

Preliminary Report

Predicting Ulcer Disease in Dyspeptic Patients by *H. Pylori* Testing Rather than Endoscopy

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ABSTRACT

Objectives: To validate accuracy of the Rapid Blood Test (RBT) in predicting peptic ulcer disease in dyspeptic patients.

Rationale: Most patients with dyspepsia have no pathology at endoscopy, thus are exposed to unjustified risk, cost, and inconvenience associated with this invasive assessment.

Setting: Medical World Polyclinic and Dar Al-Shefa Hospital, Riyadh, KSA.

Patients: One hundred patients with ulcer-like dyspepsia.

Methods: All patients underwent a RBT followed by endoscopy with antral biopsies for histology and urease slide test (CLO test).

Results: Sixty-five percent of the patients were "gold standard" *H. pylori* positive (positive CLO test, positive

histology), 30% were "gold standard" negative (negative CLO test, negative histology), and 5% had conflicting CLO test and histology results. Patients with peptic ulcer disease included 31% of all dyspeptic patients, 42% of *H. pylori*-infected patients, and 7% of non-infected individuals. RBT could determine *H. pylori* status with a sensitivity of 91% and specificity of 77%. Positive and negative predictive values of the test were 89% and 79% respectively. In predicting peptic ulcer disease, RBT was sensitive in 93% of patients and specific in 41%. Positive and negative predictive values of the test were 41% and 93% respectively.

Conclusions: RBT is reliable in determining *H. pylori* status. However, we cannot predict the development of peptic ulcer disease merely on the presence or absence of *H. pylori*.

KEYWORDS: dyspepsia, endoscopy, *H. pylori*, peptic ulcer disease

INTRODUCTION

The important role of *H. pylori* infection in the etiology of dyspepsia with ulcer disease is being recognized over the last 15 years^[1]. This has changed the way we treat dyspeptic patients. The new challenge now is: can *H. pylori* infection change the way we investigate patients presenting with dyspepsia? Conventionally, a patient with ulcer-like dyspepsia probably undergoes an endoscopy followed by the most appropriate treatment.

At endoscopy, *H. pylori* negative dyspeptic patients are found to have no pathology or only have esophagitis, whereas many of the *H. pylori* positive dyspeptic patients have peptic ulcer disease^[2,3]. Thus, knowing the *H. pylori* status could predict the likely diagnosis at endoscopy and, accordingly, the most appropriate treatment could be given without exposing the patients to unjustified risk, cost, and inconvenience associated with this invasive assessment. A number of non-invasive means of *H. pylori* testing have been developed. The Rapid Blood Test (RBT) is marketed worldwide as a simple near-patient test requiring only a drop of blood or serum to detect antibodies

to *H. pylori*. We assessed the value of RBT as a predictor of *H. pylori* status and of peptic ulcer disease in patients presenting with uncomplicated dyspepsia.

PATIENTS AND METHODS

Patients: The study involved one hundred patients seen at our clinics. Inclusion criteria consisted of age 45 years or less (mean age 32 yr; range 16-45 yr) and a presenting complaint of intermittent or persistent ulcer-like dyspepsia for 6 months or more. Dyspepsia is defined as upper abdominal pain or discomfort, heartburn, nausea, vomiting, or other symptoms considered to be related to the upper gastro-intestinal tract^[4]. Exclusion criteria consisted of alarm symptoms (such as weight loss, dysphagia, or gastro-intestinal bleeding), current intake of non-steroidal anti-inflammatory drugs, and previous intake of *H. pylori* eradication therapy. Written informed consent was obtained from patients fulfilling inclusion criteria.

Methods: At their first visit, the patients had a RBT. An appointment was then made for upper gastrointestinal endoscopy, which was performed

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Table 1*H. pylori* status and endoscopic findings in dyspeptic patients (N=100*)

Findings	Infected patients (positive CLO, positive histology) N = 65 (65%)	Non-infected patients (negative CLO, negative histology) N=30 (30%)
Pathology	n = 32 (49%)	n = 6 (20%)
Eso	5	4
DU	19	1
Duod	1	1
GU	3	-
DU + GU	2	-
Eso + DU	1	-
Eso + GU	1	-
No Pathology	n = 33 (51%)	n = 24 (80%)

* Five patients (5%) with conflicting results were excluded with no further assessment; Eso = esophagitis; DU = duodenal ulcer; GU = gastric ulcer; Duod = duodenitis

Table 2

Prevalence of PUD among dyspeptic patients

Patient Data	Total No.	No. of PUD	Prevalence of PUD (%)
Dyspeptic patients in general	95	29	31
<i>H. pylori</i> infected dyspeptic patients	65	27	42
<i>H. pylori</i> non-infected dyspeptic patients	30	2	7

PUD, peptic ulcer disease

Table 3Accuracy of RBT in determination of *H. pylori* status

	Positive RBT	Negative RBT	Total	
Infected patients (positive CLO & histology)	59	06	65	Sensitivity 91%
Non-infected patients (negative CLO & histology)	07	23	30	Specificity 77%
Total	66	29	95	
	PPV 89%	NPV 79%		

RBT, rapid blood test; PPV, positive predicative value; NPV, negative predicative value

Table 4

Accuracy of RBT in prediction of PUD

	Positive RBT	Negative RBT	Total	
Patients with PUD (confirmed by endoscopy)	27	02	29	Sensitivity 93%
Patients without PUD (confirmed by endoscopy)	39	27	66	Specificity 41%
Total	66	29	95	
	PPV 41%	NPV 93%		

PUD, peptic ulcer disease; RBT, rapid blood test; PPV, positive predicative value; NPV, negative predicative value

within 2 weeks. Rapid Blood Test (RBT; *H. pylori* STAT-PAK, Chembio Diagnostic Systems, Inc., Medford, NY, USA) is a rapid immunochromatographic test for the detection of antibodies to *H. pylori*. It involves a test card, which is composed of a membrane held in a plastic envelope containing one Test area and one Control area. The membrane has been coated with a cocktail of *H. pylori* antigen, conjugate and substrate. When the patient serum is allowed to pass over the membrane, any *H. pylori* antibodies present will bind to the *H. pylori* antigen in the Test area producing a pink band. The serum continues to migrate along the membrane and produces also a pink band in the Control area. If there is no detectable *H. pylori* antibodies in the patient serum, no pink band will be formed in the test area but there should always be a pink band in the Control area.

Endoscopy: The patients attended the clinic in a fasted state. Upper gastrointestinal endoscopy was performed in the routine manner. Antral biopsies were taken for histology and urease slide test (CLO test; Delta West Pty, West Australia).

Statistical Analysis: Data were analyzed using sensitivity, specificity, and predictive values equations^[5].

Sensitivity of a diagnostic test is the probability that a diseased individual will have a positive test result: Sensitivity = disease with positive test/all diseased.

Specificity is the probability that a disease-free individual will have a negative test result: Specificity = disease-free with negative test/all disease-free. The positive predictive value is the probability that an individual with a positive test result has the disease:

Positive Predictive Value = disease with positive test/all positive tests.

The negative predictive value is the probability that an individual with a negative test result is disease-free: Negative Predictive Value = disease-free with negative test/all negative tests.

RESULTS

At endoscopy, 65 (65%) of the 100 patients studied were "gold standard" *H. pylori* positive (positive CLO-test and positive histology) and 30 (30%) were "gold standard" negative (negative CLO-test and negative histology). Five patients (5%) could not be categorized into either gold standard group because of conflicting CLO-test and histology results and were excluded from further analysis. In 32 (49%) of the 65 *H. pylori*-infected patients, 5 had esophagitis and 27 had peptic ulcer

disease (duodenal ulcer, gastric ulcer, duodenitis) as seen on endoscopy. Of the 30 non-infected patients, four had esophagitis and 2 had peptic ulcer disease. Table 1 shows details of *H. pylori* status and endoscopic findings in all dyspeptic patients who participated in our study. Table 2 shows that the prevalence of peptic ulcer disease was markedly higher in the *H. pylori*-infected dyspeptic patients (27/65; 42%) than in the non-infected individuals (2/30; 7%).

Determination of *H. pylori* status by the RBT

Sixty-six of the 95 patients studied had a positive RBT. These included 59 of the 65 gold standard-positive cases (91% sensitivity) and seven of the 30 gold standard-negative cases (77% specificity). Positive and negative predictive values of the test were 89% and 79% respectively (table 3).

Prediction of peptic ulcer disease by the RBT

Out of the 95 patients studied, 29 had peptic ulcer disease (31%) (table 1). RBT was positive in 27 of the 29 (sensitivity 93%) and negative in 27 of the 66 patients who were free of ulcer disease (specificity 41%) (table 4). The total number of patients showing a positive RBT thus was 66. Positive and negative predictive values of the test were 41% and 93% respectively.

DISCUSSION

The accuracy of RBT in determining *H. pylori* status has been validated elsewhere. Its sensitivity has ranged from 75% to 91% and specificity from 67% to 94%^[5-7]. In this study, 100 patients presenting with dyspepsia underwent a RBT to determine their *H. pylori* status. As a gold standard evidence of current infection, we endoscoped all patients and assessed histology and the CLO test of antral mucosal biopsy specimens. RBT had a high sensitivity (91%) and specificity (77%) that were consistent with the results of previous literature^[5-8]. We noticed a somewhat low prevalence (65%) of *H. pylori* in our study population considering the high prevalence of *H. pylori* in the Saudi Arabia. In fact the number of our study population (n = 100) is too small to represent the population of the Kingdom of Saudi Arabia. In addition, the social class, income, and awareness may play a role.

The value of RBT in predicting the presence or absence of ulcer disease was also assessed in this study. We found that the ability of RBT to predict the absence of ulcer disease is better than its ability to predict the presence of ulcer disease (93% negative predictive value versus 41% positive predictive value). On the other hand, the prevalence of underlying ulcer disease (27/66; 41%) in those with a positive RBT was close to the true

proportion of ulcer disease in individuals with gold standard evidence of infection (27/65; 42%) (table 2). These data match those obtained from previous studies^[2,3].

It is important to consider the effect of using non-invasive *H. pylori* tests in determining how to manage dyspepsia. We believe that all *H. pylori*-positive dyspeptic patients should be treated with eradication therapy on the assumption that a substantial proportion will have ulcer disease that will be cured by such treatment without being subjected to the inconvenience, cost, and risks associated with endoscopy. On the other hand, *H. pylori*-negative dyspeptic patients are given symptomatic treatment postulating that they usually have no pathology or only have esophagitis (reflux disease) that will be cured by symptomatic treatment^[3,9].

The use of a positive RBT as an indication for *H. pylori* eradication therapy raises three main points for discussion:

1. Most of the *H. pylori*-positive dyspeptic patients have no ulcer disease. Is it appropriate to eradicate the infection in patients without ulcer disease?
2. Specificity of RBT is not 100%. Thus, a number of false-positive patients would be receiving a course of eradication therapy despite absence of the infection, exposing them to the potential side effects of this therapy. Is that justified?
3. A positive RBT may indicate current or previous infection. Is it warranted to give eradication therapy to all patients with a positive test?

For many reasons, recent studies support eradicating *H. pylori* infection in dyspeptic patients without ulcer disease. First, eradication of *H. pylori* infection may relieve dyspeptic symptoms at least as good as any other therapy^[10], as it is given once without the need for maintenance treatment as for other medications. Secondly, *H. pylori*-infected patients have an increased risk of developing ulcer disease in the near future^[11] and eradication therapy will, thus, remove this increased risk. It also removes a recognized risk factor for gastric cancer^[12]. Finally, many patients with non-ulcer dyspepsia will be given proton pump inhibitor therapy and there is some evidence that if this treatment is given for a long time to a patient with *H. pylori* infection, progressive gastritis may develop with subsequent gastric atrophy^[13].

The percent of false positive cases is not high and these patients may be prescribed an eradication therapy instead of doing an endoscopy; the potential side effects of eradication therapy being less hazardous than those associated with an unjustified endoscopy. Although RBT does not differentiate between current and previous

infection, eradication therapy could be given on basis of a negative history of taking such a therapy.

On the other hand, the use of a negative non-invasive test as an indication for symptomatic treatment and a means of avoiding endoscopy was examined by Asante et al^[14]. The results showed that, after 12 months of treatment, there was no difference between the endoscoped and non-endoscoped *H. pylori*-negative dyspeptic patients. Furthermore, the non-endoscoped patients who were referred later for an endoscopy were negative as would be predicted. These data and others^[15] support our postulation that *H. pylori*-negative dyspeptic patients usually have no pathology or only have esophagitis (reflux disease) that will be cured by symptomatic treatment with no need for endoscopy.

Another concern about non-endoscopic management of dyspeptic patients is the possibility of missing an underlying malignancy. Therefore we should always bear in mind the definite indications for endoscopy in patients with dyspepsia. These include patients who have alarm symptoms such as dysphagia, gastrointestinal bleeding, weight loss, or a family history of upper gastrointestinal malignancy. Similarly, old patients and those taking NSAIDs should also be endoscoped^[16,17,18]. The age above which one should probably routinely undertake endoscopy is not yet defined. It has been suggested that dyspeptic patients above 45 years of age should be endoscoped but there is little evidence to support this. Two large and very recent studies suggest that uncomplicated dyspepsia is not a symptom of gastric cancer and, thus, in the absence of alarm symptoms it is safe not to endoscope up to age 55 years^[16,17]. Taking 50 years might be appropriate because it builds in a 5-year safety margin^[18]. However these age limits are based on European studies and would have to be individualized according to the local incidence of gastric cancer.

CONCLUSIONS

Our study shows that in patients with ulcer-like dyspepsia, non-invasive *H. pylori* testing is a valuable predictor of the likely diagnosis at endoscopy in terms of *H. pylori* status. On the other hand, we cannot predict the development of peptic ulcer disease merely on the presence or absence of *H. pylori*. In high prevalence populations, like ours, this might lead to over-diagnosing peptic ulcer disease. A test with high positive and negative predictive values is required. Also, further follow-up of our studied patients is considered to determine the long-term outcome.

We, therefore, suggest that eradication therapy is to be given to all *H. pylori*-positive patients and

symptomatic treatment to all those who are *H. pylori* negative. Moreover, a negative non-invasive test could be used as a means of avoiding endoscopy. However, patients with a negative test and persistent dyspepsia despite symptomatic treatment should be endoscoped. Similarly, patients over 50 years of age, patients who have alarm symptoms, and those taking NSAIDs should also be endoscoped.

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