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RESEARCH ARTICLE

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)

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Abstract

Introduction: Gastric inflammation is a precursor to many gastrointestinal disorders including, peptic ulcer disease, atrophic gastritis and gastric cancer. Gastritis is frequent and usually severe in patients with diabetes mellitus (DMT2), probably due to the impairment of their immune status. Atrophic gastritis is usually accompanied by low hydrochloric acid, low pepsinogens and hypergastrinemia and is the most significant risk condition for gastric cancer. Studies on atrophic gastritis are scarce amongst diabetic subjects. This study aimed at detection and comparison of pepsinogen I(PGI) and gastrin-17(G-17) in serum of diabetes mellitus and non-diabetic subjects and also to find if there exists any significant correlation between these markers and DMT2.

Materials and methods: This case control study of 82 patients (51 diabetics and 31 non-diabetic subjects) was carried out in Yaounde Cameroon during the period January-April 2017. Clinical and sociodemographic information of both groups were recorded. 5 ml of blood was aseptically collected for PGI, PGII enzymes, and G-17 hormones. Assay parameters were analysed using a software application GastroSoft (www.GastroPanel.com). Data was analysed using Epi info 7.0. All statistics were realized at 95% CI. Authorizations were obtained at the Yaounde Central Hospital, and the Cite Verte District Hospital. Ethical clearance was also obtained from the National Ethics Committee.

Results: Hypergastrinemia (G-17 > 7 pmol/l) was observed in subjects with atrophic corpus gastritis (21.2 ± 24.0 pmol/l), in the diabetics (7.5 ± 0 pmol/l) and the control group (25.70 ± 26.0 pmol/l). Normal pepsinogen I (30 < PGI < 160 µg/l) levels were observed in both diabetic and control groups with nonatrophic gastritis (125.1 ± 53.9 µg/l vs. 110.5 ± 31.7 µg/l) respectively. In the diabetic subjects with atrophic corpus gastritis, pepsongen I levels were significantly reduced (26.65 ± 5.44) p = 0003 and in the control group (18.6 ± 10.3 pmol/l), p = 004. Among the diabetic complications, neuropathy was associated with atrophic corpus gastritis (p = 0.005). Atrophic gastritis (100%) and non-atrophic gastritis (55.8%) were frequent in the 52-62 age groups in the diabetic subjects.

Conclusion: The result indicates that diabetics are prone to atrophic corpus gastritis which is a risk factor for neurodegenerative disorders and gastric cancer and need continuous monitoring.

Keywords

Atrophic gastritis, Diabetes mellitus, Biomarkers, Case control

Introduction

Gastric inflammation is a precursor to many gastrointestinal disorders. Chronic active gastritis usually

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progresses into atrophic gastritis (AG) and acid free or hypochlorhydric stomach [1]. Chronic gastritis is a common life-long, serious and insidious illness amongst humans [2]. Atrophic gastritis is the single most powerful independent risk factor for distal gastric cancer which still remains a major public health problem worldwide and is fifth most frequent malignancy worldwide [3,4] and the third most cause of cancer related deaths after lung and liver cancers [5]. Autoimmune atrophic gastritis is common disorders with a prevalence of up to 2% of the general population. In patients with type 1 diabetes or autoimmune thyroid disease, the prevalence is 3- to 5-fold increased. Infection to *H. pylori* has also been implicated in the induction of autoimmune gastritis [6]. Autoimmune atrophic gastritis is characterized by atrophy of the corpus and fundus, presence of circulating autoantibodies to the parietal cell (PCA) and intrinsic factor (AIF) [6] decreased gastric acid secretion (hypo- or achlorhydria), hypergastrinemia, low pepsinogen I and iron deficiency anemia [7]. Chronic hypergastrinemia causes the enterochromaffin-like (ECL) cells in the oxyntic mucosa to undergo hyperplasia, which may progress toward dysplasia and gastric carcinoid tumors [8].

The future of prevention of gastric cancer deaths relies on the timely and early diagnosis and surveillance of patients with precancerous lesions as well as early detection of the cancer, making higher survival rates and lower healthcare costs per patient achievable [9,10]. Endoscopy with sampling of gastric biopsies is effective in screening of upper GI malignancies. However, this invasive method is uncomfortable, distressing and quite costly, emphasizing the need for rapid, reliable and inexpensive non-invasive tests [3,11]. Now a plasma biomarker test with combination of pepsinogen- I (PGI) and -II (PGII), gastrin-17 (G-17) and *H. pylori* IgG antibodies (IgG-HP) using an ELISA technique for detection (GastroPanel® test, Biohit Oyj), are now used for the screening of patients with an atrophic gastritis [1,3,4,12]. We therefore sought to determine the prevalence of atrophic gastritis using Pepsinogen I and gastrin-17 levels amongst type 2 Diabetes mellitus subjects and some controls in Yaounde Cameroon.

Material and Methods

A total of 51 type 2 diabetic patients undergoing follow up at Yaounde Central Hospital, the Cite Verte District Hospital were included during the three-month period January-April 2017. The control group consisted of 31 healthy students and health personnel with no history of diabetes and hypertension, none of the controls included was on antimicrobial agents, H2 receptor antagonist or proton-pump inhibitor for at least last 4 weeks. Age, sex, height, weight, and body mass index of all the participants were recorded. History of dyspepsia was recorded. The participants were also enquired for intake of non-steroidal anti-inflammatory drugs, history of treatment of *H. pylori* infection, use of proton pump inhibitors, H2 receptor antagonist and antacids. 5 ml of venous blood was aseptically collected in dry tubes, which was kept undisturbed for 1 hour for clot formation. The serum was transferred into sterile cryotubes and stored at -20 °C, for estimation of pepsinogen I and gastrin-17 levels using the PGI and G-17 Elisa of the Gastro Panel (Biohit Oyj Finland, www.biohithealthcare.com). All the diabetic patients in study group were observed for various diabetes mellitus related complications like diabetes retinopathy, nephropathy, neuropathy, and diabetic foot. Assay parameters were analysed using a software application GastroSoft (www.GastroPanel.com). All patients with PGI < 30 µg/l and G-17 < 1 pmol/l were considered positive for atrophic gastritis in the corpus and antrum respectively. Data was interpreted using Epi Info software 7.0. Chi-square test was applied to test the difference between two proportions; student (t) test was applied to test the difference between two means; Fisher (F) test was applied to test the difference of more than two means and

Table 1: Patient information.

	Diabetic Subjects Atrophy Prevalence				**Non-Diabetic Controls Atrophy Prevalence**				
	C *2(3.9%)*	*N* *6(11.8%)*	*S* *43(84.3%)*	p-value	*A* *2(6.5%)*	*C* *6(19.4%)*	*N* *7(22.6%)*	*S* *16(51.6%)*	p-value
Pepsinogen I(µg/l)	26.65 ± 5.44	71.8 ± 9.9	125.1 ± 53.9	0.04	93.5 ± 36.9	18.6 ± 10.3	97.9 ± 60.0	110.5 ± 31.7	
Gastrin-17 pmol/l	7.5 ± 0.0	3.9 ± 0.8	24.3 ± 19.2	0.02	0.1 ± 0.0	25.7 ± 26.6	8.8 ± 10.4	3.6 ± 2.5	0.01
Sex									
Males	0(0.0%)	2(33.3%)	14(32.6%)	0.62	1(50%)	2(33.3%)	5(71.4%)	10(62.5%)	0.03
Females	2(100%)	4(66.7%)	29(67.4%)		1(50%)	4(66.7%)	2(28.6%)	6(37.5%)	
Age(Yrs)	55.9 ± 9.8				40.3 ± 13.8				
19 - 29	0(0.0%)	0(0%)	0(0.0%)		0(0%)	2(33.3%)	2(28.6%)	6(37.5%)	
30 - 40	0(0%)	0(0%)	6(14.0%)		0(0%)	1(16.7%)	1(14.3%)	4(25.0%)	
41 - 51	0(0%)	2(33.3%)	4(9.3%)	0.61	2(100%)	2(33.3%)	2(28.6%)	3(18.8%)	0.62
52 - 62	2(100%)	4(66.7%)	24(55.8%)		0(0%)	0(0%)	1(14.3%)	3(18.8%)	
63 - 73	0(0%)	0(0%)	6(14.0%)		0(0%)	1(16.7%)	1(14.3%)	0(0%)	
74 - 84	0(0%)	0(0%)	3(7.0%)		0(0%)	0(0%)	0(0%)	0(0%)	
Dyspepsia									
No	0	2(33.3%)	8(18.6%)	0.54	1(50%)	1(20%)	1(33.3%)	1(8.3%)	0.45
Yes	2(100%)	4(66.7%)	35(81.4%)		1(50%)	4(80%)	2(66.7%)	11(91.7%)	

P value less than 0.05 was regarded as significant (P < 0.05). Ethical clearance was obtained from the National Ethics committee. All patients signed an informed consent form (Table 1).

Results

In total, 82 subjects were recruited aged 19-77 years, mean 50.0 ± 13.7 yrs. 52(63.4%) females (aged 19-77, mean 48.7 ± 14.7 years) and 30(36.6%) males aged 29-72, mean 52.3 ± 11.6 yrs. The study included 51(62.2%) diabetic patients aged 19-72 years, with mean age 55.9 ± 9.8 yrs and 31(37.2%) healthy controls aged 32-77 years, with mean age 40.3 ± 13.8 years. The Female/Male Sex ratio was 35:16 in diabetics and 17:14 in control group.

The prevalence of atrophic gastritis obtained was 10(12.2%). When the atrophy was classified into the various classes; 13(15.9%) presented with normal stomach mucosa, 59(72.0%) with non-atrophic (superficial gastritis), 8(9.8%) with atrophic corpus gastritis and 2(2.4%) with atrophic antrum gastritis. In the diabetic subjects, atrophic corpus gastritis was prevalent in 2(3.9%) compared to 6(19.4%) in the control subjects.

Atrophic gastritis (100%) and non-atrophic gastritis (55.8%) were frequent in the 52-62 age groups in the diabetic subjects. A higher prevalence of atrophic gastritis was observed in females than in males in both the diabetics (100% vs. 0%, p = 0.44) and non-diabetics (66.7% vs. 33.3%, p = 0.44).

In the subjects with dyspepsia, atrophic corpus gastritis was more prevalent 6(85.7%) than in non-dyspepsia subjects 1(14.3%). It was however, non-significant p = 0.45. Atrophic corpus gastritis was more prevalent in diabetics 100% than in the control group 80%.

Hypergastrinemia (G-17 > 7 pmol/l) was observed in subjects with atrophic corpus gastritis than in subjects with normal gastric mucosa (21.2 ± 24.0 vs. 6.55 ± 7.70 pmol/l). This difference was statistically significant in both the diabetics (7.5 ± 0.0 pmol/l vs. 3.9 ± 0.8 pmol/l, p = 0.024) and the controls (25.7 ± 26.6 vs. 8.8 ± 10.4 pmol/l, p = 0.008. However, very low gastrin-17 levels (G-17 < 1 pmol/l) were observed in subjects with atrophic antrum gastritis. Significantly decreased pepsinogen I levels were observed in subjects with atrophic corpus gastritis compared to subjects with normal stomach mucosa in both the diabetics (26.65 ± 5.44 µg/l) vs. (71.87 ± 9.97 µg/l) p = 0 = 004 and controls (18.58 ± 10.31 µg/l) vs. (97.91 ± 60.00 µg/l) p = 0 = 0003. On the other hand, raised pepsinogen I levels were observed in both groups of diabetics and controls with nonatrophic gastritis (125.1 ± 53.9 µg/l vs. 110.5 ± 31.7 µg/l) respectively. Among the diabetic complications, neuropathy was associated with atrophic corpus gastritis (p = 0.005).

Discussion

Patients with diabetes mellitus are often affected by chronic infections [13]. Few studies have evaluated the prevalence of atrophic gastritis in diabetic patients and the possible role of this condition in their metabolic control. The present study found 12.2% prevalence of atrophic gastritis in the study participants. The results for the distribution of the GastroPanel are similar with that of [3], who in a cohort in Kazakhstan obtained 14.1% prevalence of atrophic gastritis. These figures are however in sharp contrast to those reported in by Storskrubb, et al. [14] in Sweden and Telarata, et al. [15] in Finland where the overall prevalence of atrophic gastritis was only 6.5% and 3.5% respectively. These results are also similar with what has been reported previously in Cameroon by Noah, et al. [16] and Ebule, et al. [17] who obtained respectively 8.1% and 6.6% for atrophic gastritis. The prevalence of 9.8% atrophic corpus gastritis is in contrast to what has been reported earlier amongst dyspeptic subjects of 3.5%.

High prevalence of atrophic gastritis in the corpus, PGI < 30 µg/l (100%) was observed in the 52-62 age groups in the diabetic subjects. A higher prevalence of atrophic gastritis was observed in females than in males in both the diabetics (100% vs. 0%, p = 0.44) and non-diabetics (66.7% vs. 33.3%, p = 0.44). According to De Block, et al. [8] advancing age is a risk factor that has been associated with autoimmune gastritis positivity. In type 1 diabetic patients, autoimmune atrophic gastritisis present in 10-15% of children and 15-25% of adults [7]. Maclaren, et al. [18] have reported a female preponderance for autoimmune atrophic gastritis, although this has not been consistently observed [7].

Hypergastrinemia (G-17 > 7 pmol/l) was observed in subjects with atrophic corpus gastritis than in subjects with normal gastric mucosa. This difference was statistically significant in both the diabetics (7.5 ± 0 vs. 3.9 ± 0.8 pmol/l, p = 0.024) and the controls (25.7 ± 26.6 vs. 8.8 ± 10.4 pmol/l.0, p = 0.008. Significantly decreased pepsinogen I levels were observed in subjects with atrophic corpus gastritis compared to subjects with normal stomach mucosa in both the diabetics (26.65 ± 5.44 µg/l) vs. (71.87 ± 9.97 µg/l) p = 0 = 004 and controls (18.58 ± 10.31 µg/l) vs. (97.91 ± 60.00 µg/l) p = 0 = 0003. Hypergastrinemia and low pepsinogen I have been reported as a major characteristic in atrophic corpus gastritis and autoimmune atrophic gastritis [1,3,4,8,12,19]. The hypergastrinemia observed in the atrophic corpus gastritis is due to decreased acid production (hypo- or achlorhydria) (www.biohithealthcare.com) [19]. The decreased pepsinogen I levels observed in atrophic corpus gastritis is associated with loss of glands and cells in the corpus [6,20]. Very low gastrin-17 levels were observed in subjects with atrophic antrum gastritis (0.1 ± 0.0 mol/l). The low gastrin-17 levels are as a result of loss of G-cells probably due to *Helicobacter pylori* infection or high acid output [8,20] (www.biohithealthcare.com). We observed raised pepsinogen I level in both groups of diabetics and controls with nonatrophic (superficial) gastri-

tis (125.1 ± 53.9 µg/l vs. 110.5 ± 31.7 µg/l) respectively. This observation has been long reported by several authors [1,3,4,12,20]. Among the diabetic complications, neuropathy was associated with atrophic corpus gastritis (p = 0.005). All subjects with moderate or severe atrophic corpus gastritis are at risk for malabsorption of vitamin B12, and thus at risk for neurological and metabolic consequences known to be related to the vitamin B12 deficiency [1]. Impaired absorption of certain divalent micronutrients such as iron, calcium, magnesium, and zinc has also been reported in patients with diminished gastric acid secretion. The release and conversion of the micronutrients into actively absorbable ions require the presence of stomach acid. As a consequence, cognitive disturbances, neurodegenerative and vascular disorders, encephalopathies, anemias, and osteoporosis [8,19,21]. Many pharmaceuticals need the presence of stomach acid for proper absorption. For example, the absorption of calcium carbonate, dipyridamole, some iron formulations, and antifungal medicines, such as fluconazole and itraconazole, thyroxin, and atazanavir, are known to be impaired in acid-free subjects [1].

Conclusion

The study indicates that diabetics are more prone to atrophic corpus gastritis which is a risk factor for neurodegenrative disorders and gastric cancer and thus the need for continuous monitoring of atrophic gastritis in diabetic patients. However more extensive well-designed cohort studies are needed to definitely conclude the relationship of gastric inflammation with diabetes mellitus and its complications.

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