Close observation endoscopy of gastric mucosal pattern in predicting *Helicobacter pylori* infection: A single center cross sectional study

Yu Mang ZL
Pagilitan AN

Institute of Digestive
and Liver Diseases
St Luke's Medical Center
Quezon City, Philippines

Correspondence:
Dr Zhannarie L Yu Mang at
zhannarieyumang@gmail.com

Abstract

Background: Helicobacter pylori (Hp) is a major health problem causing chronic gastritis, peptic ulcer disease, gastric cancer, and affects 60% of dyspeptic patients in the Philippines. Advanced techniques such as magnifying chromoendoscopy and narrow band imaging increase detection rates but are not available in most endoscopy centers in the country. Our aim is to apply the Cho et al. classification[3] on gastric mucosal pattern by close observation with standard white light endoscopy to identify Hp infection status. *Methodology:* This is a single-center cross-sectional study of 205 dyspeptic patients undergoing gastroscopy, all without gastrointestinal bleeding, gastric mass, or liver cirrhosis. Close observation of the gastric mucosa of the corpus, rapid urease test (RUT) and histopathology were done. Patterns were categorized according to the Cho et al. criteria: without Hp infection (normal RAC (regular arrangement of collecting venules) pattern); or with Hp infection (mosaic pattern (Type A); diffuse redness (Type B); or atypical pattern (Type C)). *Results:* 97 of 205 (47%) patients were positive for Hp. The technique is 98.75% sensitive, 85.6% specific, PPV 81.44%, NPV 99.7%, and 90.7% overall diagnostic accuracy. *Conclusion:* Normal RAC pattern has good agreement with Hp status and, for these patients, further testing for Hp may no longer be necessary. Abnormal RAC and presence of Types A, B and C mucosa suggest Hp positivity but is less specific compared to RUT. Overall, Hp screening by close observation of the corpus mucosa is a cost-effective approach in Hp diagnosis and can be reliably used in clinical practice.

Keywords: Helicobacter pylori, endoscopy, gastric mucosa

Introduction

Helicobacter pylori (Hp) is the most common chronic human infection affecting approximately 4.4 billion individuals worldwide. It is a major public health problem as it is the main cause of chronic gastritis and peptic ulcer disease. Furthermore, this microorganism is also declared as a group I carcinogen by the WHO, being the principal etiologic agent for gastric cancer and gastric mucosa-associated lymphoid tissue lymphoma.[1]

In the Philippines, the incidence of Hp infection is high. According to the 2004 study by Destura et al., the local incidence of Hp infection in dyspeptic patients undergoing endoscopy is 60%.[2]

Many gastroenterologists have attempted to diagnose Hp infection by endoscopy and have recognized specific mucosal patterns characteristic of Hp-infected stomach. Most studies claim high detection rates utilizing magnifying chromoendoscopy and narrow band imaging. However, these procedures need special equipment and training, hence, are not applicable in a significant fraction of endoscopy centers in our country.

Our study aims to evaluate the accuracy of close observation of gastric mucosal pattern using conventional white light endoscopy in diagnosing Hp infection compared to rapid urease test (RUT) and/or histopathology. It aims to establish its utility in a subgroup of patients with high suspicion of Hp infection

but who are negative for RUT. It also aims to use gastric mucosal pattern to predict Hp infection negating the need for RUT or biopsy, hence, decreasing the overall cost of diagnosing the infection.

For this study, we looked for a simple and low-cost method that can be applied in all endoscopy units in the Philippines and we adapted the study of Cho et al.[3] where they utilized conventional white light endoscopy in diagnosing Hp infection.

Background

Endoscopic and non-endoscopic tests can be used for diagnosis of Hp infection. The choice depends on the clinical setup, physician skill, cost, and accuracy of test. This study was conducted in a tertiary private hospital where endoscopy is being done, and utilized endoscopic techniques for Hp diagnosis on all dyspeptic patients undergoing upper GI endoscopy.

As proposed by latest guidelines, the most commonly used diagnostic test in endoscopy centers is the RUT due to its efficiency, relatively lower cost and accuracy.[4] Based on the review of Uotani and Graham in 2015, the sensitivity of various RUT as primary diagnostic test is high and reported to vary between 80% and 100%, and specificity between 97% and 99%.[5]

One of the disadvantages of RUT is its lower accuracy in patients who have been on antibiotics and proton pump inhibitors.[6] In these cases, histopathology has higher sensitivity, which is considered to be the gold standard by some studies, albeit it still has its limitations, including optimization of site, number and size of gastric biopsies, method of staining and the expertise of the pathologist.[7] Guidelines do not recommend RUT over histopathology, citing no significant difference in their sensitivity or specificity; however, the use of both is recommended in instances of decreased accuracy, such as in patients using proton pump inhibitors and prolonged antibiotic use.

A study in Korea by Cho et. al.[3] used the following endoscopic patterns to determine presence of Hp infection: (a) Normal or without Hp: regular arrangement of collecting venules (RAC) pattern seen as numerous minute red dots; (b) type A: a mosaic-like appearance characterized by prominent, swollen area with deeper furrows or snake-skin appearance; (c) type B: a diffuse, homogenous redness; and (d) Type C: atypical pattern showing irregular redness with grooves. Pictures and description are shown in **Figure 1** and **Table 1**, respectively.
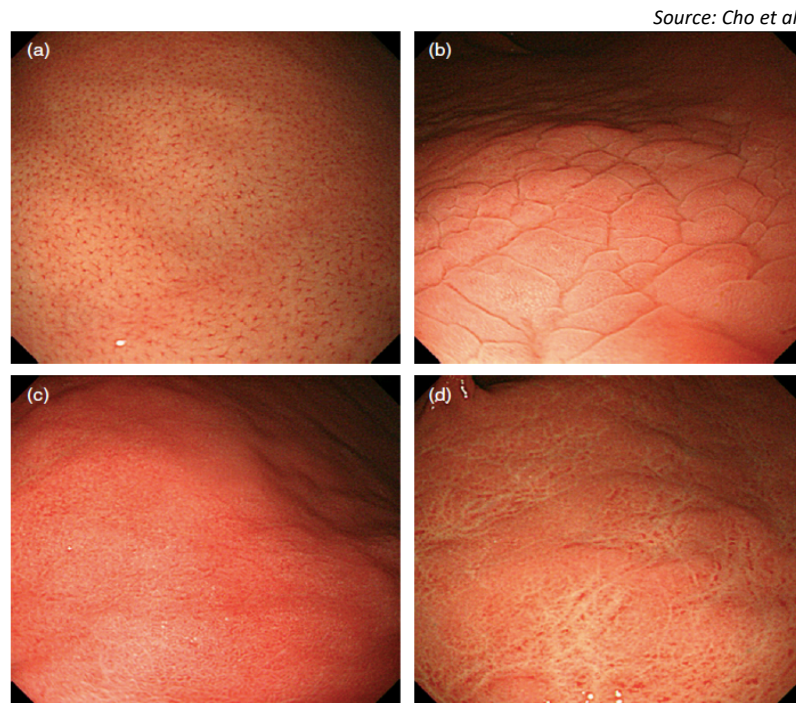
Source: Cho et al.

Figure 1. Gastric mucosal patterns using close look endoscopy. (a) Normal (RAC) pattern seen as minute dots. (b) Abnormal, Type A: mosaic pattern characterized by edematous areas with grooves, giving a snakeskin-like appearance; (c) Abnormal, Type B: homogenous redness; (d) Abnormal, Type C: atypical pattern showing irregular redness and grooves.

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Table 1. Cho et al. classification of gastric mucosal pattern by close observation with standard white light endoscopy

Classification	Description
Normal	RAC pattern seen as numerous minute red dots
Type A	Mosaic-like appearance characterized by prominent, swollen areas with deep furrows or snake skin appearance
Type B	Diffuse, homogenous redness
Type C	Atypical pattern showing irregular redness with groove

The study by Cho et al. tested their classification in 617 patients. **Table 2** below shows their summary of correlation between the endoscopic findings and Hp infection.

Table 2. Summary of Cho et al. study: Correlation between endoscopic findings and Hp infection (N=617)

Mucosal Finding	Hp Positive (%)	Hp Negative (%)
Normal	9.4	90.6
Type A	87.7	12.3
Type B	98.1	1.9
Type C	90.9	9.1

Their study yielded 93.3% sensitivity, 89.1% specificity, 92.3% positive predictive value and 90.6% negative predictive value in determining Hp status.

Our study's general objective is to determine the accuracy of close observation of gastric mucosal pattern by standard white light endoscopy in diagnosing Hp infection. It specifically aims to compare close observation of gastric mucosal pattern by conventional white light endoscopy with RUT and/or histopathology in diagnosing Hp infection.

Operational Definitions

Endoscopic Procedure

All endoscopic procedures in this study were done using the following scopes: Olympus GIF H180 and H190, Olympus GIF XP150, Fuji Film EG L590ZW and Fuji Film EG 600WR. Conventional white light imaging was utilized. Standard upper gastrointestinal endoscopy was done on each patient followed by close-up observation of the mucosal patterns at the gastric corpus of the stomach while maintaining a distance of ≤10mm between the endoscope tip and mucosal surface.

Rapid Urease Test

RUT was considered positive when the entire yellow-colored test paper strip turned pink within an hour. A negative result was when the yellow-colored test paper strip (or any part of it) remained yellow.

Histopathology

Histopathology procedure used Giemsa staining. A positive reading meant that Hp bacteria was identified by the pathologist, and a negative reading meant there was no identifiable Hp bacteria.

Mucosal Pattern

Types of mucosal pattern were based on the Cho et al. criteria, as described in **Table 2** above.

Sample Size Estimation

Sample size was calculated based on the 2013 study by Cho et al. on close observation endoscopy of gastric mucosal pattern in predicting Hp infection with sensitivity of 91.3%, as well as on the 60% prevalence rate of the 2004 study by Destura et al. on Hp infection in patients with dyspepsia undergoing endoscopy. Having a power of 80% at 95% confidence level and maximum allowable error of 0.05, the estimated sample size for this study was 205.

Ethical Considerations

The clinical protocol and all relevant documents were reviewed and approved by the SLMC Institutional Ethics Review Committee. For each subject, a unique study-generated code was assigned. No name or any other patient identifier was recorded.

The investigators are responsible for data privacy and integrity. All raw data as well as data gathering forms will be stored for ten years in a location which can be accessed only by the principal investigator and then destroyed thereafter.

Methodology

Study Design

This is a cross-sectional, prospective, observational study of subjects who underwent gastrointestinal endoscopy recruited consecutively from June 1, 2018 to February 1, 2019.

Study Participants

Filipino patients aged 18 years old and older with dyspeptic symptoms (including bothersome

postprandial fullness, early satiation, epigastric pain and epigastric burning) and who were to undergo upper gastrointestinal endoscopy were included in the study. Excluded were patients with gastrointestinal bleeding, gastric cancer, liver cirrhosis, and previous gastric surgery. Informed consent was obtained from all participants. Consent covered the endoscopy procedure, endoscopic tests, and histopathology of specimens.

During endoscopy, a minimum of three biopsy specimens were obtained from each patient: one from the angularis, a second specimen from the corpus, and a third one from the antrum. Still images of gastric mucosa were stored as JPEG files.

Processing and Interpretation of Endoscopic FIndings

A total of 100 high-quality images were taken and stored. These images were prepared as a powerpoint presentation for evaluation by three senior endoscopists with at least ten years of experience in upper gastrointestinal endoscopy. The**se** endoscopists were blinded as to the clinical data of the subjects, as well as to their RUT and histopathology results. An inter-observer assessment of.the images was done according to the criteria of Cho et al. (**Table 2**).

The mucosal pattern of each photo agreed upon by at least two out of the three senior endoscopists was recorded. In case the three readers each had different mucosal pattern reading, this was reported as either positive or negative, based on their consensus. The methodology is summarized in **Figure 2**.
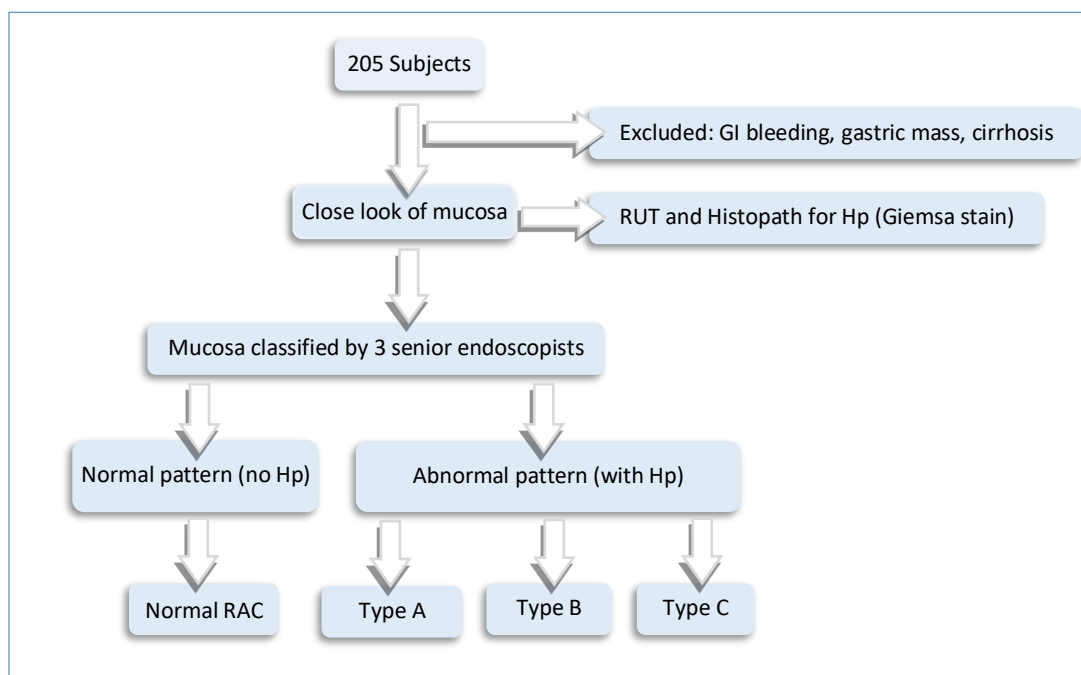

Figure 2. Methodology flow chart

Results

Study Subjects and Baseline Characteristics

A total of 205 subjects were enrolled, 107 were classified to have normal pattern with regular arrangement of collecting venules while 97 had abnormal pattern with either type A, B or C gastric mucosal pattern. The mean ages of the normal and abnormal pattern groups differed significantly (53.63 ± 13.02 versus 46.8 ± 13.46, *p* = <0.001), with the patients

with normal mucosal pattern being older. Overall, more females were included in the study (123 subjects), but it is noted that the proportion of male patients was significantly higher in the abnormal pattern group than in the normal pattern group (48.45% versus 32.41%, *p* = 0.019). Patients on proton pump inhibitors (PPI) included in the study were 62 and the proportion of subjects on PPI was not significantly different between the normal pattern group and the abnormal pattern group (37.01% versus 22.6%, *p* = 0.010) (**Table 3**).

Table 3. Baseline characteristics of subjects vs. mucosal pattern

	Normal Pattern (n=108)	Abnormal Pattern (n=97)	p-value
Age, mean (SD) years	53.53 ± 13.02	46.8 ± 13.46	<0.0001
Male Sex	35 (32.4%)	47 (48.5%)	0.019
Use of PPI	40 (37.0%)	22 (22.6%)	0.010

Close Observation Endoscopy of Gastric Mucosal Pattern

Table 4 summarizes the correlation between gastric mucosal pattern and Hp infection status.

Table 4. Gastric mucosal pattern vs. Hp infection status

Mucosal Pattern	Hp (+)	Hp (-)
Normal (n=108)	1 (0.9%)	107 (99.07%)
Abnormal		
Type A (n=58)	46 (79.3%)	12 (20.7%)
Type B (n=8)	6 (75.0%)	2 (25.0%)
Type C (n=24)	20 (83.3%)	4 (16.7%)
Combination (n=9)	8 (88.9%)	1 (11.1%)

Of the 97 patients with abnormal mucosal pattern, the most commonly seen was the type A or the mosaic pattern with 58 patients or 59.8% percent, 8 had Type B mucosa, while 24 had type C. Nine were tagged to have a combination of the three patterns.

Results show that close look endoscopy of gastric mucosa has a sensitivity of 98.75%, specificity of 85.6%, positive predictive value of 81.44% and a negative predictive value of 99.7%. The overall diagnostic accuracy is 90.7%.

Discussion

As shown in this study, the negative predictive value of close observation endoscopy was 99.7%, further strengthening the evidence that the presence of regular arrangement of collecting venules predicts absence of Hp infection. Hence in these cases further Hp evaluation is dispensable unless with high clinical suspicion of Hp infection, such as in the presence of gastric or duodenal ulcers.

In our study, the procedure's overall accuracy of 90.7% in predicting Hp infection was comparable with the results of the large-scale study of Cho et al. involving 617 participants. However, our specificity was relatively lower at 85.6% versus 89.1% of Cho et al. Similarly, our positive predictive value was lower at 81.44% versus 92.3% of the Korean study. Possible source of this difference is the lower sample size in this study.

One of the initial objectives of this study is to determine if close look observation of gastric mucosa can also be applied to patients on PPI or with antibiotic use. The number of patients on PPI included in this study, however, was small and there were variations in dosage and duration of PPI or antibiotic treatment. Hence, conclusions cannot be drawn from our data.

Conclusion

The results of this study show that close observation of gastric corpus mucosa using non-magnifying standard endoscopy has a fair specificity and positive predictive value but very high negative predictive value and therefore very sensitive in diagnosing Hp infection.

This further affirms the utility of observed gastric mucosal patterns using conventional white light endoscopy in predicting Hp infection status, and that this can be applied in routine clinical practice without additional cost for both the endoscopy center and the patient.

With these findings, we conclude that close observation of the gastric mucosa using the classification introduced by Cho et al. is a simple technique at no additional cost, and that this procedure can accurately predict Hp infection and may be applied in all endoscopy units in the Philippines.

Conflict of Interest

The authors declare no conflicts of interest.

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