Association of *Helicobacter pylori* Infection and Atrophic Gastritis with Chronic Renal Insufficiency in Yaounde Cameroon, Using Gastropanel® Serological Biomarker Panel (Pepsinogen I; Pepsinogen II; Gastrin-17; *Helicobacter pylori* IgG)

Alonge Ivo Ebule¹,²*, Valentine Ngum Ndze³, Ngouana Kammalac Thierry⁴, Guenou Etienne¹,⁵, Moche Mboudja Morel Ornella⁶, Mboletieu Ateufo Aurelien⁶, Noah Noah Dominique⁷, Minna Maki⁸ and Kari Syrjanen⁸,⁹

¹Faculty of Science, University of Buea, Cameroon.  
²School of Assistant Laboratory Technologies, Limbe, Cameroon.  
³Faculty of Health Sciences, University of Buea, Cameroon.  
⁴Antimicrobial and Biocontrol Agent Unit, University of Yaounde, Cameroon.  
⁵M.A .SANTE (meilleur Acces aux soins de santé), Younde, Cameroon.  
⁶School of Laboratory Technicians Yaounde, Cameroon.  
⁷Faculty of Medicine and Pharmaceuticals Sciences, University of Douala, Cameroon.  
⁸Department of Clinical Research, Biohit Oyj, Helsinki, Finland.  
⁹Molecular Oncology Research Center, Barretos Cancer Hospital, Barretos, SP, Brazil.

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, GE, NKT, MMO and MAA carried out sample collection, analysis, interpreted the data and drafted the manuscript. Authors NND, MM 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.

Article Information

DOI: 10.9734/JAMB/2021/v21i230328  
Editor(s):  
(1) Dr. Niranjalie Perera , Wayamba University of Sri Lanka, Sri Lanka.  
Reviewers:  
(1) Silvia Denise Peña Betancourt , UAM-X , Mexico.  
(2) Maria TURTOI , Dunarea de Jos University, Romania.  
Complete Peer review History: http://www.sdiarticle4.com/review-history/64102

Received 30 October 2020  
Accepted 02 January 2021  
Published 22 March 2021

*Corresponding author: E-mail: alongebule@gmail.com, aolevo@yahoo.com;
**ABSTRACT**

**Introduction:** *Helicobacter pylori* infection is associated with an atrophic gastritis peptic and duodenal ulcer and gastric cancer. Patients with chronic renal diseases usually have dyspeptic symptoms. Several investigations have demonstrated an association between *H. pylori* infection and chronic kidney disease, although their results are still conflicting. We therefore aimed, to clarify the prevalence of *H. pylori* infection in patients receiving dialysis.

**Materials and Methods:** Patients undergoing hemodialysis were recruited at the University Teaching Hospital of Yaounde, between January and May 2019. The clinical and sociodemographic information of the patients was recorded. 5 ml of blood were collected aseptically for Pepsinogen I and II enzymes, gastrin17 hormone and IgG anti *H. pylori* anti-body. The test parameters were analyzed using a GastroSoft software application. The data was analyzed using Epi Info 7.0. All statistics were 95% CI. Ethical clearance was also obtained from the National Ethics Committee. Authorization was obtained at the University Teaching Hospital.

**Results:** A total of 60 subjects were recruited aged 25-74 years, (mean±SD 52.03 ± 12.78) years; 22(45.16%) females, aged 29 to 71 years (mean±SD 47.45 ± 11.46) years and 38(54.84%) males aged 25 to 74 (mean±SD 56.47±12.25) years. Female / male ratio was 1.2. Overall, 26(43.33%) subjects were positive for *H. pylori* infection (IgG≥30UIU). The prevalence of atrophic gastritis obtained was (23.33%)(PG1< 30µg/l). The mean *H. pylori* IgG antibodies were significantly higher in obese than non-obese subjects (F=3.59; p=0.01). A significant increase in the mean creatinine (P=0.008), and urea (P=0.05) was observed in *H. pylori* positive than negative ones.

**Conclusion:** *H. pylori* infection is highly prevalent amongst patients with chronic renal failure and may thus require continuous follow up.

**Keywords:** Prevalence; *Helicobacter pylori* infection; atrophic gastritis; chronic renal insufficiency, gastroPanel; serological biomarker panel (pepsinogen I; pepsinogen II; gastrin17; *helicobacter pylori* IgG).

1. **INTRODUCTION**

*Helicobacter pylori* (*H. pylori*) is a spiral rod shape bacterium that primarily infects the gastric mucosa, which, if uneradicated develops atrophic gastritis (AG) in about half of the affected patients [1]. *H. pylori* infection plays a major role in the etiology of many gastroduodenal diseases including stomach cancer [2]. Chronic kidney disease (CKD) is a growing disease and public health problem worldwide [3,4]. Gastrointestinal (GI) symptoms are common among subjects with CKD, and their intensity vary slightly to very severe, altering the quality of life and potentially hindering the effectiveness of the treatment [5] and also affects their nutrition status leading to the development of malnutrition, which is a potent predictor of morbidity and mortality [6]. Patients with chronic renal failure (CRF) often have gastrointestinal symptoms caused not only by *H. pylori* infection, but also by high urea levels, decline of gastrointestinal motility, hypergastrinemia and high ammonia levels [7]. Moreover, patients with CRF may have higher risks of gastric mucosal damages compared with individuals with normal renal function because of systemic and/or local chronic circulatory failure [6]. *H. pylori* infection is crucial in many gastrointestinal conditions not only in individuals with normal renal function, but also in CRF patients receiving dialysis and kidney transplant [5]. Although associations between patients with CRF and the prevalence of *H. pylori* infection have been reported their results are still controversial [8]. We assessed the prevalence of *H. pylori* infection and atrophic gastritis amongst patients receiving dialysis at the University Teaching Hospital of Yaounde, Cameroon.

2. **METHODS**

Patients undergoing hemodialysis and consented to participate were prospectively collected between January and May 2019 at the University Teaching Hospital. Basal blood was aseptically collected by venipuncture into EDTA tubes after at least 4 hours of fasting and immediately centrifuged at 2000G for 15 minutes. The plasma samples were then distributed into cry and stored at -20 until analyzed. Plasma concentrations of PGI, PGII, G-17 and *H. pylori* IgG determined by the Gastro Panel (Biohit plc Helsinki, Finland) using the enzyme linked immunosorbenbt assay (ELISA), according to the manufacturer’s instructions for the measurement of absorbance after a peroxidation reaction at 450nm. The results of the Gastro Panel® examination were
evaluated using the GastroSoft® interpretation software.

2.1 Assay Analysis

Based on the clinically-validated cut-off values for each biomarker, the software classifies the test results into one of the five categories: 1) Normal result, 2) superficial gastritis (non-atrophic gastritis), H. pylori infection without atrophy, 3) atrophic gastritis in the corpus, 4) atrophic gastritis in the antrum, and 5) atrophic pangastritis. The recommended cut-off values were used for all 4 biomarkers as follows: pepsinogen I (PGI) <30 μg/l, the PGI/PGII ratio <2.5, and fasting G-17 <1 pmol/l (G-17b). Values below these cut-off levels implicate AG of the corpus (PGI, PGI/PGII) and AG of the antrum (G-17b), respectively. Whereas low G-17 <1 pmol/l was considered as atrophy of both antrum and corpus. H. pylori IgG antibody levels above 30 EIU (enzyme immunoassay units) were considered an indicator of H. pylori infection (ongoing or recent exposure).

2.2 Statistical Analysis

Statistical analysis was performed using the SPSS 16.0 software package (SPSS Inc. Chicago, IL, USA). Data were expressed as mean±SD. The differences between groups were analyzed by the Student’s t-test, Mann-Whitney U-test and Significance of differences between means was estimated with ANOVA, and between proportions using χ² test. In all tests, values with p<0.05 were regarded statistically significant. Ethical clearance was obtained from the national ethics committee. The study was accepted by the ethics committees of the University Teaching Hospital.

3. RESULTS

A total of 60 patients aged 25-74 years (mean±SD 52.03 ± 12.65) years, including 22 (45.16%) females aged 29-71 years (mean±SD 47.45 ± 11.46) and 38 (54.84%) males aged 25-74 years (mean±SD 56.47±12.25) were enrolled during study period. The results of the distribution of Gastropanel® test are summarized in Tables 1 and 2. Amongst the 60 subjects 20(33.33%) were interpreted as normal gastric mucosa (N), 26 (43.33%) as superficial gastritis (no atrophic gastritis) (S) and 14 (23.33%) were consistent with Atrophic Gastritis of the corpus, AGC (PGI<30μg/l and/or PGI/PGII<3). The H. pylori seropositivity was more prevalent in males 18/88 (47.37%) than females 8/22 (36.36%). This difference was however not significant (OR = 1.5750; 95%C.I 0.4759 - 5.3962) p = 0.42). No significant association of age group with H. pylori seropositivity was observed (X² = 4.3734, p=0.3578). Infection to H. pylori was associated with obesity (p = 0.01) Table 1. Significantly raised serum creatinine (p =0.008) and urea (p=0.05) levels were observed in H. pylori positive than negative ones (Table 2).

Table 1. Association of Helicobacter pylori infection with potential risk and clinical factors in the study participants

| Variable        | H. pylori positive (IgG≥30EIU) 26(43.33%) | H. pylori negative (IgG<30EIU) 34(56.67%) | OR   | 95%CI       | P-value |
|-----------------|------------------------------------------|------------------------------------------|------|-------------|---------|
| Sex             |                                          |                                          |      |             |         |
| Female          | 08(36.36%)                               | 14(63.64%)                               | Ref  | OR=1.5750   | 0.4759-5.3962 |
| Male            | 18(47.37%)                               | 20(52.63%)                               |      |             |         |
| Age group (years) |                                           |                                          |      |             |         |
| 25-35           | 4(66.67%)                                | 2(33.33%)                                | X²   | = 4.3734    |         |
| 36-46           | 4(28.57%)                                | 10(71.43%)                               |      |             |         |
| 47-57           | 12(60.00%)                               | 8(40.00%)                                |      |             |         |
| 58-68           | 2(33.33%)                                | 4(66.67%)                                |      |             |         |
| 69-79           |                                          |                                          |      |             |         |
| Retinopathy     |                                           |                                          |      |             |         |
| No              | 8(36.36%)                                | 14(63.64%)                               | Ref  | OR=1.5750   | 0.5293-4.7880 |
| Yes             | 18(47.37%)                               | 20(52.67%)                               |      |             |         |
| BMI             |                                           |                                          |      |             |         |
| 0-18.4          | 2(50.00%)                                | 2(50.00%)                                | X²   | = 10.0763   | 0.0179  |
| 18.5-25         | 14(43.75%)                               | 18(56.25%)                               |      |             |         |
| 26-30           | 0(0.00%)                                 | 10(100.00%)                              |      |             |         |
| 31-50           | 6(75.00%)                                | 2(25.00%)                                |      |             |         |

OR, odds ratio; CI, confidence interval; BMI, body mass index
4. DISCUSSION

*Helicobacter pylori* infection is crucial in many gastrointestinal conditions not only in people with normal renal function, but also in patients with renal failure undergoing chronic dialysis and kidney transplantation [9]. Patients with chronic renal failure often have a variety of clinical gastrointestinal symptoms, including nausea, dyspepsia, loss of appetite, epigastric discomfort and heartburn, as well as histological, physiological and functional disorders of the gastrointestinal system [8].

The results of Gastropanel are presented in Table 2. In this analysis of the biomarker profile of GastroPanel, atrophic corpus gastritis appeared in 14 (23.33%) of the subjects (PGI <30 μg/L). The *H. pylori* seroprevalence obtained was 26/60 (43.33%). This prevalence is in agreement to that reported in several studies in different countries with renal failure, for example [8] (48%) in Japan; [10] (44%) in Netherland, [11] (53%) in Kenya, [12] (40%) in Saudi Arabia. However, our prevalence contrasts sharply with those reported by [13] (24%) in the United Kingdom; [14] (36%) in South Korea. This prevalence of *H. pylori* is lower than previously reported in dyspeptic subjects in Cameroon by [15] (81.40%), [16] (79.80%), [17] (78.7%). The prevalence of *H. pylori* infection in patients receiving chronic dialysis or kidney transplantation has been reported to be lower than in subjects with normal renal function in various populations [4,5,18]. Dialysis patients have higher levels of pro-inflammatory cytokines, including interleukin 1β, 6, 8 and tumour necrosis factor, from activated inflammatory cells infiltrating the gastric mucosa. As a result, gastritis progress, accompanied by an increase in pH and finally *H. pylori* cannot live in the gastric mucosa [19,20]. In addition, *H. pylori* load could have been reduced by antibiotic treatment, commonly used during the first treatment periods and antibiotic concentrations are higher in the stomach [8]. We observed a high prevalence of atrophic gastritis of the corpus (23.33%) (PGI < 30 μg/l) amongst the study participants. These subjects are at risk of enteric infections, low absorption of ATBs, vitamin B12 and some divalent micronutrients, including iron, calcium, magnesium and zinc, with an increased risk of cognitive disorders, such as neurodegenerative and vascular disorders, encephalopathies, anaemia and osteoporosis [21,22]. No association of age with *H. pylori* infection was observed, although infection to *H. pylori* is usually associated with advanced age [23,24]. The *H. pylori* infection was more prevalent in males (47.37%) than females (36.36%), the association was however, not significant (p = 0.21). Most diseases related to *H. pylori* are associated with the male sex [23,25]. We observed a significant association between *H. pylori* seropositivity and obesity (P=0.0179, Table 2). It has been shown that an *H. pylori* infection is involved in the regulation of 2 hormones leptin and ghrelin involved in energy hemostasis and their interaction affects obesity, insulin sensitivity and glucose hemostasis [25]. We observed significantly high urea levels in *H. pylori* positive than negative subjects (P=0.05) (Table 2). Despite the fact that *H. pylori* is known to produce urease which degrades urea into ammonia, urea levels are toxic and inhibit the growth of *H. pylori* in the stomach [8,19,26].

5. CONCLUSION

*Helicobacter pylori* infection and atrophic gastritis are highly prevalent amongst patients with chronic renal failure and may prone these patients to risk of enteric infections, malabsorption of antibiotics, vitamin B12 and some divalent micronutrients, with an increased risk of cognitive disorders, thus require continuous follow up.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely
no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT AND ETHICAL APPROVAL

Ethical clearance was obtained from Center Regional Committee for Research on Human Health (CRERSH). An authorization was obtained 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.

ACKNOWLEDGEMENTS

We thank the staff of the Haematology unit of the General Hospital of Yaounde for their technical assistance.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Syrjänen K, Eronen K. Serological Testing in management of dyspeptic patients and in screening of gastric cancer risks. J Gastrointest Disord Liver Func. 2016;2(3):1-5.
2. Ebule IA. Gastropanel for the Diagnosis of gastritis: A tool for health emmergence. Nya Publishers. 2016;1:1-82.
3. Ardalan MR, Mardani S, Asgari-Savadjani S, Tamadon MR, Naghdifar S, Nasri H. An update on Helicobacter pylori infection in renal failure patients. Immunopathol Persa. 2016;2(2):e10.
4. Chiu GF, Chang YH, Wu DC, Wu MT, Lin HYH. Risk of chronic kidney disease after early and late Helicobacter Pylori eradication in patients with peptic ulcer disease: A population-based cohort study in Taiwan. Biol Med (Aligarh). 2017;9:402. DOI:10.4172/0974-8369.1000402
5. Sugimoto M, Sakai K, Kita M, Imanishi J, Yamaoka Y. Prevalence of Helicobacter pylori infection in long-term hemodialysis patients. Kidney Int. 2009;75:96-103 PMID:18843261. DOI: 10.1038/ki.2008.508
6. Block GA, Raggi P, Bellasi A, Kooienga L, Spiegel DM. Mortality effect of coronary calcification and phosphate binder choice in incident hemodialysis patients. Kidney Int. 2007;71:438–41. PubMed: 17200680.
7. Strid H, Simren M, Stotzer PO, Abrahamsson H, Bjomsson ES. Delay in gastric emptying in patients with chronic renal failure. Scand J Gastroenterol. 2004;39:516–20. PubMed: 15223673.
8. Sugimoto M, Yamaoka Y. Review of Helicobacter pylori Infection and Chronic Renal Failure. The Apher Dial. 2011;15 (1):1–9. DOI: 10.1111/j.1744-9987.2010.00851
9. Wijarnpreecha K, Thongprayoon C, Nissaisorakarn P, Lekuthai N, Jaruvongvanich V, Nakkala K, Rajapakse R, Cheungpasitporn W. Association between Helicobacter pylori and end-stage renal disease: A meta-analysis. World J Gastroenterol. 2017;23(8):1497-1506. DOI: doi.org/10.3748/wjg.v23.i8.1497
10. Offerhaus GJ, Kreuning J, Valentijn RM, Salvador Peña A, Endtz PH, van Duyn W, Lamers CB. Campylobacter pylori: prevalence and significance in patients with chronic renal failure. Clin Nephrol. 1989;32:239-241 PMID: 2582650.
11. Karari EM, Lule GN, McLigeyo SO, Amayo EO. Endoscopic findings and the prevalence of Helicobacter pylori in chronic renal failure patients with dyspepsia. East Afr Med J. 2000;77:406-409. PMID: 12862061.
12. Abdulrahman IS, Al-Quorain AA. Prevalence of gastroesophageal reflux disease and its association with Helicobacter pylori infection in chronic renal failure patients and in renal transplant recipients. Saudi J Gastroenterol. 2008;14:183-186. PMID: 19568535. DOI:10.4103/1319-3767.41741
13. Shousha S, Arnaout AH, Abbas SH. Antral Helicobacter pylori in patients with chronic renal failure. J Clin Pathol. 1990;43:397–399.
14. Chang SS, Hu Hy. Lower *Helicobacter pylori* infection rate in chronic kidney disease and end-stage renal disease patients with peptic ulcer disease. J Chin Med Assoc: JCMA. 2014;77:354-359.

15. Noah Noah D, Okomo Assoumou MK, Bagnaka SAFE, Ngaba GP, Alonge IE et al. Assessing gastropanel serum markers as a non-invasive method for the diagnosis of atrophic gastritis and *Helicobacter pylori* infection. Open J Gastroenterol. 2012;2:113-118.

16. Ebule IA, Longdoh AN, Paloheimo IL. *Helicobacter pylori* infection and atrophic gastritis. Afr Health Sci. 2013;13:112-117.

17. Ebule IA, Djune Fokou AK, Sitedjeya Moko IL, Tanni B, Heugueu C, Longdoh AN, Noah Noah D, Okomo Assoumou MC, Paloheimo L, Njoya O, Syrjanen K. Prevalence of *H. pylori* Infection and Atrophic Gastritis among dyspeptic subjects in Cameroon using a Panel of Serum Biomarkers (PGI, PGII, G-17, HpIgG). Sch. J. App. Med. Sci. 2017;5(4A):1230-1239.

18. Sezer S, Ibis A, Ozdemir BH et al. Association of *Helicobacter pylori* infection with nutritional status in hemodialysis patients. Transplant Proc. 2004;36:47-9. Pub Med: 15013297.

19. Khedmat H, Taheri S. Current knowledge on *Helicobacter pylori* infection in end stage renal disease patients. Saudi J.Kidney Dis Transpl. 2009;20:969-74.

20. Lin SY, Lin CL, Liu JH, Yang YF, Huang CC, Kao CH. Association between *Helicobacter pylori* infection and the subsequent risk of end-stage renal disease: A nationwide population-base cohortstudy. Int J Clin Pract. 2015;69: 604-610 PMID: 25644865. DOI:10.1111/ijcp.12602

21. Agréus L, Kuipers EJ, Kupcinskas L, Malfertheiner P, Di Mario F, Leja M, Mahachai V, Yaron N, Van Oijen M, Perez Perez G, Rugge M. Rationale in diagnosis and screening of atrophic gastritis with stomach-specific plasma biomarkers. Scandinavian journal of gastroenterology. 2012;47(2):136-47.

22. Sipponen P, Maaroos Hl. Chronic gastritis. Scandinavian Journal Gastroenterol. 2015;50(6):657-67.

23. 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. Monogr. Eval. Carcinog. Risks Hum.1994; 61:218-20.

24. De Martel C, Parsonnet J. *Helicobacter pylori* infection and gender: a meta-analysis of population-based prevalence surveys. Dig Dis Sci. 2006;51:2292-2301.

25. Francois F, Roper J, Joseph N, Pei Z, Chhada A, Blaser MJ et al. The effect of *H. pylori* eradication on meal-associated changes in plasma ghrelin and leptin. BMC Gastroenterol. 2011;11:37.

26. Ardalan MR, Mardani S, Asgari-Savadjani S, Tamadon MR, Naghdifar S, Nasri H. An update on *Helicobacter pylori* infection in renal failure patients. Immuno pathol Persa. 2016;2(2):e10.