

Association between Severity of Dyspepsia and Urea Breath Test Results in Patients with Positive *Helicobacter pylori* Serology

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ABSTRACT

Background: Active *Helicobacter pylori* (*H. pylori*) infection is considered to cause more severe dyspepsia symptoms compared to inactive infection. This study was aimed to determine the association between severity of dyspepsia and urea breath test (UBT) results in subjects with positive *H. pylori* serology.

Method: This study was a cross-sectional study in 60 subjects with positive *H. pylori* serology in Provincial General Hospital of West Nusa Tenggara. Severity of dyspepsia was measured using modified Glasgow dyspepsia severity score (GDSS) questionnaire. Diagnosis of active *H. pylori* infection was made using 14C UBT examination.

Results: Proportion of active *H. pylori* infection in subjects with positive serology was 20%. The average of modified GDSS score in all patients was 1.95 (SD \pm 1.78), with minimal score of 0 and maximal score of 7. There was a statistically significant difference between average of modified GDSS score and positive and negative UBT results, ($p = 0.027$). The cut-off point value of modified GDSS to diagnose positive UBT was 3.8. Results of diagnostic test with modified GDSS as a test and UBT results as the gold standard indicated sensitivity of 41.6% and specificity of 85.4%.

Conclusion: There was a significant difference between modified GDSS score in patients and positive and negative *H. pylori* infection. In areas which did not have UBT examination, eradication in patients with positive serology and GDSS score of more than or equal to 4 could be considered.

Keywords: dyspepsia, *H. pylori*, modified Glasgow dyspepsia severity score (GDSS), urea breath test (UBT), serology

ABSTRAK

Latar belakang: Infeksi *Helicobacter pylori* yang aktif dipikirkan akan menimbulkan gejala dispepsia yang lebih berat dibandingkan infeksi yang tidak aktif. Penelitian ini bertujuan untuk melihat hubungan antara derajat keparahan dyspepsia dengan hasil urea breath test (UBT) pada subjek dengan serologi *H. pylori* positif

Metode: Penelitian ini merupakan studi potong lintang terhadap 60 subjek dengan hasil serologi *H. pylori* positif di Rumah Sakit Umum Daerah (RSUD) Provinsi Nusa Tenggara Barat (NTB). Derajat keparahan dispepsia diukur menggunakan kuisioner Glasgow dyspepsia severity score (GDSS) yang dimodifikasi. Diagnosis infeksi *H. pylori* aktif menggunakan pemeriksaan ¹⁴C UBT.

Hasil: Proporsi infeksi *H. pylori* aktif pada subjek dengan serologi positif sebesar 20%. Rerata nilai GDSS yang dimodifikasi pada seluruh pasien adalah 1,95 (SD ± 1,78), dengan minimal skor 0 dan maksimal skor 7. Terdapat perbedaan bermakna secara statistik antara rerata nilai GDSS yang dimodifikasi dengan hasil UBT positif dan negatif, ($p = 0,027$). Nilai titik potong GDSS yang dimodifikasi untuk mendiagnosis UBT positif sebesar 3,8. Hasil uji diagnostik dengan GDSS yang dimodifikasi sebagai uji dan hasil UBT sebagai baku emas, didapatkan sensitivitas 41,6% dan spesifisitas 85,4%.

Simpulan: Terdapat perbedaan bermakna antara nilai GDSS yang dimodifikasi pada pasien dengan infeksi *H. pylori* positif dan negatif. Pada daerah yang tidak memiliki pemeriksaan UBT, dapat dipertimbangkan melakukan eradikasi pada pasien dengan serologi positif dan nilai GDSS lebih dari atau sama dengan 4.

Kata kunci: dispepsia, *H. pylori*, Glasgow dyspepsia severity score (GDSS) yang dimodifikasi, urea breath test (UBT), serologi

INTRODUCTION

Helicobacter pylori (*H. pylori*) is a bacteria colonised in half of world human population. Most of these colony do not cause symptoms; however, 15-20% of cases will develop into peptic ulcer, and a small proportion of 1-4% will develop into gastric tumour.^{1,2}

Diagnosis of *H. pylori* infection can be made using 2 methods, which are invasive and non-invasive. Invasive examination involves upper gastrointestinal tract endoscopy examination, and is more difficult to be performed in remote areas and the cost needed is relatively expensive. Non-invasive examination can be considered as an alternative, because it is easier to be performed, particularly in area in which oesophagoduodenoscopy facility is unavailable. Urea breath test (UBT) examination is one of the non-invasive examinations with very good accuracy in detecting active *H. pylori* infection, but this examination is still rarely performed due to the relatively expensive cost and limited availability. Serology examination is an alternative of non-invasive examination which is easy and cheap to be performed, with good sensitivity, but not specific. Additionally, serology examination cannot differentiate old from new infection because it only detects antibodies in the blood; thus, patients with positive serology might have been only infected in the past.³⁻⁶

Active *H. pylori* infection is predicted to cause more severe dyspepsia symptoms compared to inactive infection. Modified Glasgow dyspepsia severity score (GDSS) has been used as a measuring tool to evaluate the severity of dyspepsia thus far. This is the rationale to perform the study to determine the

association between severity of dyspepsia and active *H. pylori* infection in patients with positive serology. Modified GDSS, is expected to assist the diagnostic approach of active *H. pylori* infection, particularly in population in which only serology examination can be performed due to the unavailability of UBT or oesophagoduodenoscopy examination.^{7,8}

METHOD

This study was a cross sectional study performed in Provincial General Hospital of West Nusa Tenggara, in November 2016 to March 2017. Inclusion criteria of this study were patient aged more than 18 years, had undergone *H. pylori* infection serology examination and had positive results and did not have previous history of gastrectomy. Exclusion criteria in this study were patients who did not consent to participate in the study or had received previous *H. pylori* infection eradication therapy. Calculation of sample size in this study was performed using single proportion sample size formula with $\alpha = 0.05$, $d = 0.10$, and proportion from previous study of 11.2%, we found that the minimally required sample size was 39 samples. Patients were selected consecutively, which meant that all patients who fulfilled inclusion and exclusion criteria underwent UBT examination.^{9,10}

In this study, we used Bioramps Laboratories Immunochromatography Diagnostic Test (Bio M Pylori ®) as serology examination tool and Headway 14C-UBT (Headway ® UBT) as UBT examination tool. Severity degree of dyspepsia was measured using modified GDSS questionnaire, which consisted of frequency of dyspepsia symptoms (never = 0; 1-2

times/month = 1; 1 time/week = 2; 3-4 times/week = 3; and everyday = 4), frequency of patients felt disturbed with the dyspepsia symptoms (not bothering = 0; sometimes bothering = 1; always bothering = 2), and frequency of patients requiring medicine to overcome dyspepsia symptoms (never = 0; less than or equal to 1 time/week = 1; and more than 1 time/week = 2). The minimal score of modified GDSS was 0, and maximal score was 10. All patients were given questionnaires before undergoing UBT examination.³⁻⁸

Collected data was analysed using IBM® SPSS® Statistics version 22.0 software. We performed unpaired t-test or Mann-Whitney test to assess the comparison of modified GDSS in positive and negative UBT patients. We performed the analysis using receiver operating characteristic (ROC) curve to obtain modified GDSS cut-off point for the diagnostic approach of positive UBT results. Diagnostic test was conducted to obtain sensitivity and specificity values using GDSS score, which was obtained from cut-off point analysis in diagnosing *H. pylori* infection.

This study was a part of the *H. pylori* infection study all over Indonesia which was performed by Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia in collaboration with Department of Internal Medicine, Provincial General Hospital of West Nusa Tenggara and had obtained ethical approval from Health Research Ethics Committee Universitas Indonesia with number 417/UN2.F1/ETIK/IV/2017.

RESULTS

During the period of this study, we obtained 60 subjects who fulfilled the inclusion and exclusion criteria. The average of study subjects were 38.46 years (standard deviation (SD) ± 10.6 years). Proportion of female patients were higher compared to male, which reached 70%. Most patients were highly educated up to bachelor, master, or doctorate level (46.7%), and only small proportion was educated up to primary school/ equivalent or junior high school/ equivalent level (5%). The average income of patients was IDR 4,872,000.00 (SD ± IDR 3,407,000.00) per month. From all patients to whom UBT examination were performed, 12 patients had positive results (20.0%; 95% CI: 9.3-28.3%). Comparison of basic characteristics based on UBT results was presented in Table 1.

From all patients who were examined, we found various severity degree of dyspepsia, either from the component of frequency of dyspepsia symptoms,

frequency of patients feeling disturbed with the dyspepsia symptoms, and frequency of patients requiring medication to resolve the dyspepsia symptoms. The average of modified GDSS score in all patients were 1.95 (SD ± 1.78), with minimal score of 0 and maximal score of 7. After performing the statistical test to compare the average modified GDSS score in patients with positive and negative UBT results, we found statistically significant difference between those two groups (p = 0.027; Mann-Whitney Test), as presented in Table 2.

After performing the analysis to the average of modified GDSS score in positive and negative UBT groups, we found sensitivity and specificity of modified GDSS score towards positive UBT, which was shown using the ROC curve. Based on this curve, the cut-off point of modified GDSS score to diagnose positive UBT was 3.8 as presented in Figure 1. This cut-off

Table 1. Comparison of basic characteristics in group with positive and negative urea breath test (UBT)

Variables	Results of urea breath test (UBT) examination	
	Positive (n = 12)	Negative (n = 48)
Sex; n (%)		
Male	6 (33.3)	12 (66.7)
Female	6 (14.3)	36 (85.7)
Age (years ± SD)		
Average	44.67 ± 13.65	38.86 ± 10.81
Level of education; n (%)		
Primary or junior high school/equivalent	1 (33.3)	2 (66.7)
Senior high school/ equivalent	3 (17.6)	14 (82.4)
Diploma 1 - 3	1 (8.3)	11 (91.7)
Bachelor-master-doctorate	7 (25)	21 (75)
Average income (IDR ± SD)	4,333,333.00 ± 1,115,700.00	4,987,931.00 ± 3,663,420.00

Table 2. Comparison of average modified Glasgow dyspepsia severity score (GDSS) score in group with positive and negative urea breath test (UBT)

Variables	Results of urea breath test (UBT)	
	positive (n = 12)	negative (n = 48)
Results of modified GDSS; score (95% CI)	3.08 (1.77 – 4.39)	1.67 (1.20 – 2.13)

p = 0.027 (Mann-Whitney Test)

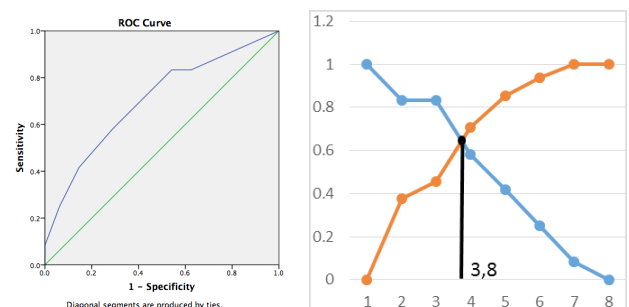


Figure 1. ROC curve and cut-off point value of modified GDSS to obtain positive results of urea breath test (UBT)

point was used to categorize modified GDSS score into 0-3 and 4-10. Diagnostic test was further conducted with severity degree of dyspepsia as test and UBT results as the gold standard, and yielded sensitivity of 41.6% and specificity of 85.4% as stated in Table 3.

Table 3. Diagnostic test of modified glasgow dyspepsia severity score (GDSS) to obtain positive urea breath test (UBT) results

Variables	Results of urea breath test (UBT)	
	Positive (n = 12)	Negative (n = 48)
Modified GDSS score 4-10	5	7
Modified GDSS score 0-3	7	41
Total number of patients	12	48
Sensitivity = 41.6%, specificity = 85.4%		

DISCUSSION

Many previous studies have shown *H. pylori* infection in regard to all sex, all age groups, all education level, and all economy status. This was in accordance with this study in which we found that *H. pylori* infection was not influenced by sex, age, education level, and economical status.^{11,12}

Compared to similar study performed by Goto et al in North Jakarta, proportion of *H. pylori* infection in this study was slightly higher which was 20%. This difference might be caused by different study population, Goto et al performed the study in dyspepsia patients who seek for treatment in District Public Hospital, while this study included patients with positive *H. pylori* serology. This indicated that only 20% of patients with history of *H. pylori* infection had active infection during the examination.^{6,12}

Although there was a difference in the average of modified GDSS score in positive and negative UBT groups, if assessed clinically, the severity of both groups were not of much difference, which were 3.06 in positive and 1.67 in negative group from a maximal score of 10. This makes it difficult to recommend modified GDSS to substitute the role of better diagnostic examinations, such as UBT or invasive examination using oesophagoduodenoscopy.^{11,12}

GDSS score more than or equal to 4, in patients with positive serology, administration of eradication therapy of *H. pylori* infection could be considered, if there was no better examination available; accounting that the cost of UBT and invasive examinations are very expensive and are not available in all hospital.

CONCLUSION

Proportion of *H. pylori* infection in patients with positive serology was 20%. There was a statistically

significant difference between GDSS score of patients with positive and negative *H. pylori* infection, but this difference was not clinically significant. In areas which did not have UBT or oesophagoduodenoscopy examination, eradication therapy administration in patients with positive serology and GDSS score of more than or equal to 4 could be considered.

ACKNOWLEDGEMENT

We would like to thank Provincial General Hospital of West Nusa Tenggara, and all staff involved in this study (Ms. Santi and Mr. Zainul Mutaqin) who have given the researchers the opportunity to perform the study.

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