Serologic and Urine Diagnostic Tests to Detect *Helicobacter pylori* Infection in Functional Dyspepsia Patients

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ABSTRACT

Background: *Dyspepsia is a collection of symptoms in the forms of discomfort, pain, nausea, vomiting, bloating, and early satiety in the stomach. This condition can be caused by various problems; one of them is Helicobacter pylori (H. pylori) infection. Dyspepsia without organic problem is known as functional dyspepsia. H. pylori examination is recommended in functional dyspepsia patients.*

Method: *In this study, we performed a diagnostic test study in dyspepsia patients in Community Health Centre of Koja District, North Jakarta, from February to April 2015. Samples were obtained through consecutive sampling method; 74 patients were included. The data was gathered by distributing questionnaires to patients, performing urea breath test (UBT) examination, serologic test, and urine test using rapid urine test (RAPIRUN).*

Results: *Prevalence of H. pylori infection by using UBT examination reached up to 36.5%; meanwhile serologic and RAPIRUN tests showed positive results in 32.4% and 24.3% patients, respectively. Serologic test has sensitivity of 74% (95% CI: 55-87%), specificity 91% (95% CI: 80-97%), positive predictive value (PPV) 83% (95% CI: 64-93%), and negative predictive value (NPV) 86% (95% CI: 74-93%). Meanwhile, RAPIRUN has sensitivity of 63% (95% CI: 44-78%), specificity 98% (95% CI: 89-100%), PPV 94% (95% CI: 74-99%), and NPV 82% (95% CI: 70-90%).*

Conclusion: *Sensitivity of serologic and RAPIRUN tests are still inadequate to be alternative to UBT examination. However, they have high specificity. Further studies are required with larger sample size and consideration of factors which may influence the results of both tests.*

Keywords: *functional dyspepsia, urea breath test, serology, rapid urine test, sensitivity, specificity*

ABSTRAK

Latar belakang: *Dispepsia merupakan kumpulan gejala berupa rasa tidak nyaman, nyeri, mual, muntah, kembung, serta rasa cepat kenyang pada perut. Kondisi ini disebabkan oleh berbagai gangguan, salah satunya*

adalah infeksi Helicobacter pylori (H. pylori). Dispepsia tanpa ditemukan gangguan organik dapat disebut sebagai dispepsia fungsional. Pemeriksaan H. pylori dianjurkan pada penderita dispepsia fungsional.

Metode: *Pada penelitian ini, dilakukan uji diagnostik pada penderita dispepsia di Puskesmas Kecamatan Koja, Jakarta Utara, sejak Februari hingga April 2015. Sampel diperoleh dengan metode consecutive sampling, berjumlah 74 pasien. Data diperoleh dengan memberikan kuisioner kepada pasien, pemeriksaan urea breath test (UBT), pemeriksaan serologi, dan pemeriksaan urin dengan rapid urine test (RAPIRUN).*

Hasil: *Prevalensi infeksi H. pylori dengan pemeriksaan UBT mencapai 36,5%, sementara itu pemeriksaan serologis dan RAPIRUN menunjukkan hasil positif pada 32,4% dan 24,3% pasien secara berurutan. Pemeriksaan serologi memiliki sensitivitas 74% (95% CI: 55-87%), spesifisitas 91% (95% CI: 80-97%), positive predictive value (PPV) 83% (95% CI: 64-93%), dan negative predictive value (NPV) 86% (95% CI: 74-93%). Sementara itu, pemeriksaan RAPIRUN memiliki sensitivitas 63% (95% CI: 44-78%), spesifisitas 98% (95% CI: 89-100%), PPV 94% (95% CI: 74-99%), dan NPV 82% (95% CI: 70-90%).*

Simpulan: *Sensitivitas pemeriksaan serologi dan RAPIRUN belum cukup baik untuk menjadi alternatif dari pemeriksaan UBT, namun memiliki spesifisitas yang tinggi. Dibutuhkan penelitian lebih lanjut dengan sampel yang lebih banyak dan untuk mengenai faktor-faktor yang memengaruhi hasil tersebut.*

Kata kunci: *dispepsia fungsional, urea breath test, serologi, rapid urine test, sensitivitas, spesifisitas*

INTRODUCTION

Dyspepsia is a collection of symptoms (syndrome) in the form of discomfort sensation, pain, nausea, vomiting, bloating, and early satiety.[1] This condition may be caused by several problems; one of them is *Helicobacter pylori (H. pylori)* infection which damages gastric mucosa and causes irritation by the gastric acid. Meanwhile, dyspepsia without the presence of organic problems is known as functional dyspepsia.[2] Examination of *H. pylori* in dyspepsia is recommended in patients aged less than 55 years old without alarm symptoms (weight loss, progressive dysphagia, recurrent vomiting, gastrointestinal bleeding, and history of gastrointestinal tract malignancy in the family) who lived in area with prevalence of *H. pylori* 10% or more.[3]

Asian consensus report on functional dyspepsia in 2011 stated that *H. pylori* examination is recommended in functional dyspepsia patients. Several previous epidemiology studies showed that *H. pylori* infection was higher in functional dyspepsia population compared to general population.[4] Several risk factors were predicted to influence *H. pylori* infection, such as higher incidence in older age group, sex, smoking, and alcohol consumption.[5,6,7]

Many diagnostic tests are available for dyspepsia condition, including histopathologic examination, microbiological culture, PCR, biopsy urea test (BUT) and urea breath test (UBT); however, serologic and urine tests have not been thoroughly studied. Serologic test is advocated in area in which the prevalence of H pylori infection reaches 60%.[8] In 2006, a study in Jakarta showed that results of serologic test of *H. pylori* infection was 52.3%.[9] While, urine examination by using ELISA or immunochromatography started to be used in developed countries, such as Japan.[10,11] Various tests on the accuracy of diagnostic methods with urine gave promising results.[11,12] In Indonesia, both of these tests have not been used widely. This study aims to compare the accuracy of serologic test and rapid urine test in diagnosing *H. pylori* infection to UBT as the gold standard. Researcher expects that both of these diagnostic tests could be alternative test to UBT because they are easy to use, accessible, and affordable in terms of cost; thus, could be applied in the future in Indonesia.

METHOD

This study was a diagnostic test study in dyspepsia patients in Community Health Centre of Koja District, North Jakarta, from February to April 2015 who agreed to participate in the study. Samples were collected through consecutive sampling method. The calculation of sample was performed using sensitivity of 90%, prevalence of disease being used in sample calculation was 52.3%; with the formula of diagnostic calculation sample needed was 67, while the drop out possibility of 10%; hence, the total sample needed was 74. The inclusion criteria include: patients who complained of dyspepsia in Primary Health Centre of Koja District, North Jakarta, during the study period and agreed to participate in the study. Exclusion criteria were patients with upper gastrointestinal tract bleeding, antibiotic and proton pump inhibitor (PPI) consumption in

the previous two weeks, and malignancy of the gastrointestinal tract. Independent variables were the results of serologic and urine tests, while dependent variable was *H. pylori* infection which was proven by results of UBT examination as a gold standard.

Data was acquired through questionnaire, serology, urine, and UBT examinations to the samples. The serologic test used 3 mL of blood, inserted into a microplate and diluted with phosphate buffer. The solution was further tested by adding 1% PHA cell suspension and agglutination reaction in the first well was observed and compared with control of PHA cell suspension. Urine test was performed using rapid urine test. We used 0.3 mL urine which was inserted into the RAPIRUN stick. Positive test of *H. pylori* infection was shown by the presence of two red bands which showed positive and control test results. Data was further analysed by using SPPS software version 16. This study has been approved by the Health Research Ethics Committee Faculty of Medicine, University of Indonesia.

RESULTS

During the period of April 2015 to June 2015, 74 patients were included in this study. Most samples (82.4%) were female. As much as 85.1% of samples were educated at high school level, 89.2% had their own toilet, 100% were smoking, 100% were using city water, and 71.6% came from low socio-economic level. Demographic data of the study samples can be seen in Table 1.

Using the UBT examination as the gold standard, 27 positive cases of *H. pylori* infection were found (36.5%). In serologic and RAPIRUN tests, we found positive in 24 (32.4%) and 18 (24.3%) cases, respectively. The results can be seen in Table 2.

Furthermore, researcher compared the results of serologic and RAPIRUN tests with UBT examination as the gold standard. Serologic test has sensitivity of 74% (95% CI: 55-87%) and specificity of 91% (95% CI: 80-97%). Positive predictive value (PPV) of the serologic test reached 83% (95% CI: 64-93%) and the negative predictive value (NPV) reached 86% (95% CI: 74-93%). Meanwhile, RAPIRUN test had sensitivity of 63% (95% CI: 44-78%) and specificity of 98% (95% CI: 89-100%). The positive predictive value (PPV) of RAPIRUN reached 94% (95% CI: 74-99%) and the negative predictive value (NPV) reached 82% (95% CI: 70-90%).

Table 1. Characteristics of study subjects

Characteristics	n (%)
Sex	
Male	13 (17.6)
Female	61 (82.4)
Age (years old), Mean (SD)	45.05 (SD 11.20)
Education level	
Primary school	1 (1.4)
Secondary school	7 (9.5)
High school	63 (85.1)
University	3 (4.1)
Ethnic groups	
Javanese	17 (23.0)
Sundanese	8 (10.8)
Betawi	11 (14.9)
Minang	13 (17.6)
Lampung	5 (6.8)
Bugis	10 (13.5)
Palembang	5 (6.8)
Lombok	4 (5.4)
Melayu	1 (1.4)
Toilet	
Own	66 (89.2)
Neighbour	8 (10.8)
Smoking	
Yes	0 (0.0)
No	74 (100.0)
Source of drinking water	
City water	74 (100.0)
Well water	0 (0.0)
Income	
Above Regional Minimum Salary (> IDR 2,700,000.00)	21 (28.4)
Below Regional Minimum Salary (< IDR 2,700,000.00)	53 (71.6)

Table 2. Proportion of results of UBT, serologic, and RAPIRUN test

Variables	n (%)
Urea Breath Test (UBT)	
Positive	27 (36.5)
Negative	47 (63.5)
Serologic test	
Positive	24 (32.4)
Negative	50 (67.6)
Rapid urine test (RAPIRUN test)	
Positive	18 (24.3)
Negative	56 (75.7)

DISCUSSION

The prevalence of *H. pylori* infection in Primary Health Centre of Koja District, North Jakarta was 36.5% with UBT examination. This prevalence was lower compared to similar study in India by Sodhi et al and in China by Xu et al.[13,14] The prevalence of *H. pylori* infection in this study was higher compared to several previous studies in North Sulawesi, Surabaya, and Jakarta which were 14.3%, 11.5%, and 9.5%, respectively.[15,16,17] The demography of population with *H. pylori* infection in this study was similar to those of several previous studies which stated that low economic status, densely populated area, not clean water, smoking, and alcohol consumption were strongly correlated with the presence of *H. pylori* infection.

In this study, the urea breath test (UBT) examination as the gold standard of *H. pylori* infection found 36.5% with positive results. In serologic test, we found 32.4% with positive results. In rapid urine test (RAPIRUN),

we found 24.3% subjects with positive results. UBT examination is a gold standard to detect *H. pylori* infection through non-invasive method which was initially found in 1987 by Graham and Bell. In terms of accuracy, UBT has acceptable sensitivity and specificity, which were more than 90%.[18]

Generally, serologic test detects IgG of *H. pylori* bacteria. Currently, there are many available ELISA tests with simple use of methods and accurate results. The problem is that the sensitivity and specificity varies geographically. A study in Jakarta using ELISA test manufactured by Roche revealed lower sensitivity and specificity compared to reports from Western countries. In the literature, antibody examination in the urine showed quite high sensitivity and specificity, which was 86% and 91%.[19] A study in China using rapid urine test (RAPIRUN *H. pylori* antibody) exhibited quite high accuracy, which was sensitivity, specificity, PPV, and NPV of 96.7%, 95.2%, 96.7%, and 95.9%, respectively.

After serologic test was performed and statistical calculation obtained sensitivity of 74%, specificity of 91%. Ideally, the sensitivity and specificity of serologic test could reach up to more than 90%; however, results of serologic test was lower. Serologic test performed by Gonzales et al had similar results with this study, which was 60-100% for sensitivity and 60-100% for specificity. Meanwhile, a study conducted by Kazemi et al revealed serologic test with results of sensitivity 50%, specificity 54 %, PPV 56 %, and NPV 61%.[20]

For RAPIRUN test, statistical calculation showed sensitivity, specificity, PPV, and NPV of 63%, 98%, 94%, and 83%. This was similar with the data from a study by Demiray et al which obtained sensitivity 71.2%, specificity 81.5% PPV 91.2%, and NPV 51.2% with similar size of sample, which was 100 patients. This result was slightly different if compared with a study by Quach et al in Vietnam which gave higher results, which were 84.7%, 89.9%, 91.2%, and 82.5% for sensitivity, specificity, PPV, and NPV, respectively, with sample size of 200 patients.[21] Further comparison was with the results of a study conducted by Kuo et al in Taiwan with sensitivity 91.7%, specificity 90.8%, PPV 96.3%, and NPV 80.6% with 317 samples.[22] From comparison with those studies, it was observed that the bigger sample size being used, then the sensitivity, specificity, PPV, and NPV would also be high.

CONCLUSION

This study obtained low results of sensitivity value. The sensitivity of serologic and RAPIRUN test are still inadequate to be an alternative to UBT examination, although they have high specificity. This is predicted to be caused by smaller sample size compared to the previous studies, despite the study samples were taken directly from the population. Meanwhile, this study gave superior results compared to previous studies in terms of specificity. Further studies are required to understand other factors which might influence those results. Limitations of this study were for exclusion criteria, evaluation procedure for digestive tract bleeding, and malignancy of the digestive tract were obtained solely from history taking, without any endoscopic and standard laboratory examinations being performed.

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