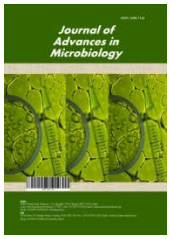

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Association of *Helicobacter pylori* Infection with Respiratory Diseases in Cameroon Patients, Using GastroPanel® Serological Biomarkers (Pepsinogen I; Pepsinogen II; Gastrin-17; *Helicobacter pylori IgG*)

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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, NKT, GE, NHIV and BTNN 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* (*H. pylori*) is a microaerophilic gram-negative bacterium that colonizes the gastric mucosa and provokes inflammation and immune responses throughout life with liberation of diversecytotoxique substances dependent on host. Infection to *H. pylori* has been associated to a number of respiratory complications, including chronic obstructive pulmonary dieases, bronchectasis, asthma, tuberculosis and lung cancer. Epidemiological data on the association of *H. pylori* infection respiratory diseases are rare in Cameroon. We sought to evaluate the prevalence *H. pylori* infection among patient with respiratory diseases.

Methodology: Blood samples were aseptically collected for the measurements *Helicobacter pylori* IgG antibodies, pepsinogene I et II levels, gastrine-17. The blood samples required for the study were collected prospectively. Ethical clairance was obtained from the Centre Regional Ethics Committee for Human Sciences. An authorization of research was obtained from the authorities of Jamot Hospital of Yaounde. All participants signed an informed consent form.

Results: The GastroPanel® results showed that the prevalence of *H. pylori* infection was 42(46.67%). We observed an *H. pylori* seroprevalence of 75%, 41.9%, 50.0% and 33,33% amongst sujects with bronchitis, Tuberculosis, Asthma and pneumonia respectively.

Keywords: Helicobacter pylori infection; respiratory diseases; gastropanel; serological Biomarkers.

1. INTRODUCTION

Helicobacter pylori (*H. pylori*) is a spiral microaerophilic gram-negative bacteria that usually colonizes the gastric mucosa and associated with inflammatory responses throughout life with liberation of diverse bacteria and cytotoxic substances dependent on host [1]. Several studies have suggested an epidemiological association between *H. pylori* and extragastroduodenal diseases including cardiovascular diseases, cutanous, rheumatism and hepatic [2-5]. It is well known that the colonization of the gastric mucosa by *H. pylori* stimulates the liberation of diverse pro-inflammatory substances such as cytokines, eicosanoïdes and acute phase proteins [6,7]. In addition cross mimicry between bacteria and host antigens exist in *H. pylori* infected individuals [8]. As a consequence, a pathogen association could exist between *H. pylori* and diseases characterized activation of inflammatory mediators and /or autoimmunity. Chronic inflammation and increased immune response have been reported amongst different respiratory diseases including chronic bronchitis [9] and bronchectasia [10]. Further, chronic obstructive pulmonary disease and pulmonary tuberculosis have been reported to be very frequent amongst patients with peptic ulcers [11,12]. Infection to H. *pylori* had been associated to a number of respiratory disorders including chronic obstructive pulmonary disease, bronchectasia, asthma, tuberculosis and lung cancer [9,13]. Data on the association between *H. pylori* infection and respiratory diseases is rare in Cameroon. We therefore sought to evaluate the prevalence of *H. pylori* infection amongst patients presenting with respiratory disorders.

2. METHODS

Patient information: Patients presenting with various respiratory complications and consented to participate were prospectively collected between January and May 2020 at the Pneumonia unit of the Jamot Hospital.

Blood samples: Basal blood was aseptically collected after at least 4hours of fasting by venipuncture into EDTA tubes and immediately centrifuged at 2000G for 15 minutes. The plasma samples were then distributed into cryo tubes and stored at -20°C until analyzed. Plasma concentrations of PGI, PGII, G- 17 and *H. pylori* IgG determined by the Gastro Panel (Biohit plc Helsinki, Finland) [14] using the enzyme linked immunosorbent assay (ELISA), according to the manufacturer's instructions for the measurement of absorbance after a peroxidation reaction at 450 nm. The results of the GastroPanel® examination were evaluated using the Gastro Soft® interpretation software [14].

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, respectively. *H. pylori* IgG antibody levels above 30 EIU (enzyme-immunoassay units) were considered as indicator of *H. pylori* infection.

Statistical analysis: Statistical analysis was performed using the EPI Info 7.0 software package. Data were expressed as mean±SD. All the statistics were realized at 95% confidence interval. In all tests, values with $p<0.05$ were regarded statistically significant. Ethical clairance was obtained from the Centre Regional Ethics Committee for Human Sciences. The study was accepted by the ethics committee of the Jamot Hospital. All patients signed an informed consent form.

3. RESULTS

A total of 90 patients were enrolled during study period, aged 10-67 years (mean±SD 36.38± 12.25) years, including 60 (66.67%) females aged 21-67 years (mean±SD 36.90 ± 12.64) and 30 (33.33%) males aged 10-55 years (mean±SD 35.33 ± 11.55). Among the subjects with respiratory diseases, 62 (68.9%) presented with tuberculosis, 6 (6.70%) with pneumonia, 16 (17.80%) had bronchitis, 04 (04.40%) asthma, and 02 (02.20%) chronic obstructive pulmonary disease. Amongst the 90 subjects, 22 (24.44%) were interpreted as normal gastric mucosa, 18 (20.00%) were interpreted as superficial gastritis (no atrophic gastritis), 50 (55.56%) were consistent with mucosal atrophy, including Atrophic Gastritis of the corpus, C (n= 12 (13.33%)(PG1< 30 µg/l and/or PGI/PGII<3), Atrophic Gastritis of the Antrum, A (n= 30 (33.33%)(PG1< 30 µg/l and/or PGI/PGII<3) and (n=8 , 8.89%) pangastritis), P(PG1< 30µg/l and/or PGI/PGII< 3 ; G-17< 1pmol/l). The prevalence of *H. pylori* in the study population was 42/90 (46.67%). The *H. pylori* seropositivity did not differ among females 28/60 (46.67%) and males 14/30 (46.67%). This difference was not significant (X2 = 1.76, p = 0.10). The positivity rate of *H. pylori* infection was higher (61.9%) for the 0-35 age group and lower in the 36-54 age group (26.30%). There was no statistically significant difference in the prevalence of *H. pylori* among different age groups (X2 = 1,45; P = 0,48). *H. pylori* positivity was higher in patients with bronchitis (75%); than in asthma(50%), tuberculosis (41.90%), and pneumonia (33.3%). This difference was however not statistically significant (X2 = 1.31 p= 0.20) (Table 1).

4. DISCUSSION

Infection to *H. pylori* has been associated to various respiratory disseases Including chronic bronchitis [7], asthma and pulmonary tuberculosis [13]. The results of the GastroPanel® indicate that the prevalence of H. *pylori* infection was 42(46,67%) (Table 1). This prevalence was lower than what had been reported earlier among dyspepsia subjects in Cameroon by [15] (81,40%), [16] (79,80%), [17]

Table 1. Patient information

Parameter	*Hélicobacter pylori*		
	positive 42(46.67. 0%)	**negative 58(53.33%)**	**p-value**
Sex			
Males	14(46.67%)	16(53.33%)	0.49
Females	28(46.67%)	32(53.32%)	
Age(yrs)			
10-35	26(61.90%)	16(38.10%)	
36-54	10(26.32%)	28(73.68%)	0.48
55-67	6(60%)	4(40%)	
Type of respiratory disease			
Asthma	2(50%)	2(50%)	
Bronchitis	12(75%)	4(25%)	0.78
Chronic obstructive pulmonary disease	0(0%)	2(100%)	
Pneumonia	2(33.33%)	4(66.67%)	
Tuberculosis	26(41.94%)	36(58.06%)	

(78,7%), and equally among diabetic subjects in Cameroon by [18] (80,5%). This low prevalence of *H. pylori* infection may be associated to high intake of antibiotics among these patients and the high prevalence of atrophic gastritis among these patients [19]. No association was observed between *H. pylori* seropositivity with sex, (X2 = 1.76, p = 0.10). and age groups (X2 = 1.31, p = 0.20). However, most *H. pylori* related diseases are associated with male gender and the elderly [20,21]. We observed an *H. pylori* seroprevalence of 75% amongst the subjects presenting with bronchitis. Reference [22], in a study amongst 60 patients presenting with chronique bronchitis observed an increase in the seroprevalence of *H. pylori* (81.6%) compared to controls (57.9%). Chronique bronchitis had been reported as the major cause of death in patients with peptic ulcers [23]. These results suggest that *H .pylori* infection in itself could be an increased risk of developing chronic bronchitis. Reference [24] in an epidemiology study among 3608 chinese adults showed that chronic bronchitis was more frequent in *H. pylori IgG* seropositive females than non infected females. It is well known that age, sex and socioeconomic are linked to both *H. pylori* infection [25] and risk of chronic bronchitis [26]. It had been reported that *H. pylori* and in particular those harboring the cagA genes stimulate the activity of liberation of a variety of proinflammatory cytokines notably interleukine-1 (IL-1), IL-8 tumour necrosis factor alpha [13,27] and the eradication of *H. pylori* could lead to normalization of levels of serum cytokines [28]. Studies have shown that cytokines could be liberated in the course of chronic bronchitis exacerbations [9]. We observd an *H. pylori* seroprevalence of 41.9% among the subjects presenting with tuberculosis. It has been reported that tuberculosis is very frequent in patients suffering from peptic ulcers [12] and that tuberculosis patients could have a high prevalence of *H. pylori* [29]. Poor socio-economic and sanitary conditions in the course of childhood could also be another factor responsable appearance of the association between the two infections [30].

We observed an *H. pylori* seroprevalence of 50.0% among the subjets with asthma. Reference [31] in a study observed an H*. pylori* seroprevalence of 47.3% *vs* 38.1 controls and they concluded that asthma could not be associated to *H. pylori infection*. Other studies have been controversial on this association [32].

5. CONCLUSION

Considering the biomarker panel results of PGI, PGII, G-17 and HpIgG in this study, we have observed a high prevalences of *H. pylori* infection (46.67%) coupled with an extremely high prevalence of atrophic gastritis (55.56%). Given that these two conditions represent the single most important risk factors of gastric cancer the is a growing need to continuously monitor *H. pylori* infection in patients with respiratory diseases. The non-invasive GastroPanel (PGI, PGII, G-17 and HpIgG) test could be a cost-effective means capable of identifying patients at risk of gastric cancer i.e those with *H. pylori* infection and atrophic gastritis.

CONSENT AND ETHICS APPROVAL

Ethical clairance 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.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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