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The Difference of Serum Gastrin-17 Level Based on Gastritis Severity and Helicobacter Pylori Infection

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Abstract

BACKGROUND: Gastritis was defined as the histological presence of gastric mucosal inflammation. One of the most common aetiology was *H. pylori*. Gastrin-17 was a hormone that was secreted by G cells. *H. pylori* infection induced increased in gastrin-17 in gastritis. Therefore, this study was to investigate the relationship of gastrin-17 with gastritis severity and *H. pylori* infection.

AIM: To determine the difference in serum Gastrin-17 level based on gastritis severity and *H. pylori* infection.

METHODS: A cross-sectional study enrolling 45 patients with gastritis was conducted in Haji Adam Malik General Hospital between April and July 2018. Endoscopy and biopsy examinations were performed to confirm the diagnosis of gastritis. Gastritis severity was assessed using the Updated Sydney System. The presence of *H. pylori* infection was detected by a Campylobacter-like organism (CLO) examination. Gastrin-17 level and demographic data were also gathered. The analysis was done using Mann Whitney and Kruskal-Wallis test. P-value of < 0.05 was considered statistically significant.

RESULTS: Serum Gastrin-17 level was significantly different based on gastritis severity (P = 0.001 according to neutrophils infiltration and P = 0.023 according to degree of atrophy), *H. pylori* infection (P = 0.038), and combined gastritis severity and *H. pylori* infection (P < 0.001). Serum Gastrin-17 level was higher in subjects with severe neutrophils infiltration, without atrophy, and with *H. pylori* infection.

CONCLUSION: There was a significant difference in serum Gastrin-17 level based on gastritis severity and *H. pylori* infection.

Introduction

Gastritis is one of the most common digestive tract problems. Worldwide, the incidence of gastritis was 1.8-2.1 million, while in South East Asia, 583,635 per year. The incidence of gastritis in Indonesia itself is very high, which is 247,396 cases from 238.452.952 population [1]. Gastritis is defined as the histological presence of gastric mucosal inflammation. In acute gastritis, the microscopic finding is neutrophilic infiltration, while in chronic gastritis, mononuclear cells, mostly lymphocytes and plasma cells and macrophages dominate the microscopic findings [2], [13]. Chronic gastritis is classified into normal, mild, moderate, severe based on mononuclear inflammatory cells infiltration, neutrophils infiltration, atrophy, intestinal metaplasia [3], [4].

H. pylori infection plays an important role in the development of peptic ulcer in gastritis patients. *H. pylori* infection in developing countries was about 25-30%, where 5-27% were found in early childhood and 50-60% were found in adults aged more than 60 years old [1]. *H. pylori* reside within the mucous layer. The stomach is a dangerous environment for most other microorganism because of its low pH. The ability of *H. pylori* to flourish in the stomach has been attributed to a protective mechanism such as its production of urease, protecting bacteria from gastric acidity by creating a basic microenvironment. *H. pylori* can cause both acute and chronic gastritis in inadequately treated *H. pylori* patients; Chronic gastritis can progress to chronic atrophic gastritis.

Gastrin prohormone is produced by G cells located within gastric antrum and corpus in response to vagal and gastrin-releasing peptide (GRP) stimulation secondary to ingestion of peptides, amino acids, gastric distention and an elevation of stomach pH. The prohormone is later processed to shorter peptides. Two major forms of gastrin are secreted which are Gastrin-17 and Gastrin-34. The major role of gastrin within gastric tissue is the regulation of acid secretion. In *H. pylori* infection, Gastrin levels are found to be consistently elevated, and normal physiological negative feedback control of secretion is lost. Furthermore, after *H. pylori* treatment, gastrin levels are decreased and normal feedback control of gastrin secretion is restored [4].

Given the high prevalence of gastritis, this study is aimed to determine the difference in serum Gastrin-17 level based on gastritis severity and *H. pylori* infection.

Methods

Study Design

A cross-sectional study was conducted in Haji Adam Malik General Hospital Medan, Indonesia between April and July 2018 following approval from the Ethics Committee of the Faculty of Medicine Universitas Sumatera Utara and Haji Adam Malik General Hospital.

Subject Recruitment

Individuals who were not pregnant, aged 18 years or older, and willing to take part in the study were enrolled in this study. Exclusion criteria included patients who had received *H. pylori* eradication therapy within the last 6 months or on antibiotic therapy commonly used in eradication therapy, concomitant use of proton pump inhibitors, H2 receptor antagonists, NSAIDs, steroids, and alcohol for the last 48 hours and patients with systemic disease.

Physical examination, routine blood count, liver and kidney function, blood sugar, amylase, and lipase evaluation, ECG, and abdominal ultrasound were conducted to assess the exclusion criteria. Subjects then underwent endoscopy and biopsy examination to establish the diagnosis of gastritis. All endoscopy examinations used scopes. Biopsy specimens were obtained from 5 places, including the greater and lesser curvature of the distal antrum, lesser curvature at incisura angularis, anterior and posterior wall of the proximal corpus. Additional biopsies were also done in suspicious regions that were not mentioned previously. Histopathologic examination was done by Anatomic Pathologists at Universitas Sumatera Utara blindly. Gastritis severity was determined using the Updated Sydney System.

Serum gastrin levels were measured in serum using the ELISA human gastrin-17 (BIOHIT OYJ, Laipattie, Fl-00880 Helsinki, Finland). Campylobacter-like Organism test (CLO) was performed to detect *H. pylori*. The changing of colour from yellow to red magenta, pink, or dark orange means positive *H. pylori* infection.

Statistical Analysis

Data from this study were analysed statistically using a descriptive study to obtain baseline characteristics. Mann Whitney U test was used to determine the difference in serum Gastrin-17 levels based on *H. pylori* infection, while the difference in serum Gastrin-17 levels based on gastritis severity was analysed using the Kruskal-Wallis test. The calculation was conducted at a 95% confidence interval and P-value of < 0.05 was considered significant.

Results

A total of 45 gastritis patients were enrolled in this study. There were 25 (55.6%) males. The mean age was 51.0 (SD 12.27) years, with mean Body Mass Index (BMI) of 23.0 (SD 4.02) kg/m^2. The majority of the ethnic background was Bataknese (71.1%).

Table 1: Baseline characteristics

Characteristics	n = 45
Gender, n (%)	
Male	25 (55.6)
Female	20 (44.4)
Mean age, years (SD)	51.0 (12.27)
Mean body mass index,kg/m^2 (SD)	23.0 (4.02)
Ethnic background, n (%)	
Acehnese	3 (6.7)
Bataknese	32 (71.1)
Javanese	10 (22.2)
Occupation, n (%)	
Housewife	11 (24.4)
Private employee	12 (26.7)
Government employee	4 (8.9)
Entrepreneur	18 (40)
Mean gastrin-17 level, pmol/mL (SD)	14.0 (12.92)
CLO, n (%)	
Positive	23 (51.1)
Negative	22 (48.9)
Chronic inflammation, n (%)	
Mild	23 (51.1)
Moderate	7 (15.6)
Severe	5 (11.1)
Neutrophil infiltration, n (%)	
Normal	22 (48.9)
Mild	18 (40.0)
Moderate	15 (33.3)
Degree of atrophy, n (%)	
Normal	36 (80.0)
Mild	4 (8.9)
Moderate	5 (11.1)

Mean serum Gastrin-17 levels in this study were 14.0 pmol/mL. The result of CLO examination

showed 23 (51.1%) gastritis patients had positive results. The result of the histopathological examination for chronic inflammation showed 51.1% of patients had mild inflammation. Based on neutrophils infiltration, 18 (40.0%) had mild infiltration and 15 (33.3%) had moderate infiltration. Based on the degree of atrophy 4 (8.9%) patients had a mild degree and 5 (11.1%) had a moderate degree (Table 1).

The difference in serum Gastrin-17 levels based on gastritis severity was shown in Table 2. There were statistically significant differences in serum Gastrin-17 levels based on gastritis severity according to neutrophils infiltration and degree of atrophy (P = 0.001 and 0.023, respectively). Patients with severe neutrophils infiltration had the highest serum Gastrin-17 level in their group, while patients without atrophy had the highest serum Gastrin-17 level in their group.

Table 2: Differences in Gastrin-17 levels based on gastritis severity

	N	Gastrin-17, median (min-max)	p*
Chronic inflammation			
Mild	23	6.0 (0.8-33.0)	0.806
Moderate	7	2.6 (0.8-40.0)	
Severe	15	19.5 (1.1-40.0)	
Neutrophil inflammation			
Normal	22	4.2 (0.8-40.0)	0.001
Mild	18	14.0 (1.1-40.0)	
Severe	5	27.6 (15-40.0)	
Atrophy			
Normal	36	13.65 (0.8-40.0)	0.023
Mild	4	5.85 (5.8-6.0)	
Moderate	5	1.5 (1.1-2.6)	

*Kruskal Wallis test.

There was a statistically significant difference in serum Gastrin-17 levels based on *H. pylori* infection (P = 0.038). Median serum Gastrin-17 levels are shown in Table 3.

Table 3: Serum Gastrin-17 levels differ based on *H. pylori* infection

CLO	Gastrin-17, median (min-max)	P*
Positive	14.2 (1.1-40.0)	0.038
Negative	9.0 (0.8-33.0)	

*Mann Whitney U test.

We also analysed the difference in serum Gastrin-17 level based on *H. pylori* infection in each gastritis severity group.

Table 4: Differences in serum Gastrin-17 levels based on *H. Pylori* infection in each gastritis severity group

Gastrin-17 Level, median (range)		N	*H. pylori* (+)	*H. pylori* (-)	P*
Chronic inflamation	Mild	23	5.8 (1.5-6.0)	10.0 (0.8-33.0)	0.218
	Moderate	7	8.6 (2.6-40.0)	1,65 (0.8-24.0)	0.157
	Severe	15	19.5 (1.1-40.0)	-	-
Neutrophil infiltrasion	Normal	22	5.8 (1.5-40.0)	2,2 (0.8-33.0)	0.480
	Mild	18	13.8 (1.1-40.0)	21.8 (10.3-26.1)	0.750
	Severe	5	27.6 (15-40.0)	-	-
Atrophy	Normal	36	19.8 (8.6-40.0)	9.7 (0.8-33.0)	< 0.001
	Mild	5	5.9 (5.8-6.0)	5.8	0.346
	Severe	5	1.5 (1.1-2.6)	-	

*Mann-Whitney U test.

Based on the statistical analysis, we found a significant difference in serum Gastrin-17 levels in patients without atrophy between positive and negative *H. pylori* infection with a P value of < 0.001. Significantly higher serum Gastrin-17 level was observed in patients with positive *H. pylori* infection without atrophy (Table 4).

Discussion

Gastrin is secreted by G cells, which are presented in gastric antrum and duodenum. Gastrin is secreted in response to vagal and gastrin-releasing peptide (GRP) stimulation secondary to ingestion of peptides, amino acids, gastric distention and an elevation of stomach pH. The secret gastrin into the systemic circulation is delivered to parietal cells and enterochromaffin-like cells (ECL) in gastric fundus and cardia. Gastrin stimulated parietal cells to secrete gastric acid and ECL to secret histamine which also results in gastric acid production [14].

H. pylori infection mostly is found in antrum at an early stage and in both corpus and antrum in the later stage of infection. It causes gastric inflammation which released cytokines (TNFα, IL1β, IFN gamma, IL8) [4], [12]. Gastric inflammation/gastritis are described by neutrophils infiltration level, lymphocytes level, present of intestinal metaplasia and atrophy. High level of TNFα is related to a severe degree of neutrophils infiltration. Because of its potent chemotactic and stimulatory activity on neutrophils and lymphocytes, high IL8 count is related to severe degree of chronic inflammation, neutrophils infiltration, atrophy and intestinal metaplasia [16]. Cytokines caused elevation of gastrin production. Increment of gastrin levels in *H. pylori* gastritis is also contributed by reduced somatostatin secreting D-cells [19]. In this study, Gastrin-17 levels were significantly higher in patients with positive *H. pylori* infection compared to negative *H. pylori* infection (p = 0.038). This result was supported by the previous study which was conducted by Park et al., [4] They reported fasting serum gastrin concentrations were significantly higher in patients with *H. pylori* infection compared to patients without infection (80.3 ± 23.5 vs 47.6 ± 14.1 pg/ml, p < 0.001).

In Sheykholeslami et al., study, Gastrin-17 was increased in corpus-predominant gastritis (p < 0.01) [5]. However in this study, Gastrin-17 level was significantly higher in severe neutrophil infiltration. Meanwhile, in chronic inflammation, Gastrin -17 was higher in the severe category but was not significantly different.

In our study, Gastrin-17 level tends to be lower in moderate atrophy (1.5 pmol/mL), and the highest value was observed in subjects without atrophy (13.63 pmol/mL) (p = 0.023). This result was consistent with a study that was done by Vaananen et

al., [7], Ebule et al., [11]. In most cases, *H. pylori* colonisation occurs, causing peptic ulcer disease in the antrum, gastric atrophy and achlorhydria in gastric corpus. *H. pylori* induce chronic inflammation eventually lead gastric to become atrophic. In atrophic gastritis, the mucosal gland is replaced by immature gland and epithelial cells which is intestinal type gland (intestinal metaplasia), fibrous tissue and/or pyloric type (resembling pyloric glands and epithelium that has no G cell inside) [17]. The decrement in G cell population causes gastrin production to decrease as the atrophic progress [8], [15]. Serum Gastrin-17 is significantly reduced in antral atrophy and coexistence of corpus atrophy [18].

In conclusion, we found a significant difference in serum Gastrin-17 level based on gastritis severity and *H. pylori* infection. Serum Gastrin-17 level is higher in subjects with severe neutrophil infiltration, without atrophy, and with *H. pylori* infection.

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