

# Detection of *Helicobacter pylori* by rapid urease test and histology: Impact of acid suppression therapy

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## ABSTRACT

**Introduction:** *Helicobacter pylori* (*H. pylori*) infection is very common particularly in the developing countries. It is strongly associated with gastric ulcer diseases, chronic gastritis, gastric adenocarcinomas and mucosal associated lymphoid tissue (MALT) lymphoma. *H. pylori* can be detected by various invasive (rapid urease test (Pronto-dry) and Histology) and non-invasive tests (stool antigen test, urea breath tests and serology). Our aims are to assess whether biopsy or rapid urease test is superior in diagnosing *H. pylori*, and to study the impact of acid suppression therapies on these two tests. **Material and Methods:** Patients who had endoscopy at the RIPAS Hospital over a period of six months and had testing for *H. pylori* were included. Only patients who were tested by both histology and Pronto-dry (n = 233, mean age 45.0 ± 16.1 years, male; 57.5%) were included in the study. Positivity for *H. pylori* was considered when either or both tests were positive. **Result:** The overall positivity rate (either or both positive) for *H. pylori* was 38.2%. Pronto-dry (24%, n = 56) and histology (33%, n = 77). The concordant rate was 80.9% (both +ve; 18.9%, both -ve 61.8%) and discordant rate was 19.4% (histology +ve/ Pronto-dry -ve in 14.2% and histology -ve/ Pronto-dry +ve in 5.2%). Use of acid suppression therapy (either proton pump inhibitor [PPI] or Histamine-2-receptor antagonist [H<sub>2</sub>RA]) resulted in false negative rates of 34.1% and 15.9% respectively for Pronto-dry and histology. The false negative rates were higher for PPI (52% for Pronto-dry and 24% for histology) compared to H<sub>2</sub>RA (10.5% for Pronto-dry and 5.3% for histology) **Conclusion:** Both Pronto-dry and histology are associated with false negative. Use of PPI and H<sub>2</sub>RA before endoscopy reduces the sensitivity of antral and corpus biopsies for *H. pylori* detection with both Pronto-dry and histological examination.

**Keywords:** *Helicobacter pylori*, detection, acid suppression, rapid urease test, histology

## INTRODUCTION

*Helicobacter pylori* (*H. pylori*) is a microaerophilic, gram negative, slow growing and path-

ogenic bacterium which produces urease enzyme which allows it to survive in the hostile environment of the stomach.<sup>1</sup> In most patients, *H. pylori* infection does not cause symptoms and the infection often persists without any clinically evident disease. However, 10-20% of *H. pylori* infected patients may

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go on to develop severe disease during their lifetime, which include peptic ulcer disease, mucosal associated lymphoid tissue (MALT) lymphoma (<1% risk) and adenocarcinoma of the stomach (3-6 fold increase).<sup>2, 3</sup> *H. pylori* have been classified as class 1 gastric carcinogen the World Health Organisation.<sup>4</sup>

The prevalence of *H. pylori* has been reported to reach 70% or more in developing countries, and to be less than 40% in developed countries.<sup>5-8</sup> Similar to what have been reported elsewhere, the prevalence of *H. pylori* is also declining in Brunei Darussalam.<sup>9</sup>

Diagnosis of *H. pylori* can be made by either invasive or non-invasive tests.<sup>10</sup> Invasive methods require endoscopy and biopsy of the gastric mucosa to detect the presence of *H. pylori* by either a rapid urease test (RUT), histopathology, culture and even genetic amplification, while non-invasive tests include urea breath test (UBT), serology and stool antigen.<sup>11</sup> Isolation of *H. pylori* from gastric biopsy specimen constitutes the most specific way to establish the diagnosis. RUT and histology are the commonly used methods for the diagnosis of *H. pylori* infection in most centres. RUT is easy to perform and convenient to use as it provide a rapid result and can be used at room temperature.<sup>12</sup> The diagnostic yield of RUT can be enhanced by increasing the number of biopsies and number of sites that are biopsied.<sup>13</sup> The sensitivity of these tests are however reduced in patients taking acid suppression medications such as proton pump inhibitors (PPIs) or Histamine-2-Receptor antagonist (H<sub>2</sub>RA), antibiotics or bismuth compounds. PPIs are known to decrease *H. pylori* density in the stomach and to shift their distribution proximally.<sup>14, 15</sup>

In general practice, most dyspeptic patients are using PPIs prior to undergoing diagnostic endoscopy. The aims of this study are to assess whether biopsy or rapid urease test is superior in diagnosing *H. pylori*, and to study the impact of acid suppression therapies on these two tests.

## MATERIALS AND METHODS

Over the six months period, 550 patients who had undergone endoscopy in the Endoscopy Unit, RIPAS Hospital and had testing for *H. pylori* by both Pronto-dry® and histology were eligible for the study. A detailed questionnaire was handled by the pre-procedure assessment nurses. Data on the demography, drug therapies including use of acid suppressions (PPIs and H<sub>2</sub>RA) and comorbid conditions were enquired. *H. pylori* were considered positive when either or both tests were positive. Patients who had already been treated for *H. pylori* and came for repeated assessment were excluded.

Biopsy specimens were taken from two areas; the antrum and corpus. Two specimens (one from the antrum and one from the corpus) were evaluated by Pronto-dry and histopathology. Pronto-dry was performed according to the manufacturer's instructions. Specimens were placed into the test dots. After resealing the test, the label was pressed over the test dot with the finger to squeeze the tissue fluid out of the specimens. The tissue fluid is absorbed by the filter paper. Results were monitored at room temperature after one hour and 24 hours. A positive result was defined as the colour change from yellow to pink-magenta.

Biopsy specimens for histology were

fixed with formalin and sent to Department of Pathology, RIPAS Hospital to be analysed. The sections were stained with haematoxylin and eosin (H&E) and Giemsa solution for detection of *H. pylori*. The presence of spiral organism on the slide was considered positive for *H. pylori*.

The data was analysed using Statistical Package for Social Sciences (SPSS) software, version 13.0. Results were presented as mean ± standard deviation (SD) and percentages as appropriate.

## RESULTS

A total of 233 patients were included in the study; 134 (57.5%) were male and 99 (42.5%) were female. The mean age at endoscopy was 45.0 ± 16.1 years. The majority were Malays (80.3%) followed by Chinese (15.5%) and others (4.3%), consistent with the national breakdown. Most of patients were not on any antibiotics (95.3%). Overall, 54.5% were on acid suppression therapy when they had their endoscopy; PPIs (34.3%) and H<sub>2</sub>RA (21.9%). Four patients (1.7%) were on both PPI and H<sub>2</sub>RA. The indi-

cations for undergoing upper gastrointestinal endoscopy are shown patients is shown in Figure 1.

The endoscopic findings are shown in Table 2. The most common findings were gastritis, oesophagitis and peptic ulcer.

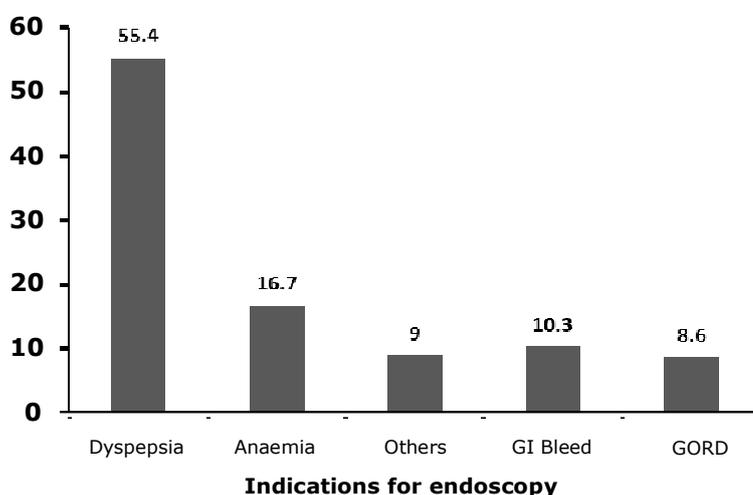
The prevalence of *H. pylori* was 38.1% (89), of which 33% (n=77) were detected on histology and 24% (n=54) on Pronto-dry. The concordant rate was 80.9% and the discordant rate was 19.4%. These are shown in Table 2.

Use of acid suppressions (either PPI or H<sub>2</sub>RA) resulted in false negative rates of 34.1% and 15.9% for Pronto-dry and histology respectively. The false negative rates were

**Table 1: Endoscopic findings.**

Findings	Frequency (%)
Hiatus Hernia	5 (2.1)
Oesophagitis	52 (22.3)
Gastritis	164 (70.4)
Gastric Ulcer	15 (6.4)
Duodenitis	14 (6.0)
Duodenal ulcer	19 (8.2)
Cancer	1 (0.4)

### Percentages



**Fig. 1: Indications for endoscopy.**

**Table 2: The concordant and discordant rates for histology and Pronto-dry test for *H. pylori*.**

	Pronto dry -ve	Pronto dry +ve	Total
Histology -ve	144 (61.8%)	8 (5.2%)	156 (67%)
Histology +ve	33 (14.2%)	44 (18.9%)	77 (33%)
<b>Total</b>	177 (76%)	56 (24.1%)	233 (100%)

higher for PPI (52% for Pronto-dry and 24% for histology) compared to H<sub>2</sub>RA (10.5% for Pronto-dry and 5.3% for histology).

The effect of PPI on histology and Pronto-dry is shown in Table 3, which showed fewer positive rate in patients on PPI for both the histology and Pronto-dry test.

## DISCUSSION

The overall prevalence of *H. pylori* infection was 38.1% in our study based on either RUT or histology being positive. Our previous study showed 24.1% based on CLO<sup>®</sup> test, another RUT.<sup>16</sup> High prevalence of *H. pylori* have been reported in South America (70%-90% of adults) and Asia (50%-80% of adults).<sup>17</sup> These are also areas with a high incidence of gastric cancer.<sup>18</sup> A recent review of *H. pylori* epidemiology also reported high prevalence in Eastern Europe, North Africa, and the Middle East.<sup>19</sup> In the Southeast Asia region, a study on ethnic minority in Malaysian part of Borneo reported prevalence rate of

37.7%.<sup>20</sup> In Thailand the prevalence of *H. pylori* infection varies from 40-60%.<sup>21</sup> We previously reported on the rate of *H. pylori* infection which was also high, 53.5% in 1994 but declining to 25.6% in 2005.<sup>9</sup> High rates and declining trends have also been reported in the other countries in the Southeast Asia region.

Out of the total 89 (38.1%) patients who were positive for *H. pylori*, 77 (33%) were positive on histology and 54 (24%) positive on Pronto-dry. Many studies have shown that histology is more sensitive than RUT, especially when using immunohistochemistry staining.<sup>22, 23</sup> However, non-*pylori* Helicobacter species may also be detected by histology and this can lead to false positive.<sup>24</sup> A major advantage of histological examination over other techniques is that it provides information on the gastric mucosal pathology. In our previous study, we showed that *H. pylori* was detected in 41.6% by histology and 25.7% by CLO test, showing different perfor-

**Table 3: Impact of PPI histology and Pronto-dry test for detection of *H. pylori*.**

	Histology		Pronto-dry	
	+ve	-ve	+ve	-ve
On PPI	19 (76%)	6 (24%)	12 (48.0%)	13 (52%)
Off PPI	58 (90.6)	6 (9.4%)	44 (68.8%)	20 (31.3%)
P value	0.020		0.013	

mance of these two tests. <sup>16</sup>

RUT is frequently used for the diagnosis of *H. pylori* infection. This method has several advantages which include prompt result within an hour, reasonable high diagnostic accuracy as well as its low cost. RUT (Pronto-dry) has been shown that have sensitivity, specificity, PPV, NPV, and diagnostic accuracy of 98%, 100%, 100%, 98%, and 99% respectively. <sup>25</sup> One study showed that the sensitivity and specificity of Pronto-dry against culture were 98% and 97% respectively. <sup>26</sup> The sensitivity and specificity of Pronto-dry with and without PPI was found to be 43.3% and 86.4% vs. 71.9% and 80%. <sup>27</sup>

Our concordant and discordant rates were 80.9% and 19.4% respectively. A study on diagnostic accuracy of RUT observed almost similar concordance and discordance rates, 84.8% and 15.1% respectively. <sup>28</sup> Use of PPIs increases the numbers of false negative tests through two possible mechanisms; direct inhibition of *H. pylori* urease activity and the changing patterns of *H. pylori* colonisation after acid suppression may delay the positivity of RUT. <sup>29</sup> The presence of blood may also adversely affect the performance of RUT leading to a false negative result likely due to buffering effect of serum albumin on the pH indicator. <sup>28</sup> Therefore, PPIs should be discontinued before the endoscopy. <sup>14</sup> However in clinical practice, it often not possible to stop the medications for too long especially for symptomatic patients. Furthermore, patients quite often self-medicate. It has been previously recommended that PPI should be stopped for at least 2 weeks, H<sub>2</sub>RA for 48 hours and antibiotics for 1 month. However, if it is not possible to stop acid suppressions

before endoscopy, biopsies should be taken from the antrum and corpus, as what we have done to increase the diagnostic yield.

In conclusion, both RUT and histology have false negative and the use of PPIs before endoscopy reduces the sensitivity of antral and corpus biopsies for *H. pylori* detection.

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