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Upper gastrointestinal bleeding: Diagnosis of *Helicobacter pylori* infection—Descriptive study

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Abstract

Background and Aim: The presence of blood in the stomach has been thought to affect the performance of diagnostic tests used in detecting *Helicobacter pylori* (*H. pylori*) in the stomach. This study evaluates the effect of upper gastrointestinal bleeding on the efficacy of a rapid urease test (RUT) and compares the results with the pathologic method.

Methods: In this descriptive study, 100 patients presented with upper gastrointestinal bleeding, confirmed from endoscopy, referred to Shahid Rahimi Hospital in Khorramabad were enrolled. Antral biopsy was performed in all the patients and the samples were extracted for histopathology and RUT. A questionnaire was used to collect rapid urease test outcomes and associated parameters (antibiotic, bismuth, and proton pump inhibitors), histology and demographic data. Histopathology was used as the gold standard for diagnosis of *H. pylori*.

Results: Of the 52 patients who were reported positive for *H. pylori* in pathology, 36 had RUT-positive *H. pylori*, sensitivity 69.2%, and of 48 patients whose pathology was negative, 25 had negative RUT, specificity 52.1%. Of 59 RUT, 36 had positive pathology, positive predictive value was 61% and from 41 with negative RUT, 25 had negative pathology, negative predictive value was 61%. The prevalence of *H. pylori* infection was significantly associated with the age of 50 years and above, $p = 0.042$, and previous history of bleeding, $p = 0.019$.

Conclusion: Gastrointestinal bleeding can reduce the sensitivity of RUT. The negative results of these tests in acute upper gastrointestinal bleeding should therefore be interpreted carefully.

KEYWORDS

gastritis, gastrointestinal, *Helicobacter pylori*, infection, pathologic, rapid urease test (RUT)

1 | INTRODUCTION

Helicobacter pylori (*H. pylori*) is considered a grade I carcinogen that is responsible for gastric cancer, gastric and duodenal ulcers, and gastritis.[1] Although the prevalence of *H. pylori* infection is declining in developing and developed countries, it imposes a great health burden in Asia.[2,3] *H. pylori* is estimated to affect 50% of the global population.[4] In developing countries, childhood *H. pylori* infection usually turns into adulthood chronic infection, and the prevalence of infection increases with the advancement in the age.[5,6] Peptic ulcer disease as a result of the infection is complicated by gastrointestinal bleeding that can lead to mortality in 0.8%–14% of patients.[7]

The diagnosis of *H. pylori* infection typically relies on noninvasive methods such as the urea breath test and stool antigen testing. However, invasive methods like histology, culture, and the rapid urease test (RUT) are also employed for accurate diagnosis.[8,9] Esophago-gastro-duodenoscopy is a common procedure used to diagnose gastrointestinal bleeding, where it can indicate the need for tissue biopsy and guide treatment planning.[7] Notably, RUT is conducted using biopsy samples obtained from the stomach lining, specifically the antrum and corpus. However, several factors, including bleeding events, the presence of blood in the stomach, and uneven distribution of bacteria in the stomach, can influence the outcomes of the test.[8]

Despite the clinical relevance of diagnosing *H. pylori* infection, the accuracy of the RUT, a widely used method, may be compromised in the presence of upper gastrointestinal bleeding. This study addresses this critical gap in our understanding by evaluating the sensitivity and accuracy of the RUT specifically among patients with upper gastrointestinal bleeding who are suspected of having *H. pylori* infection. Furthermore, this research aims to compare the results of the RUT with histopathological examination, considered a more reliable diagnostic method for *H. pylori* infection.

By investigating the impact of upper gastrointestinal bleeding on the performance of the RUT, this study aims to shed light on whether healthcare professionals should interpret negative RUT results differently in cases of acute upper gastrointestinal bleeding. The findings of this research have the potential to contribute valuable insights to the field of gastroenterology, potentially leading to improved diagnostic guidelines for *H. pylori* infection in patients with upper gastrointestinal bleeding. Ultimately, this study strives to enhance the precision of *H. pylori* diagnosis, thereby facilitating timely and appropriate medical interventions for affected patients.

2 | METHODS

This descriptive-analytical study was conducted on *H. pylori* patients who were referred to Shahid Rahimi Hospital, Khorramabad in the year 2019 due to upper gastrointestinal bleeding associated with peptic ulcers.

The inclusion criteria were patients presented with gastrointestinal bleeding, referred to our center during the study period. Patients who did not consent to participate along with those having hematological disorders and undergoing anticoagulant therapy were excluded from the study.

A checklist was designed for the study that included demographic data (age, smoking, and sex) and RUT result variables along with the use of PPI, antibiotics, and bismuth subcitrate over the past month. Note that intake of PPI for 2 weeks and antibiotics for 4 weeks was stopped before performing RUT.

All patients underwent an endoscopy procedure and a RUT for the detection of *H. pylori* infection. Notably, before endoscopy, all patients received intravenous proton pump inhibitor (PPI) therapy to prepare for the examination.

During the endoscopy procedure, three biopsy samples were meticulously obtained from the antrum of the stomach for each patient. These biopsy samples served distinct purposes in our study: one was designated for the RUT, while the remaining two were intended for histopathological examination.

The biopsy sample allocated for RUT was directly provided to the patient, and clear instructions were given for its proper handling. Patients were advised to observe any color changes in the sample within the initial 24 h following collection. The patients were given a detailed briefing on how and when to conduct the changes and they were asked to record the changes in the color seen in the chart, provided by the research team.

A positive result was defined by a noticeable color change from yellow to pink or red. Patients were encouraged to report any color changes during this timeframe. If color changes occurred beyond 24 h, it was considered a potential false-positive result due to non-*H. pylori* bacterial activity. For a biopsy, staining was performed in staining in semisolid (0.1% agar) normal saline with hematoxylin and eosin stain and modified Giemsa stain.

In addition to the RUT, the two other biopsy samples were dedicated to histopathology. These samples allowed for a comprehensive assessment of the gastric tissue, enabling us not only to confirm the presence of *H. pylori* but also to evaluate associated inflammatory changes and potential complications.

2.1 | Method of data analysis

The data were analyzed using SPSS v22. Descriptive statistics were computed to summarize patient demographics, including means and standard deviations. Sensitivity and specificity were calculated to assess the performance of the RUT in diagnosing *H. pylori* infection. Gender-based analyses were conducted to determine variations in RUT sensitivity and specificity among female and male patients. Additionally, the sensitivity and specificity of RUT were evaluated based on age groups, distinguishing patients aged above 50 years from those under 51 years. Further analyses included assessing RUT performance in dyspeptic and nondyspeptic patients and comparing patients with a history of PPI usage to those without. The impact of antibiotic usage history on RUT performance was also assessed.

Fisher's exact test was employed to examine the relationship between *H. pylori* infection prevalence and gender, age, PPI usage, antibiotic usage, smoking history, and a history of abdominal bleeding. These analyses provided valuable insights into the diagnostic accuracy of RUT and its associations with various patient characteristics.

2.2 | Ethical

The written consent was obtained from all participating patients before their inclusion in the study, ensuring their informed and voluntary participation. Additionally, this research was conducted in accordance with the ethical guidelines and received approval from the board of research ethics at the Shahid Rahimi Hospital. This study was approved by the Research Ethics Board of Lorestan University of Medical Sciences (IR.LUMS.REC.1397.012) (https://ethics.research.ac.ir/ProposalCertificateEn.php?id=12578&Print=true&NoPrintHeader=true&NoPrintFooter=true&NoPrintPageBorder=true&LetterPrint=true).

3 | RESULTS

3.1 | Demographics of patients

Of 100 patients referred with gastrointestinal bleeding, 59 patients were aged above 50 years. Seventy patients were male and 30 were female and 10 patients were smokers.

Patient clinical and drug history is reported in Table 1.

3.2 | H. pylori infection in patients

From 52 patients positive for *H. pylori* in pathology, 36 samples were positive for *H. pylori* from RUT so the sensitivity of the test was 69.2%. From 48 patients who were negative for *H. pylori*, 25 patients were negative for the RUT test so the specificity of the test was 52.1%.

Of 59 *H. pylori* positive cases in RUT, 36 had positive pathology (positive predictive value: 61.0%) and from 41 RUT negative cases, 25 were negative in pathology (negative predictive value: 61%). From 100 patients, overall, 61 patients were positive for *H. pylori* infection from RUT and pathology.

3.3 | RUT and pathology based on gender

From 11 female patients with positive pathology, the sensitivity of the RUT test was 72.7% and the specificity was 52.6%, respectively. The positive predictive value was 47.1% and the negative predictive value was 76.9% among these patients. The sensitivity and specificity of the test among 42 men was 66.7% and 53.6%, respectively.

3.4 | RUT and pathology based on age

Out of 36 patients aged above 50 years with positive pathology, the sensitivity and specificity of the test were 66.7% and 52.2%. Furthermore, the positive predictive value stood at 68.6%, while the negative predictive value was recorded at 50%. Overall, 25 patients in the group had the same results from RUT and pathology, therefore, 60.9% were diagnosed correctly. The sensitivity and specificity of the test in patients under 51 years of age were 75% and 25%, respectively.

3.5 | RUT and pathology among dyspepsia patients

Among 36 patients with dyspepsia, the sensitivity and specificity of the test were 66.7% and 57.9%, respectively. The positive predictive value was 60%, and the negative predictive value was 64.7%. In total, 46 patients with dyspepsia exhibited congruent results between the RUT and pathology, resulting in a correct diagnosis rate of 62.1% among these patients. Among the 16 nondyspeptic patients, the sensitivity and specificity of the test were 75% and 30%, respectively, with positive and negative predictive values of 63.2% and 57.6%, respectively.

3.6 | Patients with a history of PPI use

The sensitivity and specificity of RUT among patients with a history of use of PPI was 69.4% and 48.5%, respectively. The positive

TABLE 1 Distribution of the frequency of patients under study according to demographic and contextual characteristics.

Variables	Factors	Frequency
Sex	Female	30
	Male	70
Age	< 50	41
	50 ≤	59
Smoking	No	90
	Yes	10
Gastrointestinal bleeding	Yes	18
	No	82
History of PPI	Yes	68
	No	32
History of the usage of antibiotics	Yes	30
	No	70
History of the usage of bismuth subcitrate	Yes	0
	No	100

predictive value was 64.1% and the negative predictive value was 62.1% among these patients.

In the subset of 16 patients who did not have a history of PPI usage and exhibited positive pathology results, the sensitivity and specificity of the test were both recorded at 68.8%. Additionally, the positive predictive value was 43.8%, while the negative predictive value stood at 55%.

3.7 | RUT and pathology among patients with the use of antibiotics

The sensitivity and specificity of RUT among patients with a history of use of antibiotics were 80% and 60%, respectively. The positive predictive value was 66.7% and the negative predictive value was 75% among these patients.

Among patients who did not have a history of antibiotic usage, the sensitivity and specificity of the test were found to be 64.9% and 48.5%, respectively. Furthermore, the positive predictive value in this group was 58.5%, and the negative predictive value was 55.2%.

3.8 | Correlation between *H. pylori* infection and other variables

The results from Fisher's exact test showed that the prevalence of *H. pylori* infection was not significantly different between male and female genders, $p = 0.052$; however, the frequency of infection was higher in men than women (58.6% vs. 36.7%).

The prevalence of *H. pylori* infection was significantly different among the patients aged 50 and above than those under 50 years, $p = 0.042$. The frequency of infection was higher among those aged 50 and above (61% vs. 39%).

The prevalence of *H. pylori* infection was not significantly different among the patients with a history of PPI usage compared to those without a history of PPI usage in the past month, $p = 0.832$. The frequency of the infection among the two groups was 52.9% vs. 47.1%.

Similarly, the history of the usage of antibiotics a month before the study did not significantly affect the prevalence of the infection, $p = 0.830$.

The frequency of the infection among smokers and nonsmokers was 48.9% and 51.1%, respectively. The difference was not statistically significant among the two groups, $p = 0.94$. The frequency of infection among the patients with a previous history of abdominal bleeding and those without the history was 77.8% and 46.3%. The difference was statistically significant among the two groups, $p = 0.019$ (Table 2).

4 | DISCUSSION

RUT is a high-sensitivity, fast, simple, and low-cost method, and is an optional test for patients with uncomplicated peptic ulcer. However, the diagnostic value of this test is uncertain in patients with hemorrhagic peptic ulcer. The false-negative results have been reported in these cases. This study evaluates the diagnostic value of RUT and compares its results with pathology, as a more reliable method in patients with upper gastrointestinal bleeding. Some of the

TABLE 2 Investigation of the prevalence of *Helicobacter pylori* infection with demographic and contextual variables of the patient.

		Pathology results				
		Negative		Positive		
Variables	Factors	Frequency	Percent	Frequency	Percent	*p*-Value
Sex	Female	19	63.3	11	36.7	0.052
	Male	29	41.4	41	58.6	
Age	< 50	25	61	16	39	0.042
	50 ≤	23	39	36	61	
Smoking	No	46	51.1	44	48.9	0.094
	Yes	2	20	8	80	
Gastrointestinal bleeding	Yes	4	22.2	14	77.8	0.019
	No	44	53.7	38	46.3	
History of PPI	Yes	32	47.1	36	52.9	0.832
	No	16	50	16	50	
History of the usage of antibiotics	Yes	15	50	15	50	0.830
	No	33	47.1	37	52.9	
History of the usage of bismuth subcitrate	Yes	0	0	0	0	

common factors that can affect the outcome RUT are the use of PPI before the examination, bleeding leading to bactericidal effects or inhibitors that can suppress the urease activity and change in blood pH as a result of buffering effects can alter color changes.[10,11]

The results of our study demonstrated that the RUT exhibits a sensitivity of 69.2% and a specificity of 52.1% in diagnosing *H. pylori* infection. While these findings provide valuable insights into the diagnostic performance of RUT, it is important to consider that the test's sensitivity and specificity can vary across different studies and clinical settings.

Comparing our results to studies published in various journals, we observe variations in reported sensitivity and specificity figures. For example, a study emphasized the diverse diagnostic methods available for *H. pylori* infection, each with its own sensitivity and specificity profiles, making test selection contingent on factors such as clinical conditions, clinician experience, and cost considerations.[12] Another study published in Clinical Infectious Diseases reported significantly higher sensitivity (95%) and specificity (100%) figures for RUT; however, these results underscore the influence of patient populations and clinical contexts on test performance.[13] A study drawing from epidemiological data, presented sensitivity values ranging from 74.2% to 90.8% and specificity values ranging from 95.1% to 97.2% for RUT when using immunohistochemistry (IHC) as a gold standard.[14]

Our study unveiled variations in RUT sensitivity and specificity based on factors like gender, age, the presence of dyspepsia, and a history of PPI or antibiotic use. These findings align with the understanding that RUT's accuracy is multifaceted and can be influenced by numerous variables.

The overall accuracy of RUT showed no significant difference except in patients with a history of dyspepsia. The diagnostic value of RUT in patients with a history of dyspepsia is lower than in individuals without a history of dyspepsia, which can be attributed to the use of drugs involved in eradicating *H. pylori* such as antibiotics and PPI by the patient before endoscopy.[15,16] Papatheodoridis, Papadelli[17] reported that previous dyspepsia, history of bleeding and peptic ulcer are the risk factors of gastrointestinal bleeding.[18] Our study showed that previous bleeding and age above 50 years are significant factors that can be attribute to the upper gastrointestinal bleeding due to *H. pylori* infection.

A number of studies have indicated that the presence of blood in the stomach can influence the sensitivity of RUT.[16] Mittal et al.,[19] reported that in the absence of blood, 55.6% of patients tested *H. pylori* positive from two RUT duplicates whereas, in patients with bleeding, 38.9% from the first duplicate and 47.2% of patients from the second duplicate tested positive. The decrease in *H. pylori* detection in the presence of blood was significant in the study from RUT but was insignificant from pathological findings.[20] The sensitivity of RUT in the presence of blood was 15%, while in the absence of blood it was 75%. However, increasing the number of biopsy samples can increase the sensitivity of this test.[10,21]

Castro Fernández M et al.,[22] reported that among nonbleeding duodenal ulcer patients RUT sensitivity was 93%, whereas, among patients with bleeding, it is 83%. The difference was reported to be statistically significant. The reduced sensitivity is more in patients presenting with upper gastrointestinal bleeding. Similarly, Tang JH et al.,[23] reported that the presence of *H. pylori* infection among the patients with bleeding ulcers is lower, compared to those without bleeding 53.7% versus 65.2%.[24] The bleeding group was also associated with greater false-negative RUT results. Bleeding was seen to have a significant impact on the sensitivity of RUT.[25] However, the presence of blood in the stomach and the use of PPI did not affect the results of the test.

5 | CONCLUSION

Rapid urease test is effective test for uncomplicated peptic ulcer disease; however, factors like age and gastrointestinal bleeding are likely to affect the outcomes of the test. We recommend studies evaluating severity of upper gastrointestinal bleeding based on different etiologies and the effect of rapid urease tests.

AUTHOR CONTRIBUTIONS

Saleh Azadbakht: Conceptualization; data curation; formal analysis; resources; software; supervision. **Salehe Azadbakht**: Investigation; methodology; project administration; visualization; writing—original draft; writing—review and editing. **Morteza Azadbakht**: Data curation; formal analysis; funding acquisition; investigation; software; supervision; validation; visualization.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

TRANSPARENCY STATEMENT

The lead author Morteza Azadbakht affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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