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

Lee-Guan Lim, Khay-Guan Yeoh, Bow Ho, Seng-Gee Lim

**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

**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[2-8]. 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)[9]. 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 centimetre 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 13C 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.

### 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

| Number          | PS | QV | BM | PS | UG | All |
|-----------------|----|----|----|----|----|-----|
| Male/female     | 56/33 | 63/36 | 119/89 |
| C:IM2*          | 91/124:2 | 83/7:63 | 174/19:10:5 |
| Mean age (range) | 44.7 (18–73) | 41.3 (20–68) | 43.1 (18–73) |

* C = Chinese; I = Indian; M = Malay; O = Others.

### Table 1 Characteristics of recruited patients

| Kits used     | BM | QV | UG | PS |
|---------------|----|----|----|----|
| Sensitivity (%) | 67.2 | 45.3 | 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 | 25.2 | 31.2 | 41.3 | 19.1 |
| Negative likelihood ratio | 0.338 | 0.567 | 0.441 | 0.207 |

The Maastricht 2-2000 Consensus report 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 \textit{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.

ACKNOWLEDGMENTS

We would like to thank Mrs Lim Thiew Peng who performed the \textit{H pylori} serology and our research nurse Ms Lai Shuet Ting, for their kind assistance.

REFERENCES

1 Lam SK, Talley NJ. Report of the 1997 Asia Pacific Consensus Conference on the management of \textit{Helicobacter pylori} infection. \textit{J Gastroenterol Hepatol} 1998; 13: 1-12
2 Leung WK, Chan FK, Falk MS, Suen R, Sung JJ. Comparison of two rapid whole-blood tests for \textit{Helicobacter pylori} infection in Chinese patients. \textit{J Clin Microbiol} 1998; 36: 3441-3442
3 Wong BC, Wong W, Tang VS, Lai K, Yuen S, Hu WH, Chan C, Lau GK, Lai C, Lam S. An evaluation of whole blood testing for \textit{Helicobacter pylori} infection in the Chinese population. \textit{Aliment Pharmacol Ther} 2000; 14: 331-335
4 Chen TS, Chang FY, Lee SD. No difference of accuracy between capillary and venous blood in rapid whole blood test for diagnosis of \textit{Helicobacter pylori} infection. \textit{Dig Dis Sci} 2002; 47: 2519-2522
5 Wong WM, Lam SK, Xia HH, Tang VS, Lai KC, Hu WH, Chan CK, Cheung KL, Wong BC. Accuracy of a new near patient test for the diagnosis of \textit{Helicobacter pylori} infection in Chinese. \textit{J Gastroenterol Hepatol} 2002; 17: 1272-1277
6 Graham DY. \textit{Helicobacter pylori}: its epidemiology and its role in duodenal ulcer disease. \textit{J Gastroenterol Hepatol} 1991; 6: 105-113
7 Hua J, Ng HC, Yeoh KG, Ho KY, Ho B. Characterization of clinical isolates of \textit{Helicobacter pylori} in Singapore. Microbios 1998; 94: 71-81
8 Höök-Nikanne J, Perez-Perez GI, Blaser MJ. Antigenic characterization of \textit{Helicobacter pylori} strains from different parts of the world. \textit{Clin Diagn Lab Immunol} 1997; 4: 592-597
9 Kang JY, Yeoh KG, Ko KY, Quan R, Lim TP, Quak SH, Wee A, Teo D, Ong YW. Racial differences in \textit{Helicobacter pylori} seroprevalence in Singapore: correlation with differences in peptic ulcer frequency. \textit{J Gastroenterol Hepatol} 1997; 12: 635-639
10 Browner WS, Black D, Newman TB, Hulley SB. Estimating sample size and power. In: Hulley SB, Cummings SR, editors. Designing clinical research: an epidemiological approach. 1st ed. Williams and Wilkins, 1988: 139-150
11 Feldman RA, Evans SJ. Accuracy of diagnostic methods used for epidemiological studies of \textit{Helicobacter pylori}. \textit{Aliment Pharmacol Ther} 1995; 9 Suppl 2: 21-31
12 Hawthorne AB, Morgan S, Westmoreland D, Stenson R, Thomas GA, Newcombe RG. A comparison of two rapid whole blood tests and laboratory serology, in the diagnosis of \textit{Helicobacter pylori} infection. \textit{Eur J Gastroenterol Hepatol} 1999; 11: 863-865
13 Chey WD, Murthy U, Shaw S, Zawadski A, Montague J, Linscheer W, Laine L. A comparison of three fingerstick, whole blood antibody tests for \textit{Helicobacter pylori} infection: A United States, multicenter trial. \textit{Am J Gastroenterol} 1999; 94: 1512-1516
14 Glupczynski Y. Microbiological and serological diagnostic tests for \textit{Helicobacter pylori}: an overview. \textit{Br Med Bull} 1998; 54: 175-186
15 Talley NJ, Lambert JR, Howell S, Xia HH, Lin SK, Agreus L. An evaluation of whole blood testing for \textit{Helicobacter pylori} in general practice. \textit{Aliment Pharmacol Ther} 1998; 12: 641-645
16 Malfertheiner P, Megraud F, O’Morain C, Hungin AP, Jones R, Axon A, Graham DY, Tytgat G. Current concepts in the management of Helicobacter pylori infection—the Maastricht 2-2000 Consensus Report. \textit{Aliment Pharmacol Ther} 2002; 16: 167-180