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• *BRIEF REPORTS* •

Validation of four *Helicobacter pylori* rapid blood tests in a multi-ethnic Asian population

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Abstract

AIM: To validate the accuracy of four rapid blood tests in the diagnosis of *Helicobacter pylori*.

METHODS: Consecutive dyspeptic patients scheduled for endoscopy at the National University Hospital, Singapore, were interviewed and had blood drawn for serology. The first 109 patients were tested with BM-test (BM), Pyloriset Screen (PS) and QuickVue (QV), and the next 99 subjects were tested with PS and Unigold (UG). Endoscopies were performed blinded to rapid blood test results and biopsies were taken for culture and rapid urease test. Urea breath tests were performed after endoscopies. The rapid blood test results were compared with four reference tests (rapid urease test, culture, serology, and breath test).

RESULTS: The study population composed of 208 patients (mean age 43.1 years; range 18-73 years; 119 males; 174 Chinese). The number of evaluable patients for BM, QV, UG and PS were 102, 102, 95, and 197, respectively. The sensitivity and specificity, respectively were: PS 80.2%, 95.8%; UG 55.9%, 100%; QV 43.3%, 100%; BM 67.2%, 97.1%.

CONCLUSION: The rapid blood test kits showed high specificity and positive predictive value (97-100%), while sensitivity and negative predictive value ranged widely (43%-80% and 47%-73%, respectively). Among test kits, PS showed the best sensitivity (80%), best negative predictive value (73%) and best negative likelihood ratio (0.207). PS had a specificity of 96%, positive predictive value of 97% and positive likelihood ratio of 19.1.

Key words: *Helicobacter pylori*; Rapid blood test

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INTRODUCTION

There are a variety of methods available for the detection of *Helicobacter pylori (H pylori)*, but many of these are invasive (such as biopsies for rapid urease test, culture, histology, and polymerase chain reaction) or require laboratories (such as urea breath test and serology). Recently, *H pylori* rapid test kits have become available. Rapid blood tests detect *H pylori* antibodies in whole or capillary blood, are easy to use, and yield results in a few minutes, making it a convenient point-of-care test for screening *H pylori*.

The 1997 Asia Pacific Consensus Conference on the management of *H pylori* infection[1] recommended that any blood test must be locally validated, with two or more alternative means of testing, before its widespread application.

Rapid blood test kits have not been widely validated in the Asian populations[2-5]. Local validation is important because the performance characteristics of blood test kits and population prevalence of *H pylori* vary in different populations. In Asian countries, the prevalence of *H pylori* infection is generally higher than in the developed Western nations (such as the United Kingdom, Australia, and France)[6]. In addition, the test performance of rapid blood kits may vary because local *H pylori* strains may be different[7,8].

Our prospective study aimed to validate four rapid blood test kits in the diagnosis of *H pylori* infection in a multi-ethnic Asian population. Amongst the Asian studies till date[2-5], none was conducted in a multi-ethnic population, and all were tested with less than four rapid blood test kits.

MATERIALS AND METHODS

Consecutive patients who were referred from general practice or outpatient clinics and scheduled for endoscopy for initial evaluation of dyspepsia at the National University Hospital, Singapore, were included for the

study. Exclusion criteria included patients with known peptic ulcer or gastric cancer, subjects with prior *H pylori* treatment, and those who had taken antibiotics, bismuth or proton pump inhibitors in the previous one month.

At entry, patients were interviewed using a standard questionnaire. Ten cubic centimeter of blood was drawn from each patient for serology. Each of the first 109 patients were tested with BM-test (BM, Boehringer Mannheim, East Essex, UK), QuickVue (QV, Quidel, CA, USA) and Pyloriset Screen (PS, Orion Diagnostica, Espoo, Finland). The kit with the best sensitivity was retained for continued testing in the next 99 patients together with an additional kit, Unigold (UG, Trinity Biotech, NY, USA). Endoscopy was then performed in the routine fashion by experienced endoscopists blinded to earlier results and three antral biopsy specimens were taken from each patient. Two biopsy specimens were sent for culture and one specimen was sent for the rapid urease test.

A ^{13}C urea breath test was performed directly after endoscopy. The technician doing the urea breath test was blinded to the results of the endoscopy. The results from the rapid blood test, rapid urease test, serology, culture, urea breath test and endoscopy were recorded on a standard data form.

The results of the rapid blood tests were compared with four reference tests: serology using HEL-p Test kit (AMRAD Operations Pty. Ltd, Australia), which had been validated locally[9], culture, rapid urease test, and urea breath test. *H pylori* infection was diagnosed, if any two reference tests were positive. If all the four reference tests were negative, it was assumed that infection was absent. Patients with a single positive test out of the four reference tests were classified as having indeterminate results.

Sample size was estimated based on reference tables[10]. Based on sensitivity of 80% and specificity of 90%, absolute precision of 0.10 and confidence interval of 95%, we needed a minimum of 62 *H pylori*-positive and 35 *H pylori*-negative patients.

The study was approved by the Research and Ethics Committee, National University Hospital, Singapore.

RESULTS

The characteristics of recruited patients are described in Table 1. One hundred and nine patients were tested with BM, QV, and PS (102 evaluable, 7 indeterminate results), and the next 99 subjects with PS and UG (95 evaluable, 4 indeterminate results).

Table 2 shows the sensitivity, specificity, predictive values and likelihood ratios of the respective rapid blood tests for *H pylori*. The rapid blood kits tested all showed specificities above 95% and very good positive predictive values exceeding 97%. There was a wide range in sensitivity between 43% and 80%, negative predictive value ranged from 48% to 73%, and negative likelihood ratios ranged from 0.207 to 0.567. PS had the best sensitivity of 80%, the best negative predictive value of 73%, and the best negative likelihood ratio of 0.207. PS had a high specificity of 96%, a good positive predictive value of 97.1% and a high positive likelihood ratio of 19.1.

Table 1 Characteristics of recruited patients

Kits used	PS, QV, BM	PS, UG	All
Number	109	99	208
Male:female	56:53	63:36	119:89
C:I:M:O[1]	91:12:4:2	83:7:6:3	174:19:10:5
Mean age (range)	44.7 (18–73)	41.3 (20–68)	43.1 (18–73)
H pylori positive	67	59	126
H pylori negative	35	36	71
Indeterminate results	7	4	11

[1]C = Chinese; I = Indian; M = Malay; O = Others.

Table 2 Sensitivity, specificity, predictive values, and likelihood ratios of rapid blood test for *H pylori* infection

Performance characteristics	BM	QV	UG	PS
Sensitivity (%)	67.2	43.3	55.9	80.2
Specificity (%)	97.1	99	99	95.8
Positive predictive value (%)	97.8	98	99	97.1
Negative predictive value (%)	60.7	47.9	58.1	73.1
Positive likelihood ratio	23.2	31.2	41.3	19.1
Negative likelihood ratio	0.338	0.567	0.441	0.207

DISCUSSION

Among the kits tested in our study, PS showed the best sensitivity (84%). Our study showed a wide range in the performance characteristics of the rapid tests. This may be attributable to the antigens used[11] or test kit designs.

The same rapid blood test kit might vary in performance between different populations. For example, QV's sensitivity for *H pylori* was 43.3% in our Singapore population, compared with 81% in Europe[12] and 82% in America[13]. These factors make it important that kits are locally tested and validated before use. A meta-analysis had shown that rapid tests are less accurate than reference tests, with sensitivity and specificity averaging 80-85% and 75-80%, respectively[14].

We conducted this study in an institution. For better evaluation of the potential of rapid blood test as a screening method in primary care, local studies conducted in general practice would be needed. Talley *et al*[15] reported that when used in general practice in Australia, rapid blood test had a sensitivity of 60% and specificity of 90% Data on the performance characteristics of *H pylori* rapid blood test kits in general practice in the Asian population is lacking.

The Maastricht 2-2000 Consensus report[16] recommended a 'test and treat' approach in the primary care for *H pylori* infection. However, there is a strong association between *H pylori* infection and gastric cancer, especially in the Asian population, which has a high incidence of gastric cancer. Therefore, the use of 'test and treat' approach in Asians remains controversial and awaits further study. PS had a good sensitivity and specificity for the detection of *H pylori* infection, with the positive likelihood ratio of above 10, providing convincing diagnostic evidence, and negative likelihood ratio of 0.2, giving a strong diagnostic evidence. PS might therefore be potentially useful for 'test

and referral' strategy in general practice. Our study, which validated the point-of-care rapid blood test kits in a multi-ethnic Asian population, is an important step for future studies in this area.

In conclusion, there was a wide range in the performance characteristics of rapid blood test, making it important for the kits to be tested and validated locally before being used. Of the rapid blood kits tested, the best sensitivity for *H pylori* detection was 80% (PS). The validation of rapid blood test kits in the local population facilitates future studies on the 'test and treat' or 'test and referral' approach in the Asian population.

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