The Differences Level of Resistin between Positive and Negative *Helicobacter pylori* Gastritis and its Correlation with Nutritional Status

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ABSTRACT

Background: H. pylori gastritis can be related to people with obesity and metabolic syndrome. The mechanism underlying the relationship between them is suspected to be caused by adipocytokine called resistin. Objective: to analyze the difference level of resistin between positive and negative H. pylori gastritis patients and their relationship with nutritional status.

Method: This cross sectional study was done in the Gastroenterology department of General Hospital Adam Malik, Medan, from May to October 2019. Patients with gastritis diagnosed by endoscopy underwent rapid urease test (RUT), resistin, albumin, hemoglobin tests, also body mass index (BMI) and waist circumference (WC) were measured.

Results: Sixty gastritis patients found by endoscopic examination, 29 (48.33%) was H. pylori positive and 31 (51.67%) was negative. No significant differences were found between BMI, WC, and albumin against H. pylori gastritis with p values 0.099, 0.055, and 0.528, respectively. Hemoglobin was found significant with a p 0.009. The mean resistin in the positive H. pylori group was 7.62 ng/mL while the negative was 3.23 ng/mL, and statistically significant (p < 0.001). There was a strong positive correlation between resistin levels with BMI and WC (BMI p 0.01, r 0.577; WC p 0.001, r 0.592).

Conclusion: Resistin levels in gastritis with H. pylori positive are higher than H. pylori negative, body mass index and waist circumference have a strong relationship with resistin levels in patients with positive H. pylori gastritis, hemoglobin is lower in H. pylori positive than negative gastritis.

Keywords: resistin, gastritis, Helicobacter pylori, body mass index, obesity

ABSTRAK

Latar belakang: Gastritis H. pylori dapat dikaitkan dengan orang dengan obesitas dan sindrom metabolik. Mekanisme yang mendasari hubungan di antara mereka diduga disebabkan oleh adipositokin yang disebut resistin. Tujuan: untuk menganalisis perbedaan tingkat resistin antara pasien gastritis H. pylori positif dan negatif dan hubungannya dengan status gizi.

Metode: Penelitian cross sectional yang dilakukan di departemen Gastroenterologi Rumah Sakit Umum Adam Malik, Medan, dari Mei hingga Oktober 2019. Pasien dengan gastritis yang didiagnosis dengan endoskopi menjalani pemeriksaan rapid urease test (RUT), resistin, albumin, hemoglobin, serta pengukuran indeks massa tubuh (IMT) dan lingkar pinggang (LP).

Hasil: Enam puluh pasien gastritis ditemukan dengan pemeriksaan endoskopi, 29 (48.33%) adalah H. pylori positif dan 31 (51.67%) negatif. Tidak ada perbedaan signifikan yang ditemukan antara IMT, LP, dan albumin terhadap H. pylori gastritis dengan nilai p masing-masing 0.099, 0.055, dan 0.528. Hemoglobin ditemukan signifikan dengan p 0.009. Kadar rerata resistin pada kelompok H. pylori positif adalah 7.62 ng/mL sedangkan pada kelompok negatif adalah 3.23 ng/mL, dan signifikan secara statistik (p <0.001). Dijumpai korelasi positif kuat antara kadar resistin dengan IMT dan LP (IMT p 0.01, r 0.577; LP p 0.001, r 0.592).

Simpulan: Kadar resistin pada gastritis H. pylori positif lebih tinggi daripada H. pylori negatif, indeks massa tubuh dan lingkar pinggang memiliki hubungan yang kuat dengan kadar resistin pada pasien dengan gastritis H. pylori positif, hemoglobin lebih rendah pada H. pylori positif daripada negatif.

Kata kunci: resistin, gastritis, Helicobacter pylori, indeks massa tubuh, obesitas

INTRODUCTION

Gastritis is inflammation of the gastric mucosa, caused by *Helicobacter pylori*, bile reflux, non-steroidal anti-inflammatory or allergic respons.[1] The incidence of gastritis in Southeast Asia around 583,635 of the total population every year.[2] *H.pylori* is the most common cause of gastritis. The prevalence of *H. pylori* infection in peptic ulcer patients varies between 90-100% in Indonesia.[3]

Adipose tissue in obesity have a biological role, not only play a role in triglycerides metabolic processes but also acts as an endocrine gland that secretes various cytokines and peptide hormones which play a role not only in regulating the balance of body weight and energy metabolism, but also in the inflammatory process. Some of these substances are adiponectin, leptin, resistin, interleukin-6, tumor necrosis factor-α (TNF-α).[4] Resistin is thought to have a role in the condition of insulin resistance.[5]

Together with adiponectin, resistin has been a research topic for the past several decades. Hypoadiponectinemia is associated with various diseases, including gastritis. In previous studies it was said that the anti-inflammatory properties of adiponectin have a protective effect against gastrointestinal diseases. In contrast resistin has a proinflammatory effect.[6] In addition, Samuel et. al showed that subjects who were lean and resistant to insulin might have higher levels of pro-inflammatory markers (MCP-1, IL-6 and resistin) than subjects who were overweight and still insulin sensitive.[7]

There has been no report exploring resistin levels in *H. pylori* gastritis patients, we therefore studied the difference level of resistin between positive and negative *H. pylori* gastritis patients and their relationship with nutritional status (body mass index, waist circumference, hemoglobin, and albumin.

METHOD

This cross sectional study was conducted at the Endoscopic Unit of H. Adam Malik Hospital and other network hospital in Medan, North Sumatera, after obtaining approval from the Health Research Ethics Commission and related institutions. The time of the study was carried out on May to October 2019.

The inclusion criterias were men and women who are not pregnant aged 18-70 years, diagnosed with gastritis from endoscopic examination results histopathology. The exclusion criterias were patients who received *H. pylori* eradication therapy in the last 6 months or currently on antibiotic therapy which commonly used in eradication therapy, take Proton Pump Inhibitor, H2-receptor antagonist, non-steroid anti inflammation drugs, steroids, alcohol for the past 48 hours, patients with systemic diseases and malignancies, and the subject refused to participate.

Dyspepsia according to Rome III criteria is one or more symptoms: fullness after eating, feeling full quickly, epigastric pain, or burning sensation in the epigastrium that occurs in the last 3 months, with the onset of symptoms occurring at least 6 months before diagnosis.

A 4 mL blood sample was inserted into the vacutainer tube without anticoagulation. Blood that has been taken is stored at room temperature for 30-45 minutes until the blood clots and then centrifuged at a speed of 3000 rpm for 15 minutes. The serum formed

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was put into 3 serum tubes, each as much as 0.5 mL for measurement of resistin, hemoglobin, albumin. Store at -20 ° C (each given identity: name, gender, date and type of serum sample).

BMI is measured by comparing weight (in kilograms) to height (in meters squared). Waist circumference is measured on the abdomen above the umbilicus in centimeters (cm).

All endoscopic examinations using scopes (Olympus, Tokyo, Japan) in the endoscopic unit of H. Adam Malik Hospital. The endoscopic procedure was performed by an experienced endoscope who is the same at each subject examination. Endoscopy was done after the subject has fasted overnight (10-12 hours). Endoscopy was performed to look at the gastric mucosa whether it has edema, erythema (spotted, patchy, linear)/exudate/bleeding/ erosive; and retrieving networks for CLO checks.

To detect *H. pylori*, two biopsy specimens were each collected from the major curvature in the middle of the body and antrum of gastric. Serology (CLO) was performed by a gastroenterohepatologist who did the endoscopy.

This study used univariate analysis by analyzing the frequency distribution of independent and dependent variables, while bivariate analysis uses an independent T test if the data is normally distributed, and if the data is not normally distributed using the Mann Whitney test. Nutritional status variables would be tested for correlation with resistin levels using Spearman correlation.

RESULTS

Sixty patients who met the inclusion criteria included in this study. A total of 34 patients (56.7%) were male and 26 patients (43.3%) were female. The average age is 46.5 years. The majority of respondents in the Batak ethnicity were 37 people (61.7%). Most of the patients who were respondents in this study were 27 employees (45%). The highest level of education is high school, 32 people (53.3%).

The mean BMI of respondents was 23.35 ± 3.98 kg/m^2. The mean waist circumference was 84.45 ± 8.24 cm, the median hemoglobin was 14 (10.4-16) g/dL, the average albumin was 4.5 ± 0.57 g/dL, and the median value resistin was 5.12 (2.12-10) ng/mL.

By using the independent T-test, there were no significant differences found between BMI, waist circumference, and albumin in *H. pylori* gastritis with p values of 0.099, 0.055, and 0.528, respectively. Statistical analysis of hemoglobin with the Mann Whitney test found a difference between positive and negative *H. pylori* with a p value of 0.009.

Table 1. Research subjects characteristics (n = 60)

Variable	n (%)
Gender	
Men	34 (56,7)
Women	26 (43,3)
Age, median (min-max), years old	46,5 (24-66)
Ethnic	
Batak	37 (61,7)
Java	18 (30)
Aceh	5 (8,3)
Occupation	
Employees	27 (45)
Housewife	14 (23,3)
Entrepreneur	16 (26,7)
Civil servants	3 (5)
Education	
Elementary school	3 (5)
Middle school	14 (23,3)
High school	32 (53,3)
University	11 (18,3)
BMI, (mean ± SD), kg/m2	23,35 ± 3,98
WC, (mean ± SD), cm	84,45 ± 8,24
Hb, median (min-max), g/dL	14 (10,4-16,0)
Albumin, (mean ± SD), g/dL	4,5 ± 0,57
Resistin, median (min-max), ng/mL	5,12 (2,12-10)

BMI: body mass index, WC: waist circumference, Hb: Hemoglobin

Table 2. Relationship characteristics of research subjects based on positive and negative *H. pylori* groups

Variable	*H. pylori* positive (n = 29), n (%)	*H. pylori* negative (n = 31), n (%)	p
Gender			
Men	17 (58,6)	17 (54,8)	0,768a
Women	12 (41,4)	14 (45,2)	
Age, median (min-max), years old	49 (25-66)	44 (24-63)	0,154c
Ethnic			
Bataknese	16 (55,2)	21 (67,7)	0,597a
Javanese	10 (34,5)	8 (25,8)	
Acehnese	3 (10,3)	2 (6,5)	
Occupation			
Employees	10 (34,5)	17 (54,8)	0,227a
Housewife	7 (24,1)	7 (22,6)	
Entrepreneur	11 (37,9)	5 (16,1)	
Civil servants	1 (3,4)	2 (6,5)	
Education			
Elementary school	3 (10,3)	0	0,005a
Middle school	10 (34,5)	4 (12,9)	
High school	15 (51,7)	17 (54,8)	
University	1 (3,4)	10 (32,3)	
BMI, (mean ± SD), kg/m2	24,22 ± 4,52	22,5 ± 3,25	0,099b
WC, (mean ± SD), cm	86,55 ± 8,67	82,48 ± 7,43	0,055 b
Hb, median (min-max), g/dL	12,5 (10,4-16)	14,6 (10,4-16)	0,009 c
Albumin, (mean ± SD), g/dL	4,55 ± 0,59	4,46 ± 0,54	0,528 b

Note: a. Chi-square test; b. Independent T-test; c. Mann-Whitney U test

BMI: body mass index, WC: waist circumference, Hb: Hemoglobin

There were significant mean differences ($p < 0,001$) of resistin levels in patients with positive and negative *H. pylori*. The mean resistance in the positive *H. pylori* group was higher with an average of 7.62 ng/mL while in the group with *H. pylori* negative with an average of 3.23 ng/mL.

By using the Spearman correlation test to determine the relationship between resistin and body mass index and waist circumference in group of patients with *H. pylori* positive, showed there was a strong and

positive relationship between resistin levels with body mass index and waist circumference and statistically significant (BMI p 0,01, r 0,577, WC p 0,001, r 0,592)

Table 3. Resistin levels based on positive and negative *H. pylori* groups

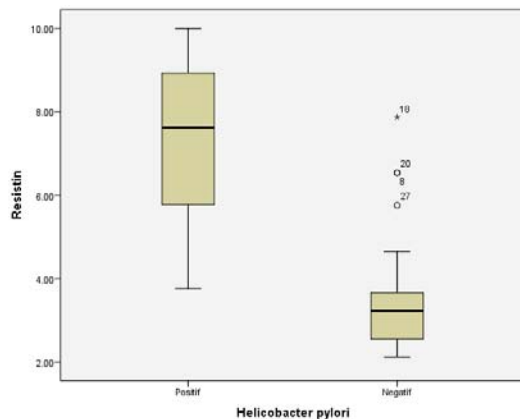| Variable	*H. pylori* positive	*H. pylori* negative	p
Resistin, median (min-max), ng/mL	7,62 (3,76-10)	3,23 (2.12-7,87)	< 0,001

Figure 1. Differences in Resistin Levels between groups of patients with positive and negative *H. pylori*

Table 4. Relationship of BMI, WC, Hb, Albumin to resistin levels in the group with positive *H. pylori*

Variable	Resistin	
	p	r
Body mass index (BMI)	0,01	0,577
Waist circumference (WC)	0,001	0,592
Hemoglobin (Hb)	0,842	0,039
Albumin	0,543	0,118

DISCUSSION

The average age is 46.5 years in this study but not statistically significant between two groups (p = 0.154). The characteristic baseline data in this study is also based on gender where the results of this study were 34 patients (56.7%) were male and 26 patients (43.3%) were female. Statistical analysis of sex relations with positive or negative *H. pylori* did not show significant results (p = 0.768). This is in accordance with the study of Al-Zubaidi[8], in obese and non-obese patients with positive *H. pylori* infections, found 65% were male, but gender was not significantly related to *H. pylori* (p = 0.200).

In terms of socio-economic demographic factors, most of the patients who were respondents in this study were 27 private employees (45%). The highest level of education is high school, 32 people (53.3%). However, a statistical analysis of the employment relationship with positive and negative *H. pylori* was found to be insignificant, while a statistical analysis of the educational level with *H. pylori* was found to be significantly different from the results of p 0.005 (p < 0.05). Demographic and socioeconomic factors were assessed in a study by Genta et al of 487,587 Americans who underwent endoscopy with a biopsy.[9] High income levels and higher education are associated with a decrease in the prevalence of *H. pylori* gastritis, as well as intestinal metaplasia and gastric atrophy.

One important factor affecting the upper gastrointestinal tract is BMI which is known to be associated with gastritis. From this study, BMI and WC of positive *H. pylori* group was higher than *H. pylori* negative, however, bivariate analysis found no significant differences (p: 0.099 and 0.055, respectively). In line with the study of Akeel et. al[10] found a non-significant difference in prevalence among various categories of BMI.

Bivariate analysis of hemoglobin in this study found a difference between positive and negative *H. pylori* (p = 0.009), Hb was lower in *H. pylori* positive group. In line with Mwafy & Afana, it shows that the average level of hemoglobin is significantly lower in *H. pylori* infection and *H. pylori* infection seems to cause a decrease in vitamin B12 levels, iron levels and several haematological parameters.[11] Albumin showed no significant differences between two groups (p: 0.528). In line with research by Rasane et al found that *H. pylori* negative group had lower serum albumin levels (2.97 ± 0.96 vs. 3.86 ± 0.91; p = 0.0001).[12]

To determine the mechanism underlying the relationship between obesity and *H. pylori* gastritis, we examined the serum concentration of resistin in the same subject previously analyzed for the relationship of BMI with *H. pylori* gastritis, and found that the prevalence of *H. pylori* gastritis increased when resistin levels increased, using the Mann Whitney test found a significant mean difference (p < 0.001) of resistin levels in patients with positive and negative *H. pylori* gastritis. The mean resistin in the group with *H. pylori* positive was higher with an average of 7.62 ng/mL while in the group with *H. pylori* negative with a mean of 3.23 ng/mL.

Higher levels of resistin was found in *H. pylori* gastritis. Although it has not been able to clarify the role of resistin in the pathogenesis of *H. pylori* gastritis in this study, it is suspected that resistin is indeed pro-inflammatory in gastritis. Previous research examining resistin levels in *H. pylori* infection in humans has not yet been established.

Resistin regulation in carbohydrate metabolism is thought to be associated with insulin resistance. Resistin is able to regulate the metabolism of insulin-stimulated carbohydrates in many insulin target organs.[13] Since the discovery of resistin, most studies have focused the relationship of resistance to obesity and diabetes.

Resistin has also been involved in inflammatory conditions and has been shown to be secreted in sufficient quantities by mononuclear cells. Its role in inflammation is the induction of expression and release of IL-1b, IL-6, IL-8, IL-12, TNF-α, and Toll-like-receptor-2 (TLR-2) through the NF-kB pathway.[14]

Together with adiponectin, resistin has been a research topic for the past several decades. Hypoadiponectinemia is associated with various diseases, including gastritis. In previous studies it was said that the anti-inflammatory properties of adiponectin have a protective effect against gastrointestinal diseases. In contrast resistin has a proinflammatory effect.[6] In addition, Samuel et al showed that subjects who were lean and resistant to insulin might have higher levels of pro-inflammatory markers (MCP-1, IL-6 and resistin) than subjects who were overweight and still insulin sensitive.[7]

By using the Spearman correlation test of resistin with BMI in a group of patients with *H. pylori* positive, r 0.577 with p = 0.01, and with WC r 0.592 with p = 0.001 was found, meaning that there was a strong relationship between resistin levels with BMI and statistically significant. Hassan and Azim showed that there were statistically significant differences between the levels of resistin in the three groups (p < 0.001), group I: BMI less than 25%, and hemoglobin levels less than 11 g/dL, group II: BMI more than 30% and the hemoglobin level is less than 11 g/dL, group III: healthy control with BMI less than 25%.[15] In group II there was a statistically significant direct correlation between serum resistin levels and BMI. There is a statistically significant inverse correlation between resistin level and hemoglobin level which indicates that an increase in hemoglobin level is associated with a decrease in resistin levels and vice versa.

However, to investigate whether resistin is related to *H. pylori* gastritis independently of body mass index, a multivariate analysis should be undertaken which includes other potential risk factors for gastritis, such as living habits (smoking, food, and drinking alcohol) as well as markers of serum metabolism (cholesterol, triglycerides, glucose, and insulin levels), in addition to body mass index, waist circumference, and resistin.

CONCLUSION

Resistin levels in gastritis with *H. pylori* positive are higher than *H. pylori* negative. Body mass index and waist circumference have a strong relationship with resistin levels in patients with positive *H. pylori* gastritis. Hemoglobin is found to be lower in *H. pylori* positive than negative gastritis.

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