Original Article

Diagnostic Accuracy of *Helicobacter pylori* Antibody Testing in Uninvestigated Dyspeptic Patients, Thailand

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Background: The non-invasive *Helicobacter pylori* antibody (Hp Ab) test is convenient, cost-effective, and helpful for early detection and treatment.

Objective: To evaluate the accuracy of Hp Ab test for the diagnosis of Hp infection compared with the rapid urease test (RUT) and histology via Esophago-gastro-duodenoscopy (EGD).

Materials and Methods: Uninvestigated dyspeptic patients 18 to 80 years-old without contra-indicated to EGD were included in this study. On EGD day, all patients had received Hp Ab testing via blood and gastric biopsy sample via EGD for RUT and histological examination. Patients were considered Hp positive if one of the two invasive tests, either RUT or histology, was positive.

Results: Among the 269 patients, female were more predominant with mean age 55.2±14.8 years. The endoscopic findings were gastritis at 85.9%, gastric ulcer at 13.8%, duodenal ulcer at 7.1%, normal finding at 3.7%, and no gastric cancer. The prevalence of Hp infection was 40.1%. The diagnostic indices of Hp Ab test were sensitivity at 81.5%, specificity at 75.2%, positive predictive value at 68.8%, negative predictive value at 85.8%, and accuracy at 77.7%.

Conclusion: The Hp Ab testing is accurate for the diagnosis of Hp infection in uninvestigated dyspeptic patients. Positive cases can receive Hp eradication without EGD. In the negative cases, they should undergo EGD to determine the cause of dyspepsia.

Keywords: Uninvestigated dyspepsia; *Helicobacter pylori*; *H. pylori* antibody test; Rapid urease test; Histology; Gastroscopy

Received 5 January 2022 | Revised 8 June 2022 | Accepted 23 June 2022

J Med Assoc Thai 2022;105(8):748-53

Website: http://www.jmatonline.com

Helicobacter pylori (Hp) colonizes in the human stomach. More than 50% of the global population has been infected with this organism[1-3]. Since 1994, World Health Organization (WHO) has classified the bacterium Hp as a class 1 carcinogen[4]. Chronic infection with Hp is associated with acid-related disorders such as gastritis, peptic ulcer diseases (PUDs), and gastric cancer (GCA), and is associated with dyspepsia[5-8]. Dyspepsia is a common condition in medical practice with global and Thailand prevalence of at least 20%[9] and 66%[10], respectively. Uninvestigated dyspepsia refers to dyspeptic symptoms in people who have not yet undergone specific diagnostic investigations[11]. One-third of the Thai population have been infected with Hp that is increasingly drug resistant[12-14]. Thailand guideline of dyspepsia 2018 recommended that Hp should be eradicated in all dyspeptic patients with Hp infection[15]. Hp test strategy, especially non-invasive technique, and eradication, can reduce PUDs or GCA occurrence. The non-invasive technique reduces the waiting time as compared to the invasive Hp assessment via Esophago-gastro-duodenoscopy (EGD), and it is cost-effective[6,15-19].

Hp infection can be demonstrated by two assessments[2,14,15]. The first method is invasive via EGD with gastric biopsy for evaluation of urease enzyme as rapid urease test (RUT). The histology can demonstrate Hp in tissue by Gram stain, Giemsa stain, hematoxylin-eosin stain, culture with special media, or polymerase chain reaction (PCR). The second method is non-invasive tests such as urea breath test (UBT), stool Hp antigen test, or Hp antibody (Ab) test[20]. Routinely Hp assessment method in Maharat Nakhon Ratchasima Hospital (MHRH), in the North-Eastern Part of Thailand is direct testing for

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How to cite this article:

Luangjaru S, Vipatakul N, Malikhao S. Diagnostic Accuracy of *Helicobacter pylori* Antibody Testing in Uninvestigated Dyspeptic Patients, Thailand. J Med Assoc Thai 2022;105:748-53.

DOI: 10.35755/jmedassocthai.2022.08.13476

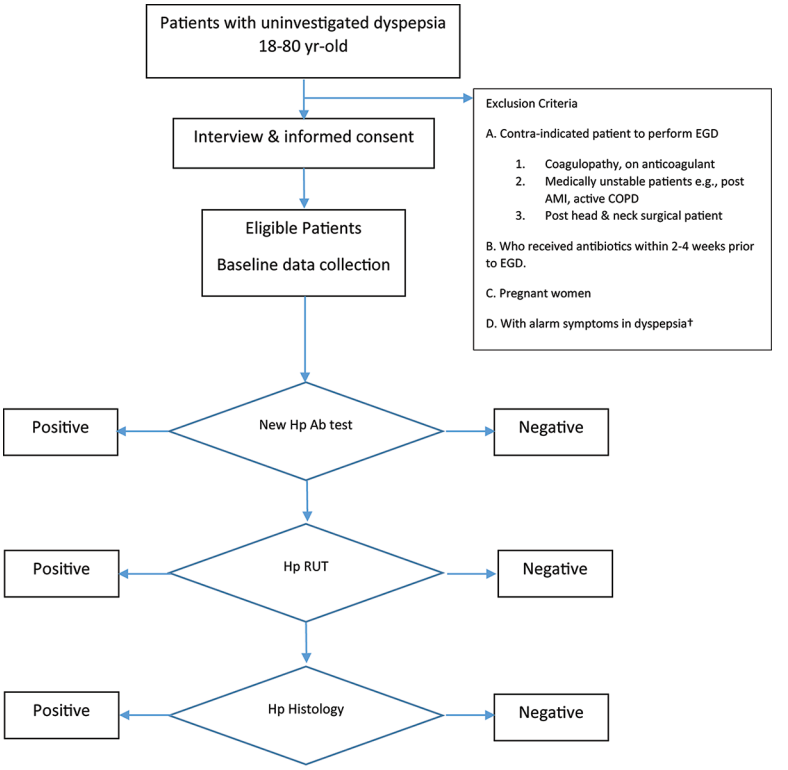

Figure 1. Study flow.

EGD=esophagogastroduodenoscopy; AMI=acute myocardial infarction; COPD=chronic obstructive pulmonary disease; Hp=*Helicobacter pylori*; Ab=antibody; RUT=rapid urease test

† Alarm symptoms: intractable vomiting due to unknown cause, early satiety, dysphagia, GI bleeding, iron deficiency anemia, unintended weight loss over 10% and family history of upper GI cancer in 1st-degree relatives

Hp, including a RUT or histology via EGD. Patients were considered to have Hp infection if one of the two tests was positive. The disadvantages and limitation of Hp test via EGD are the need for an expert and long waiting time for EGD. Use of antibiotics or proton pump inhibitor can cause false negative. Non-invasive Hp tests have advantages and limitation such as the UBT cost is 80 U.S. dollars per test while the cost of the stool Hp antigen test is 10 U.S. dollars but it needs fresh stool, not more than two hours after collection, which in most people minds, this is disgusting.

Currently, the Hp Ab test-kit is inexpensive at 10 U.S. dollars per test, with a small amount of blood sample and can assess within 15 minutes. The MP Diagnostic ASSURE Hp rapid test, Singapore, is an immunochromatographic test device intended for the rapid detection of IgG antibodies and antibodies to a recombinant current infection marker (CIM), which is indicative of current infection and show its high sensitivity and specificity. It was studied in Thailand in children population[20]. If this Hp Ab testing had a good diagnostic accuracy, especially in adults, it may be beneficial in the clinical practice including avoidance of unnecessary EGD and reduction of waiting time for the invasive Hp assessment via EGD, and it can reduce PUDs or GCA occurrence in the future.

The objective of the present study was to evaluate the accuracy of the non-invasive Hp Ab test for the diagnosis of Hp infection compared with the RUT and histology via EGD.

Materials and Methods

The present study was a diagnostic accuracy, cross-sectional, population-based research conducted in uninvestigated dyspeptic patients at Maharat Nakhon Ratchasima Hospital, Thailand between August 2020 and July 2021.

The present study population were uninvestigated dyspeptic patients, aged 18 to 80 years of age at Maharat Nakhon Ratchasima Hospital between August 2020 and July 2021. Participants eligible for this diagnostic study if they had dyspeptic symptoms

for at least four weeks before enrollment. Exclusion criteria were patients with contraindication for EGD or received antibiotics therapy two to four weeks prior to the study, pregnancy, or alarm symptoms of gastrointestinal (GI) malignancy such as intractable vomiting due to unknown cause, early satiety, dysphagia, GI bleeding, iron deficiency anemia, unintended weight loss over 10%, and family history of upper GI cancer in 1st-degree relatives. All patients had never been treated for Hp infection.

Calculation of the sample size was based on a pilot study conducted in January 2020, in which the sensitivity of the Hp Ab test was determined to be 88.9%. Therefore, based on the expected sensitivity of this test was not less than 75%, one-sided test, 5% alpha error, and 80% power, at least 50 Hp infected cases would be needed. As the prevalence of Hp infection was 32.1%, at least 156 patients were needed for the present study.

The study participation was voluntary and purpose of the present research and procedures, risks and benefits of study participation, potential study-associated costs had been explained. The participants could withdraw at any time. The study started after the participants signed the informed consent as Figure 1.

The baseline clinical data were collected from the medical records and interviewed such as age, gender, medical right, co-morbid disease, risk factors, presenting symptoms of dyspepsia, previous acid blocker use especially H2 antagonist, and proton pump inhibitor (PPI).

All participants underwent fingertip blood draw for ASSURE Hp Ab test and then EGD with antral biopsy for RUT and histopathologic examination. Patients were considered to have Hp infection if either RUT or histopathologic examination was positive.

Statistical analysis

Data were presented as number, percentage and mean ± standard deviation. Diagnostic performance of the tests such as sensitivity, specificity, positive predictive value, negative predictive value, and accuracy, were presented as percentages and 95% confidence interval. Statistical analyses were performed using Stata Statistical Software, version 16.1 (StataCorp LLC, College Station, TX, USA; Serial number: 501606204774).

The present study was approved by the Local Ethics Committee of Maharat Nakhon Ratchasima Hospital Institution Review Board, Ministry of Public Health, Thailand, number 044/2020.

Table 1. Baseline clinical data (n=269)

Variable	
Sex: female; n (%)	154 (57.2)
Age (year); mean±SD	55.2±14.8
Medical right; n (%)	
UCS	213 (79.2)
SSS	32 (11.9)
CSMBS	21 (7.8)
Others	4 (1.1)
Risk factors; n (%)†	
Aspirin/NSAIDs use	44 (16.4)
Alcohol ingestion	33 (12.3)
Smoking	13 (4.8)
Raw food intake	9 (3.4)
Steroids use	7 (2.6)
Co-morbidity; n (%)†	
None	161 (59.9)
Hypertension	73 (27.1)
Dyslipidemia	42 (15.6)
Diabetes mellitus	40 (14.9)
Liver cirrhosis	20 (7.4)
End-stage renal disease	8 (3.0)
Presenting symptoms; n (%)†	
Epigastric pain	241 (89.6)
Bloating, belching	168 (62.4)
Epigastric burning sensation	149 (55.4)
Nausea, vomiting	24 (8.9)
Constipation	19 (7.0)
Acid blocker use; n (%)	
Proton pump inhibitor	164 (61.0)
Histamine blocker	12 (4.5)

UCS=Universal Coverage Scheme; SSS=Social Security Scheme; CSMBS=Civil Servant Medical Benefit Scheme

† Row % (some patients have two or more conditions)

Results

Baseline clinical data

Two hundred sixty-nine uninvestigated dyspeptic patients were enrolled in the present study. Mostly were female, 57.2% with a mean age of 55.2±14.8 years. The risk factors were aspirin or NSAID use for 16.4%, alcohol ingestion for 12.3%, and smoking for 4.8%. The co-morbidity was presented at 49.5% with hypertension at 27.1%, dyslipidemia at 15.6%, and diabetes mellitus at 14.9%. The presenting symptoms were epigastric pain at 89.6%, bloating/belching at 62.4%, and epigastric burning sensation at 55.4%. Most of them (65.5%) were using acid blockers especially using PPI with 61.0%, as shown in Table 1.

The upper GI endoscopic findings in most cases (96.3%) were abnormal such as gastritis in 85.9%,

Table 2. Endoscopic findings of 269 cases

Endoscopic finding†	n (%)
Mucosal damage	
Gastritis	
• Mild/non-erosive gastritis	98 (36.4)
• Severe/erosive gastritis	133 (49.4
Duodenitis	11 (4.1)
Esophagitis	8 (3.0)
Gastric ulcer	37 (13.8)
Duodenal ulcer	19 (7.1)
Gastric/duodenal polyp	1 (0.4)
Other relevant diseases‡	32 (11.9)
Malignancy of upper GI tract	0 (0.0)
No abnormality	10 (3.7)

GI=gastrointestinal

† Row % (some patients have two or more lesions), ‡ Other relevant diseases: achalasia, esophagogastric varices, hiatal hernia, gastroesophageal reflux disease

Table 3. Result Hp Ab test compared with RUT and histology

Hp Ab test	Positive RUT and/or histology	Negative RUT and histology	Total
Positive	88	40	128
Negative	20	121	141
Total	108	161	269

Hp=*Helicobacter pylori*; Ab=antibody; RUT=rapid urease test

gastric ulcer in 13.8%, and duodenal ulcer in 7.1%. All mild or non-erosive gastritis by endoscopy were confirmed by pathologist. If patients with mild or non-erosive gastritis were categorized as normal, then percentage of normal would be 40.2%. The malignancy of upper GI tract was not detected in the present study, as shown in Table 2. The histopathologic reports were gastric intestinal metaplasia in 27 cases (10.0%).

The prevalence of Hp infection was 40.1%. Hp Ab test for the diagnosis of Hp infection compared with RUT and histological examination had sensitivity of 81.5% (95% CI 72.9 to 88.3), specificity of 75.2% (95% CI 66.7 to 81.6), positive predictive value of 68.8% (95% CI 60.0 to 76.6), negative predictive value of 85.8% (95% CI 78.9 to 91.1), and accuracy of 77.7% (95% CI 72.2 to 82.5), as shown in Table 3.

Discussion

Nowadays, HP is an important organism and is correlated with malignant change of the stomach. It is commonly found in dyspeptic patient more than in the asymptomatic persons[21]. According to Asian dyspepsia data, the test and treatment strategy of Hp are cost-effective[14-16,22,23] and has symptomatic improvement more than 50% after Hp eradication[7].

In the present study, the presenting symptoms are epigastric pain, bloating, and epigastric burning sensation commonly found in the clinical practice in Thailand. The majority of the cases were used acid blockers (65.5%) especially the PPI (61.0%) but could not improve the symptom. These data suggest that acid may not play a significant role in these patients. Although the mean age of the authors' patients was 55.2±14.8 years, which was more than the age of early endoscopy for malignancy according to the Thai dyspepsia guideline for EGD, no malignancy of upper GI was recognized in the present study. This fact differed from those of patients thorough out Thailand. This may be a special finding in this region of the country. As Rome IV diagnostic criteria[24], functional dyspepsia in the present study was detected in 81%, which is the same as the Thai data[10,15].

The prevalence of Hp infection in the present study was 40.1%, higher than mean prevalence of the Thai population[12-14]. The prevalence of Hp infection has high variation in each region of Thailand, low in the southern part (14.4%) and highest in the north-eastern part (60.6%)[12,25,26].

Diagnostic indices of this Hp Ab test had high sensitivity, specificity, and negative predictive value although the majority of these patients took PPI, which might be the limitation of other Hp test. In Taiwan data, Hp Ab test is one of the Hp detection methods that had high efficiency and cost-effectiveness[27]. PPI does not alter the Ab test result[28]. Negative cases from this Hp Ab test can be highly assured that the patients do not have Hp infection. The false positive of the present study is 24.8%. This group may unnecessarily expose to short-period antibiotics with risk of allergy for Hp eradication. The false negative of the present study is 18.5%. Therefore, only this small amount of subgroup should undergo EGD with Hp re-evaluation.

When expense, convenience, and time consumption are considered, Hp Ab test takes only 15 minutes and costs only 10 U.S. dollars. In MNRH, the total cost of the standard test via EGD is 185 U.S. dollars, which include EGD, RUT, and histopathology at 165, 11.6, and 8.4 U.S. dollars, respectively. This test can reduce waiting time of the invasive and more expensive diagnostic method via EGD. According to World recommendation including Asian & WHO, Hp infection should be screened early. It is useful and can reduce GCA occurrence in the future[14,29-32]. This Hp Ab test is one of the methods that should be chosen.

Conclusion

This Hp Ab testing is accurate for the diagnosis of Hp infection in uninvestigated dyspeptic patients without alarming symptoms. Positive case can receive Hp eradication without EGD. The negative cases should undergo EGD to determine the cause of dyspepsia. Hp Ab test can also help to reduce the cost of EGD.

What is already known on this topic?

Thailand guideline of dyspepsia 2018 recommended that Hp should be eradicated in all dyspeptic patients with Hp infection.

What this study adds?

The Hp Ab test is one of the methods that should be used in Hp screening because it is simple, affordable, and does not require an EGD. It can also be used if the patient was using a proton pump inhibitor.

Ethical statement

All clinical data in the present research were collected in the research medical file of the medical department, Maharat Nakhon Ratchasima Hospital.

Funding disclosure

This research was supported by the Research Center, Maharat Nakhon Ratchasima Hospital, Thailand and Hausen Bernstein Co., Ltd., a distributor of test kits in Thailand. The company was not involved in any process in the present research including test processes and study results.

Conflicts of interest

The authors declare no conflict of interest.

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