THE HIV-status on serum gastrin levels [13]. The role of *H. pylori* infection in HIV-infected subjects has been conflicting. Several studies have reported

low prevalence of *H. pylori* amongst HIV- positive subjects [1,2,14-17]. In contrast, higher *H. pylori* prevalence has been reported in some other studies [4,18,19].

Endoscopy with targeted mucosal biopsies is effective in screening of the upper GI-tract malignancies. However, this invasive method is uncomfortable, distressing and quite costly, emphasizing the need for rapid, reliable and inexpensive non-invasive tests [20,21]. Recently, a plasma biomarker panel with combination of PGI,–PGII, G-17 and *H. pylori* IgG antibodies using an ELISA technique was developed, known as GastroPanel® test (BiohitOyj, Helsinki, Finland). GastroPanel is intended for the first-line diagnosis of dyspeptic patients and for screening of the risk groups of GC, i.e. to detect the subjects with AG [22-25]. In the present study, GastroPanel test was used to assess the prevalence of *H. pylori* infection, AG and hypochlorhydriain HIV/AIDS patients (in Yaounde, Cameroon), with biomarker levels related to the CD4 counts.

2. METHODS

We undertook a cross sectional study and patients presenting with HIV/AIDS and followed up at the Jammot Hospital of Yaounde Cameroon and consented to participate were prospectively recruited during the five-month period January-May 2018. Authorizations were obtained at the Jammot Hospital of Yaounde, and ethical approval was granted by the National Ethics committee (No 0174/CRERSHC of February 05th 2018). All patients signed an informed consent.

Clinical and socio-demographic information of patients were recorded. As an essential anamnestic data for GastroPanel test, the participants were enquired for their intake of non-steroidal anti-inflammatory drugs, treatment of antibiotics, use of proton pump inhibitors (PPI), H2-receptor antagonists and anti-retroviral therapy.

For the GastroPanel test, an aliquot of 5 ml of blood was aseptically collected in EDTA anticoagulated tubes, which was kept undisturbed for 1 hour for plasma formation. The tubes were subsequently centrifuged at 1500rpm for 5 minutes. The plasma obtained was transferred into sterile cryotubes and stored at -20°C, for GastroPanel analysis, following the manufacturer's instructions. The biomarker profiles for PGI, PGII, G-17, and *H.pylori*

IgGwere interpreted using theGastroSoft software application [26]. All patients with *H. pylori* IgG≥ 30 EIU were considered positive for *H. pylori* infection. All patients with PGI < 30 µg/l and/or PGI/PGII < 3.0 and those with G-17 < 1pmol/l were considered positive for AG of the corpus and AG of the antrum,respectively. Subjects with G-17 >7pmol/l were considered as having hypochlorhydria.

All statistical analyses were conducted by Epi Info software 7.0 (the Centers for Disease Control and Prevention, CDC, Atlanta, GA, USA). All statistics were realized at 95% CI and a p-value <0.05 was regarded as statistically significant.

3. RESULTS

Altogether, 84 subjects with HIV/AIDS were recruited, aged between 17-63 years, with a mean age of 37.6 ± 8.9 (SD) years. Of the 84 patients, 54(64.3%) were females (aged 21-63,mean 36.7 ± 8.6 years) and 30(35.7%) were males aged 17-60, mean 39.1 ± 9.6 years. Elevated levels of Anti *H. pylori* antibodies (IgG ≥ 30 EIU) were detected in 68/84 (81.0%) of the patients. In all age groups, higher seroprevalence of anti *H. pylori* antibodies were noticed in the HIV subjects Table 1, with *H. pylori* seroprevalence of 83.3%, 77.3% and 100.0% in HIV+ age groups 17-35, 36-54 and 55-73 years, respectively (p=0.48). *H. pylori* IgG seropositivity was not associated with the sex; females (85.2%) and males (73.3%), (p=0.10).*H. pylori*seropositivity was significantly associated with low CD4 counts (p=0.01). When AG was classified into various grades, 52(63.9.0%) presented with non-atrophic (superficial Hp-gastritis) while 26(31.0%) were diagnosed with AGof the corpus. In addition, 32(38.1%) of the subjects presented with hypochlorhydria Table 2. AG and hypochlorhydria were associated with low CD4 counts<200µl/l (p=0.01) and (p=0.005), respectively. High G-17 levels (G-17 >7pmol/l) were more frequently associated with AG of the corpus than with superficial gastritis (16.44±18.40 vs. 10.03±9.2pmol/l; p=0.03). The same is true with G-17 levels and hypochlorhydria as compared with normal acid levels (15.26±16.73 vs. 10.02± 9.73pmol/l).

4. DISCUSSION

The role of *H. pylori*infection among HIV-infected subjects remains controversial [1,19]. In the present study, seropositivity of*H. Pylori* was

68/84 (81,0%), which is very similar as previously reported among dyspeptic subjects in Cameroon [27] (81,40%), [28] (79,80%), [22] (78,7%) and in some other countries e.g. 76,5% in Kazakhstan [20]. This *H. pylori* seroprevalence is also similar with that (80.5%) reported previously in diabetic subjects in our country [29]. This high prevalence of *H. pylori* among HIV/AIDS subjects is in alignment with the figures reported from other countries including: Malawi using histology (71,6%) [4], as well as Ethiopia using IgG serology (85,6%) [19].

However, the seroprevalence of 81% in the present study is substantially higher than detected among HIV/AIDS patients in some other countries using different detection techniques, including histology and a rapid urease test (RUT) in Cameroon (59%) [30], and 50% [1], respectively. The figures were even lower (37.2%) in Brasil [15], those obtained by

histology (22,1%) in China [14]; stool antigen test (SAT) in Uganda (22,5%) [17], or those (46.8%) in Nigeria [16]. Undoubtedly, these divergent figures in the prevalence of *H. pylori* reported among HIV-subjects are due to different diagnostic techniques. Histology, UBT and SAT used in most studies are associated with false negative results especially in certain medical conditions such as peptic ulcer, AG, MALT lymphoma and partial gastrectomy [24,25,31-34]. In addition, decreased bacterial load may result from prolonged use of certain medications with antimicrobial properties including PPI, NSAIDs and antibiotics, and lead to false negative results in many studies [24]. On the other hand, UBT may also give false positive results in cases where acid-free stomach is colonized by urease-positive bacterial species other than *H. pylori* [35]. These false negative and false positive results in *H. pylori* diagnosis can now be avoided with the simple GastroPanel test [23,24,35].

Table 1. Socio-demographic data of the HIV- subjects related to *H. pylori* serostatus

	<i>H. pylori</i> Positive (IgG\geq30EIU) 68(81.0%)	<i>H. pylori</i> Negative (IgG<30EIU) 16(19.0%)	P-value
Pepsinogen(PGI/ μ g/l)	94.63 \pm 87.73	126,8 \pm 126,2	0.23
Pepsinogen(PGII / μ g/l)	50.53 \pm 38.06	30,18 \pm 24,63	0.045
PGI/PGII ratio	4.49 \pm 11.07	3.68 \pm 1.33	0.80
Gastrin-17(G17/pmol /l)	13.2 \pm 14.23	7.76 \pm 2.79	0.15
<i>H. pylori</i> (IgG / EIU)	260.27 \pm 203.27	21.00 \pm 4.78	0.00001
CD4	54(84.4%)	10(15.6%)	0.01
0-199	10(83.3%)	2(16.7%)	
200-499	2(33.3%)	4(66.7%)	
500-1000			
Sex	22(73.3%)	8(26.7%)	0.10
Males	46(85.2%)	8(14.8%)	
Females			
Age(yrs)	30(83.3%)	6(16.7%)	0.48
17-35	34(77.3%)	10(22.7%)	
36-54	4(100%)	0(0.0%)	
55-73			
ATB	26(76.5%)	8(23.5%)	0.20
Yes	42(84.0%)	8(16.0%)	
No			
NSAIDS	4(50%)	4(50%)	0.04
Yes	64 (84.2%)	12 (15.8%)	
No			
PPI	22(100%)	0(0%)	0.004
Yes	46(74.2%)	16(25.8%)	
No			
HAART	18(69.2%)	8(30.8%)	0.07
Yes	50(86.2%)	8(13.8%)	
No			

ATB: antibiotics, NSAIDS: non steroidal anti inflammatory drugs, PPI: proton pump inhibitors, HAART: highly active antiretroviral therapy

Table 2. Atrophic gastritis (AG) and hypochlorhydria in HIV-positive subjects

	Atrophic Gastritis C:(PGI <30µg/l) 26(31.0%)	Non atrophic Gastritis S: 58(69.0%)	p-value	Hypochlorhydria Yes(G17>7pmol /l) 32(38.1%)	Hypochlorhydria No 52(61.9%)	p-value
Pepsinogen PGI (µg/l)	28.37 ± 8.93	133.31 ± 99.84	0.00001	56.32 ± 86,12	128.2 ± 92.4	0.001
Pepsinogen PGII (µg/l)	42.29 ± 41.58	48,61± 34,43	0,47	42,14±39,92	49.42±34.59	0.38
PGI/PGI ratio	1.19 ± 1.02	5.62±11.75	0.06	1.74 ± 1.49	5.79 ± 12.41	0.07
Gastrin-17 G17(pmol /l)	16.44±18.40	10.03±9.2	0.03	15.26±16.73	10.02 ± 9.73	0.07
H. pylori IgG(EIU)	204.4± 254.9	219.3± 181.7	0.76	170.8 ± 239.7	241.7± 178.7	0.13
CD4	26(40.6%)	38(59.4%)	0.005	28(43.8%)	36(56.3%)	0.006
0-199	0(0%)	12(100%)		0.00	12(100)	
200-499	0(0%)	6(100%)		4(66.7%)	2(33.3%)	
500-1000						
Sex	10(33.3%)	20(66.7%)	0.36	12(40.0%)	18(60.0%)	0.40
Males	16(29.6%)	38(70.4%)		20(37.0%)	34(63.0%)	
Females						
Age(yrs)	14(38.29%)	22(61.71%)	0.21	16(44.4%)	20(55.6%)	0.21
17-35	12(27.3%)	32(72.7%)		16(36.4%)	28(63.6%)	
36-54	0(0%)	4(100%)		0(0%)	4(100%)	
55-73						

Although the majority of *H. pylori* infections and AG have been associated with age and male gender [9,36,37], we did not find any association of *H. pylori* prevalence with age($p=0,48$) or sex ($p=0,10$). However, we observed an elevated *H. pylori* prevalence among subjects with low CD4 ($p=0.01$) Table 1. This observation was not confirmed in some studies [1,2,30]. Given that *H. pylori* infection is usually contracted at childhood, it could have facilitated the destruction of CD4 cells by HIV-virus. According to Magen et al. [18], *H. pylori* stimulates the activation of CD4+, CCR5+ and CCR4+ which are receptors and co-receptors for HIV.

In the present analysis of GastroPanel biomarker profile, AG of the corpus occurred in 26 (31,0%) of the subjects (PGI $<30\mu\text{g/l}$) and low acid output (hypochlorhydria) in 32 (38,1%) ($G-17>7\text{pmol/l}$) of the study subjects. This high prevalence of AG of the corpus and hypochlorhydria among HIV subjects substantiate the figures reported in previous studies [1,15,30]. Such a high prevalence of AG is, however, in contrast to what has been reported among dyspeptic subjects [22,23,27,28,38,39,40]. This high prevalence ($>30\%$) of corpus AG implicates that HIV/AIDS patients are at substantially higher risk of GC as compared to the general population.

In addition, we observed a close association between low CD4 counts and 1) AG ($p=0,005$) as well as 2) hypochlorhydria ($p=0,01$). Similar observations have been reported before [4,30]. AG and hypochlorhydria (low acid output) observed in HIV/AIDS subjects may suggest the risk of enteric infections, poor absorption of ARV, Vitamin-B12, and certain divalent micronutrients including iron, calcium, magnesium and zinc [3-10,41], with increased risk of clinically important sequels, like cognitive disorders, neurodegenerative and vascular disorders, encephalopathies, anemias and osteoporosis.

5. CONCLUSIONS

We report high prevalence of *H. pylori* infection amongst HIV/AIDS subjects similar to those in dyspeptic and diabetic subjects. We also report high prevalence of atrophic corpus gastritis and hypochlorhydria in these patients. *H. pylori* infection and AG represent the most important risk factors for GC and oesophageal cancer. Accordingly, HIV/AIDS subjects may be at increased risk of GC and impaired absorption of micronutrients and some medicines, thus requiring continuous monitoring

and follow-up. This can be neatly accomplished by non-invasive GastroPanel test, closely reflecting both the structure and function of the stomach, in addition of being the most comprehensive test for *H. pylori* infections, devoid of the limitations of UBT and SAT tests [35].

CONSENT AND ETHICAL APPROVAL

Ethical clearance was obtained from Center Regional Committee for Research on Human Health (CRERSH) No 0174/CRERSHC/2018 of 05 February 2018. An authorization was obtained from the authorities of the Jamot Hospital of Yaounde. All patients signed an informed consent form.

DECLARATION

Availability of data and materials : All data used during the current study are available from the corresponding author on reasonable request.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Andoulo FA, Kowo M, Ngatcha G, Ndam AN, Awouoyiegnigni B, Sida MB. Prévalence de l'infection à *Helicobacter pylori* au travers de l'endoscopie digestive haute chez les patients VIH/sida avec des symptômes gastro-intestinaux dans les hôpitaux universitaires au Cameroun, Med Sante Trop. 2016;26:278-82.
2. Nevin T. Daniel, Morgan J. Christopher, Graham Y. David and Genta M. Robert. *Helicobacter pylori* gastritis in HIV- infected patients: A review. Helicobacter; 2014. DOI: 10.1111/hel.1213
3. Agréus L, Kuipers EJ, Kupcinskas L, Malfertheiner P, Di Mario F, Leja M. Rationale in diagnosis and screening of atrophic gastritis with stomach-specific plasma biomarkers. Scand J Gastroenterol. 2012;47(2):136-47.
4. Geraghty J, Thumbs A, Kankwatira A, Andrews T, Moore A, Malamba R, et al.

- Helicobacter pylori*, HIV and gastric hypochlorhydria in the Malawian population. PLoS One. 2015;10(8):0132043.
DOI:10.1371/journal.pone.0132043
5. Parsons BN, Ijaz UZ, D'Amore R, Burkitt MD, Eccles R, Lenzi L. Comparison of the human gastric microbiota in hypochlorhydric states arising as a result of *Helicobacter pylori*-induced atrophic gastritis, autoimmune atrophic gastritis and proton pump inhibitor use. PLoS Pathogens. 2017;13(11):1006653.
 6. Hong SJ, Kim SW. *Helicobacter pylori* infection in gastroesophageal reflux disease in the Asian countries. Gastroenterology Research and Practice; 2015.
 7. Harris PR, Serrano CA, Villagrán A, Walker MM, Thomson M, Duarte I. *Helicobacter pylori*-associated hypochlorhydria in children, and development of iron deficiency. Journal of Clinical Pathology. 2013;66(4):343-347.
 8. Kwon YH, Kim N, Yoon H, Shin CM, Park YS, Lee DH. Effect of citric acid on accuracy of 13C-urea breath test after *Helicobacter pylori* eradication therapy in a region with a high prevalence of atrophic gastritis. Gut and liver. 2019;13(5):506.
 9. Di Mario F, Franzè A, Cavallaro LG. Non-invasive approach to diagnosis of upper gastrointestinal diseases. 1st ed. Area Qualità s.r.l. 2008;5-64.
 10. Ebule IA. GastroPanel for the diagnosis of gastritis: A tool for health emergence. 1st ed. Yaounde: NYA PUBLISHERS. 2016;1: 1-82.
 11. Herzlich BC, Schiano TD, Moussa Z, Zimbalist E, Panagopoulos G, Ast A, et al. Decreased intrinsic factor secretion in AIDS: Relation to parietal cell acid secretory capacity and vitamin B12 malabsorption. Am J Gastroenterol. 1992; 87(12):1781-8. PMID:1449141
 12. Fabris P, Pilotto A, Bozzola L, Tositti G, Soffiati G, Manfrin V, et al. Serum pepsinogen and gastrin levels in HIV-positive patients: Relationship with CD4+ cell count and *Helicobacter pylori* infection. Aliment Pharmacol Ther. Blackwell Science Ltd. 2002;16(4):807-11.
 13. Shaffer RT, LaHatte LJ, Kelly JW, Kadakia S, Carrouger JG, Keate RF, et al. Gastric acid secretion in HIV-1 infection. Am J Gastroenterol. 1992;87(12):1777-80. PMID:1449140
 14. Lu FJ, Luo XL, Meng X, Jin R, Ding HG, Zhang ST. A low prevalence of *H pylori* and endoscopic findings in HIV-positive Chinese patients with gastrointestinal symptoms. World J Gastroenterol. 2007; 13(41):5492-5496.
 15. Fialho ABC, Braga-Neto MB, Guerra Eder JC, Fialho AMN, Fernandes KC, Sun JLM. Low prevalence of *H. pylori* Infection in HIV-Positive patients in the Northeast of Brazil. BMC Gastroenterol. 2011;11(13). Available:www.biomedcentral.com/1471-230X/11/13
 16. Anejo-Okopi AJ, Audu O, Adaiche AR, Okojokuw OJ, Ali M, Adekwu A. Prevalence of *Helicobacter pylori* infection among HIV-1 infected patients using stool antigen tests in Jos, North-Central, Nigeria. Govaresh. 2016;21:55-63.
 17. Hestvik E, Tylleskar T, Ndeezi G, Grahnsquist L, Olafsdottir E, Tumwine KJ. Prevalence of *Helicobacter pylori* in HIV-infected, HAART-naïve Ugandan children: A hospital-based survey. J Int AIDS Soc. 2011;14(34):1-9. Availablefrom:www.jiasociety.org/content/14/1/34
 18. Magen E, Elbirt D, Agmon-Levin N, Mishal J, Sthoeger Z. Eradication of *Helicobacter pylori* can facilitate immune reconstitution in HIV-1-infected immunological non-responders. Int J Infect Dis. 2010;14:322-327.
 19. Moges F, Kassu A, Mengistu G, Adugna S, Andualem B, Nishikawa T. Seroprevalence of *Helicobacter pylori* in dyspeptic patients and its relationship with HIV infection, ABO blood groups and life style in a university hospital, Northwest Ethiopia. World J Gastroenterol. 2006;12(12):1957-1961. Available:www.wjgnet.com/1007-9327/12/1957.asp
 20. Benberin V, Bektayeva R, Karabayeva R, Lebedev A, Akemeyeva K, Paloheimo L. Prevalence of *H. pylori* infection and atrophic gastritis among symptomatic and dyspeptic adults in Kazakhstan. A hospital-based screening study using a panel of serum biomarkers. AnticancerRes. 2013; 33(10):4595-602.
 21. Bornschein J, Selgrad M, Wex T, Kuester D, Malfertheiner P. Serological assessment of gastric mucosal atrophy in gastric cancer. BMC Gastroenterol. 2012; 12:10.

22. Ebule IA, Djune FAK, Njeambosay BA, DohG N, Befolo MHDM, Nkayo M, et al. Atrophic gastritis and gastric cancer risk amongst diabetes mellitus type 2 subjects and controls in Yaounde Cameroon. Using a Panel of Serum Biomarkers (PGI,G-17).J Clin Gastroenterol Treat. 2017;3:052. DOI: org/10.23937/2469-584X/1510052
23. Kurilovich S, Belkovets A, Reshetnikov O, Openko T, Malyutina S, Ragino Y. Stomach-specific biomarkers (GastroPanel) can predict the development of gastric cancer in a caucasian population: A longitudinal nested case-control study in Siberia. Anticancer res. 2016;36(1):247-53.
24. Syrjänen K. False positive and false negative results in diagnosis of *Helicobacter pylori*infection can be avoided by a panel of serum biomarkers (GastroPanel®). M J Gast. 2017;1(1):007.
25. Syrjänen K. Serological biomarker panel (GastroPanel®): A test for non-invasive diagnosis of dyspeptic symptoms and for comprehensive detection of *Helicobacter pylori* infection. Biomark J. 2017;3:1(2). DOI:10.21767/2472-1646.100024
26. Available:www.gastropanel.net/www.biohit healthcare.com
27. Noah Noah D, Marie Claire OA, Servais Albert Fiacre EB, Guy PN, Ebule IA, Lea P. Assessing GastroPanel serum markers as a non-invasivemethod for the diagnosis of atrophic gastritis and *Helicobacter pylori* infection. O J Gast. 2012;2:113-118.
28. Ebule IA, Longdoh AN, Paloheimo IL. *Helicobacter pylori* infection and atrophic gastritis. Afr Health Sc. 2013;13(1):112-117.
29. Ebule IA, Djune FAK, Njeambosay BA, Doh GN, Metaghue G, Majuikouo L, et al. Association of *Helicobacter Pylori* infection and diabetes mellitus type 2 subjects in Yaounde Cameroon. Using a Panel of Serum Biomarkers (PGII, HplgG): A Case Control Study. J ClinGastroenterol Treat. 2017;3:053. DOI:org/10.23937/2469-584X/1510053
30. Firmin A, Mathurin K, Antonin WNN, Benjamin A, Oudou N, Magloire BS. The prevalence of *Helicobacter Pylori* infection and peptic ulcer disease in HIV-positive patients with gastrointestinal symptoms isnot related to absolute CD4 counts: A case-control study. Health Sci. Dis. 2016;17(1):1-5. Available:www.hsd-fmsb.org
31. Kokkola A, Rautelin H, Puolakkainen P, Sipponen P. Diagnosis of *Helicobacter pylori* infection in patients with atrophic gastritis: Comparison of histology, 13C-urea breath test, and serology. Scand J Gastroenterol. 2000;35(2):138-141.
32. Barkun AN, Bardou M, Kuipers EJ. International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding. Ann Intern Med. 2010;152(2): 101-113.
33. Malfertheiner P, Megraud F, O'morain CA, Atherton J, Axon AT, Bazzoli F. Management of *Helicobacter pylori* infection—The maastricht IV/florence consensus report. Gut. 2012;61(5):646-64.
34. Zagari RM, Romano M, Ojetti V, Stockbrugger R. Guidelines for the management of *Helicobacter pylori*infection in Italy: The III working group consensus report. Dig Liver Dis. 2015;47(11):903-912.
35. Syrjänen K. Caveats in diagnosis of *Helicobacter Pylori* infection can be avoided by a panel of serum biomarkers (GastroPanel®). J Carcinog Mutagen. 2016;7:123. DOI:10.4172/2157-2518.1000e123
36. International Agency for Research on Cancer, World Health Organization schistosomes, liver flukes and *Helicobacter pylori*. IARC working group on the evaluation of carcinogenic risks to human. MonogrEvalCarcinog Risks Hum. 1994;61:218-20.
37. Oldenburg B, Diepersloot RJ, Hoekstra JB. High seroprevalence of *Helicobacter pylori* in diabetesmellitus patients. Dig Dis Sci. 1996;41:458-461.
38. Storskrubb T, Aro P, Ronkainen J, Sipponen P, Nyhlin H. Serum biomarkers provide an accurate method for diagnosis of atrophic gastritis in a general population: The kalixanda study. Scand J Gastroenterol. 2008;43:1448-1455.
39. Telaranta-Keerie A, Kara R, Paloheimo L, Härkönen M, Sipponen P. Prevalence of undiagnosed advanced atrophic corpus gastritis in Finland: An observational study among 4,256 volunteers without specific complaints. Scand J Gastroenterol. 2010; 45:1036-1041.
40. Syrjänen K, Eronen K. Serological testing in management of dyspeptic patients and in screening of gastric cancer risks. J

GastrointestDisord Liver Func. 2016;2(3): 41. Sipponen P, Maaros HI. Chronic gastritis. ScandJ Gastroenterol. 2015;50(6):657-67. 1- 5.

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