



## **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)**

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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, GE, NKT, MMMO 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.*

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## 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 socio-demographic 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≥30EIU). 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; gastrin-17; *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 immunosorbent 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  $\chi^2$  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 < 30 µg/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% CI 0.4759-5.3962)  $p = 0.42$ . No significant association of age group with *H. pylori* seropositivity was observed ( $\chi^2 = 4.3734$ ,  $p = 0.3578$ ). 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	<i>H. pylori</i> positive (IgG ≥ 30 EIU) 26 (43.33%)	<i>H. pylori</i> negative (IgG < 30 EIU) 34 (56.67%)	OR	95% CI	P-value
Sex					0.42
Female	08 (36.36%)	14 (63.64%)	Ref	0.4759-5.3962	
Male	18 (47.37%)	20 (52.63%)	R=1.5750		
Age group (years)			$\chi^2 = 4.3734$	/	0.35
25-35	4 (66.67%)	2 (33.33%)			
36-46	4 (28.57%)	10 (71.43%)			
47-57	4 (28.57%)	10 (71.43%)			
58-68	12 (60.00%)	8 (40.00%)			
69-79	2 (33.33%)	4 (66.67%)			
Retinopathy					
No	8 (36.36%)	14 (63.64%)	Ref	95% CI	0.2124
Yes	18 (47.37%)	20 (52.67%)	OR=1.5750	0.5293-4.7880	
BMI			$\chi^2 = 10.0763$		0.0179
0-18.4	2 (50.00%)	2 (50.00%)			
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

**Table 2. Mean serum creatininand urea levels ( $\pm$ SD) according to *Helicobacter pylori* serostatus**

Variable	Anti- <i>H. pylori</i>		p-value	Atrophic gastritis class			p-value
	Negative (IgG < 30 EIU) 26(43.33%)	Positive (IgG $\geq$ 30 EIU) 34(56.67%)		AGC14 (23,33%)	N20 (33.33%)	S, 26(43.33%)	
Creatinine (mg/L)	123.60 $\pm$ 40.43	184.10 $\pm$ 12.10	0.008	94.13 $\pm$ 31.5	141.36 $\pm$ 25.69	186.32 $\pm$ 121.55	0.005
Urea (mg/L)	2.18 $\pm$ 0,66	2.57 $\pm$ 0.85	0.05	2.18 $\pm$ 0.77	2.26 $\pm$ 0,61	2.51 $\pm$ 0.56	0.34

*N*, normal stomach mucosa; *AGC*, atrophic gastritis of the corpus; *S*, superficial (non atrophic gastritis); mg/L, milligram per litre

#### 4. DISCUSSION

*H. 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  $\mu$ g /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 1 $\beta$ , 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%)(PG1 < 30 $\mu$ g/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 8/22(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

*H. 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 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.

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