The Comparison of Serum Malondialdehyde Level Between *H. pylori Positive* and *H. pylori Negative Gastritis* Patients

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ABSTRACT

Background: *Helicobacter pylori is the most common cause of chronic gastritis in the world, meanwhile gastritis caused by non-steroidal anti-inflammatory drugs (NSAIDs) is the most encountered type of gastritis. Increased free radicals caused by Helicobacter pylori can cause damage in gastric mucous. Tissue damage due to free radicals can be examined by measuring malondialdehyde compound. There are many studies that proves the increased malondialdehyde in gastritis, but those studies commonly done in animal experimentation and malondialdehyde examination in gastric mucous.*

Method: *This is a cross-sectional study of 40 dyspepsia patients who came to endoscopic unit of Adam Malik General Hospital Medan and networking hospitals by using Rome III criteria. Further examination with gastroscopy and biopsy was done to determine gastritis. H. pylori examination was done by using Campylobacter-like organism test (CLO) test. Serum malondiasldehyde level was examined with high performance liquid chromatography (HPLC) method.*

Results: *From total of 40 patients,24 (60%) were men and 16 (40%) were women with an average age of 47 years, the majority of the ethnic was Bataknese (57.5%). From 20 patients with H.pylori (+), the average level of malondialdehyde was 1.58 umol/mL while in 20 other patients with H. pylori (-), malondialdehyde level was 1.19 umol/mL with p value 0.013.We found the mean serum levels of malondialdehyde was higher in H. pylori positive gastritis than H. pylori negative.*

Conclusion: *Serum Malondialdehyde level was significantly higher in patient with positive H. pylori gastritis compared to H. pylori negative gastritis.*

Keywords: *gastritis, Malondialdehyde, Helicobacter pylori*

ABSTRAK

Latar belakang: *Helicobacter pylori merupakan penyebab tersering gastritis kronik di seluruh dunia, sementara gastritis akibat NSAIDs merupakan penyebab gastritis yang sering dijumpai. Peningkatan radikal bebas yang disebabkan Helicobacter pylori mengakibatkan terjadinya kerusakan mukosa gaster. Kerusakan jaringan akibat radikal bebas diperiksa dengan mengukur senyawa malondialdehyde. Banyak studi yang membuktikan peningkatan malondialdehyde pada gastritis. Namun, penelitian-penelitian tersebut umumnya dilakukan pada hewan coba dan pemeriksaan malondialdehyde di mukosa gaster.*

Metode: *Penelitian dilakukan dengan desain cross sectional terhadap 40 penderita dispepsia yang datang ke unit endoskopi Rumah Sakit H. Adam Malik Medan dan Rumah Sakit jejaring dengan menggunakan kriteria Rome III. Selanjutnya dilakukan gastroskopi dan biopsi untuk menentukan adanya gastritis dan pemeriksaan H. pylori dengan menggunakan Campylobacter-like organism test (CLO) test. Kadar malondialdehyde serumdiperiksa dengan menggunakan metode high performance liqiud chromatography (HPLC).*

Hasil: *Dari 40 subyek, 24 orang (60%) pria, 16 orang perempuan (40%), rerata umur 47 tahun, mayoritas bersuku Batak 23 o rang (57,5%). Pada 20 orang penderita gastritis H. pylori positif didapatkan nilai rerata malondialdehyde sebesar 1,58 µmol/mL sedangkan pada 20 penderita gastritis H. pylori negatif yaitu sebesar 1,19 µmol/mL dengan p 0,013. Ditemukan rerata kadar malondialdehyde serum lebih tinggi pada gastritis H. pylori positif dibandingkan gastritis H. pylori negatif (p = 0,013).*

Simpulan: *Kadar malondialdehyde serum lebih tinggi secara signifikan pada pasien gastritis H. pylori positif dibandingkan dengan gastritis H. pylori negatif.*

Kata kunci: *gastritis, Helicobacter pylori, Malondialdehyde.*

INTRODUCTION

Gastritis is an inflammation process in gastric mucous and submucous as a response to acute or chronic injury. *Helicobacter pylori* infection is the most common cause of active chronic gastritis in the world, meanwhile chemical gastritis due to NSAID is the second most common risk factor in gastritis.[1]

H. pylori prevalence in the western world keep decreasing due to improvement of quality of life, good hygiene, lower density, and antibiotic usage. Meanwhile in Asia, *H. pylori* infection rate is very high, including Indonesia.[2,3] Reactive Oxygen Species that was produced by the bacteria is one of many important factor whereas oxydative stress has an important role in the pathogenesis of worsening gastritis and gatric ulcer.[4] *H. pylori* infection will cause neutrofil and macrofage/monosit recruitment which in turn increase free radical that implied in gastric mucous damage. Radical Anion Superoxyde (O2-) resulted by neutrofil infiltration to cellular lipid membrane which produce lipid peroksidase that metabolized to malondialdehyde. Lipid tissue damage due to free radical that can be measured with malodialdehyde compound measurement which is a lipid peroxidase product. Free radical production indirectly measured by lipid peroksidase level. Malondialdehyde is a biomarker to assess oxydative stress condition.[5]

Turkkan et al proved that severe chronic inflammation correlate with higher malondialdehyde level in study subject.[6] Navvabi et al that studies *H. pylori* effect on oxydative stress in chronic gastritis patient showed that malodialdehyde and oxydised glutation level increased significantly in *H. pylori* patient, meanwhile total antioxydant level and reduced glutathion significantly decreased.[7] Many studies have proved the role of free radical to gastritis. But, many of these studies usually done in animal and the malondialdehyde level was examined from gastric mucous. The aim of this study is to compare serum malondialdehyde level in *H. pylori* positive gastritis and *H. pylori* negative gastritis patients.

METHOD

This is a descriptive analytic study with cross sectional design, which is done from April to June 2017 and was conducted in Endoscopy Unit Adam Malik General Hospital Medan and Faculty Medicine of Universitas Sumatera Utara. Patients age 18 years and older who diagnosed with gastritis from endoscopic and histopathologic examinations were enrolled in this study. The exclusion criteria were patients who have received previous treatment for *H. pylori* infection in the last six months, use of proton pump inhibitor (PPI) and H2 receptor antagonist during 2 days before the study, and currently on antibiotic theraphy for *H. pylori* eradication, diabetes melitus, hypertension, obesity, renal failure, hepatitis, liver cirhossis, coronary artery disease, congestive heart failure, rheumatic disease, infection diseases, gastrointestinal bleeding, peptic ulcer and malignant diseases.

The sample size was determined by using the formula of unpaired numerical comparative analytical 2 groups, with 95% confidence level, 90% power, and 10% increment to avoid design error, 20 samples are needed in each group. With the total sample size is 40 people.

Affiliate hospital after approval from ethical commission and related institute. Dyspepsia patient, defined with Rome III criteria, was then examined by using endoscopy and biopsy. To

detect *H. pylori*, serology examination (CLO) was done. Malondialdehyde examination was done by HPLC examination (high performance liquid chromatography). Data was analyzed by using Mann Whitney Test with standard deviation (a) 0.05. The data was processed and analyzed by using SPSS version 22.

RESULTS

This study include 40 patient that has fulfilled inclusion criteria dan divided to two group, each with 20 patient in *H. pylori* (+) gastritis patient and 20 patient in *H. pylori* (-) gastritis patient. 24 patient (60%) was male and 16 (40%) patient was female with average age 48 years old. Median malodndialdehyde level was 1.27 ng/mL. Baseline characteristic and clinical profile of the subject was showed in Table 1.

Table 1. Baseline characteristic and clinical profile of the subject (n = 40)

Characteristic	n (%)
Sex	
Male	24 (60) [a]
Female	16 (40)
Age, mean, years	47,85 (14,85) [b]
Ethnicities	
Bataknese	23 (57,5) [a]
Javanese	11 (27,5)
Acehnese	6 (15)
Religion	
Moslem	24 (60) [a]
Christian	11 (27,5
Hinduism	5 (12,5)
Education level	
Elementary school	6 (15) [a]
Junior high school	8 (20)
Senior high school	22 (55)
Bachelor degree	4 (10)
Jobs	
Entrepreneur	16 (40) [a]
Housewife	12 (30)
Employees	10 (25)
Farmer	2 (5)
Body mass index (BMI), mean, kg/m^2	21,53 (3,93) [b]
< 18,5	2 (5)
18,5-24,9	38 (95)
≥ 25	0 (0)
Malondyaldehide, median (min-max), μ mol/mL	1,27 (0.78-2.91) [c]

[a]Cathegorical Data: n(%) [b] Numeric data, normal distribution: median (min – max), [c]numeric data, non-normal distribution: median (min-max)

From this data, the mean malondialdehyde level in *H. pylori* (+) patient was 1.58 and the *H. pylori* (-) was 1.19 with p 0.013. This is shown in Table 2 and Figure 1.

Table 2. Serum Malondialdehyyde comparison between *H. pylori* positive gastritis and *H. pylori* negative gastritis

	H. pylori (+)	*H. pylori* (-)	p
MDA (μmol/mL median (min-max)	1.58 (0.78-2.91)	1.19 (0.96-2.19)	0.013*

*p < 0,05, *Mann Whitney U-test*

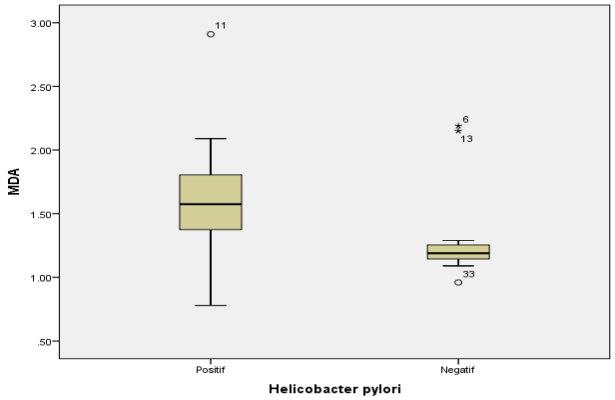

figure 1. Boxplot diagram of Malondialdehyde level in *H. pylori* positive gastritis and *H. pylori* negative gastritis

DISCUSSION

This study includes 40 patient which has fulfilled inclusion criteria and divided into 2 group with 20 patient each group based on the presence of *H. pylori* infection. Male subject is more commonly found in *H. pylori* (+) gastritis which is 12 (60%) patient meanwhile in *H. pylori* (-) gastritis the amount of male and female was the same which is 10 patient (50%). This is consistent with Naja F study which include 1,306 patient where *H. pylori* positve gastritis was more common in male compared to female (56.1% : 43.9%).[8] But this is reversed from studies by Zhu where from 5,417 sample with *H. pylori* (+), female patient was more frequent than male (64.47:38.26).[9] Draker et al studies about reactive oxygen species activity and lipid peroksidase in *H. pylori* gastritis, from 161 subject, male patients was more frequent than female with average age 47 years old.[10]

After statistic analysis was done, this study shows that average malondialdehyde level was higher in *H. pylori* (+) gastritis which is 1.58 (0.78-2.91) compared to *H. pylori* (-) gastritis which is 1.19 (0.96-2.19). Vijayan et al studies shows plasma malondialdehyde level in *H. pylori* patient with anemia increased significantly in study group (5.41 ± 2.16) compared to control group (2.26 ± 0.5; $p < 0.05$).[11] This is consistent with Santra et al study that shows gastric mucous malondialdehyde level in patients with duodenal ulcer *H. pylori* (+) was increased significantly compared to *H. pylori* (-).[12]

Drake et al states that malondialdehyde level was higher significantly in gastritis patient mucous in *H. pylori* patient with chronic gastritis compared to normal histology. *H. pylori* gastritis with more severe inflammation has significantly higher malondialdehyde level ($p < 0.05$) and in patient with neutrophil infiltration

in grade 2 or 3 gastric mucous has significantly higher malondialdehyde compared to normal ($p < 0.05$).[10] Turkkan proves that more severe chronic inflammation has significantly higher malondialdehyde level in study subject ($p = 0.04$).[6]

Aksoy et al report that average malondialdehyde concentration in preeclampsia patient with *H pylori* (+) was significantly higher compared to *H. pylori* (-). Preeclampsia patient has higher serum malondialdehyde level compared to healthy pregnant woman, 80% preeclampsia women infected by *H. pylori*, meanwhile prevalence of *H. pylori* infection in healthy pregnant woman was 60% (OR = 2.86), so it is suspected that increased serum MDA concentration in preeclampsia woman was due to *H. pylori* infection.[13]

Navvabi et al that studies *H. pylori* effect to oxydative stress in chronic gastritis patient shows that malondialdehyde and oxidized glutathione level was increased significantly in *H. pylori* patient, meanwhile total antioxidant and reduced glutathione level was decreased significantly.[7] Khanzode et al that study gastritis patient and gastric cancer showed consistent result, which is increased serum malondialdehyde level significantly in patient with *H. pylori* infection compared to control.[14] This study also showed that malondialdehyde level was significantly higher in gastric cancer patient compared to gastritis.

Up until now, MDA level still didn't have a normal value which can be used as standard. MDA level can be affected by age, enzyme activities (*superoxide dismutase*, *catalase*, and *glutathione perioxidase),* antioxidant supplement (vitamine C, E, βeta-karoten, etc), diseases and environment (pollution and radiation). Malondialdehyde level as a biomarker to assess oxydative stress in each disease was diffferent.[15]

CONCLUSION

Serum Malondialdehyde level was significantly higher in patient with positive *H. pylori* gastritis compared to *H. pylori* negative gastritis.

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