Does nodular gastropathy always indicate Helicobacter pylori infection?

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Abstract

Background: Nodular gastropathy (NG) is a common finding during esophagogastroduodenoscopy (EGD), and Helicobacter pylori (*H. pylori*) infection is an endemic infection in developing countries. Aims: To define the relationship between NG and *H.pylori* as a causative agent, assess the presence of NG in relation to various demographic parameters of patients, and determine the prevalence of *H. pylori* among patients who underwent EGD.

Patients and Methods: This is a descriptive retrospective study that included 353 patients, classified into two groups: nodular and non-nodular gastropathy (NNG), based on the presence of nodularity
of the gastric mucosa during EGD. Various methods document the existence of *H. pylori*. Other information, such as the patient's age, BMI, smoking status, and history of *H. pylori* eradication, was included.

Result: *H.pylori* was present in 213 patients (60.3%); 229 (64.9%) patients were female, with a significant association between female sex and NG ($p < 0.001$). The mean age of our patients is 33.7 ± 15.2 years. There is a significant negative association between smoking and NG (P value <0.001). Most patients with NG had a BMI of less than 30 (68 patients, 87.2%), and 72 patients (92.3%) with NG had *an H. Pylori* infection. NG had a sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 33.8%, 95.7%, 92.3%, and 48.7%, respectively.

Conclusion: A strong association exists between NG and *H. pylori* during EGD. NG should be regarded as clear indicator of H.*pylori* infection, particularly in young female patients.

Keywords: Nodular gastropathy, H.pylori, Nodular gastritis.

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Introduction:

Nodular gastritis, or nodular gastropathy (NG), is a form of chronic gastritis characterized by lymphoid hyperplasia in the gastric mucosa with moderate inflammation and eosinophilic infiltration in the superficial lamina propria. It has been associated with H. pylori infection, and endoscopically, NG exhibits a unique cobblestone, corn-like appearance; these changes are more pronounced at the gastric antrum than in the corpus. Gastric lymphonodular hyperplasia and nodular antritis are other names for NG (1). Upper gastrointestinal symptoms such as epigastric pain, indigestion, nausea, abdominal bloating, or abdominal discomfort are present in some individuals. Still, most cases are detected accidentally during EGD because they are asymptomatic (2, 3). The earliest endoscopic findings for NG, as published in the literature, were characterized by Miyagawa et al. as "goose-like flesh" (4). Dixon and colleagues (1996) revised the Sydney System's classification, characterizing the follicles as clusters of lymphoid germinal centers that are characteristic of H. pylori (5). The endoscopic and histopathological changes of nodular gastropathy will disappear after H. pylori eradication (6).

Helicobacter pylori (H. pylori) is a gram-negative, spiral-shaped bacterium that colonizes the gastric mucosa. It is the most prevalent chronic bacterial infection in humans and the leading cause of infection-associated cancer (7). It is widely acknowledged that this infection, which is typically contracted in childhood, can cause diseases at later ages and, if untreated, last a lifetime. H. pylori infection remains a concern for both developed and developing countries, and its seroprevalence differs between countries and even within a single country. While the prevalence of H. pylori infection ranges from 5 to 20% in developed countries, it is between 70% and 90% in developing countries (8). In Iraq, the prevalence varies from 47.8% to 70.4% using different methods (9). H. pylori mainly colonizes the gastric antrum and corpus and can cause intestinal metaplasia, chronic gastritis, duodenal and stomach ulcers, as well as gastric adenocarcinoma and gastric lymphoma. Although the exact mechanism underlying gastric inflammation remains unknown, the production of active secretions that directly or indirectly damage the mucosa, the persistence of the inflammatory response, and the breakdown of acid secretion regulation are all thought to be contributing factors to H. pylori-induced mucosal damage (10).

Patients and methods:

This is a retrospective descriptive study conducted over three months (November 2024–January 2025) in a private endoscopy center in Mosul, Iraq. This study includes 353 patients, all of whom underwent esophagogastroduodenal (EGD) endoscopy for various reasons. Seventy-eight patients had nodular gastropathy during EGD, and 275 patients had no nodularity. All patients agreed and signed a consent form regarding participation in this research. We include various patient data, such as the indication for EGD, age, weight, height, smoking habit, endoscopic findings, whether the patient has had a previous *H. pylori* infection, and whether the patient has undergone previous *H. pylori* eradication. Regarding the indication for EGD, it was variable and included chronic dyspepsia, upper gastrointestinal bleeding, vomiting, reflux symptoms, loss of appetite, and acidity.

All 353 patients were tested for *H. pylori* during EGD, either by a rapid urease test (RUT) or by taking a gastric biopsy and sending it for histopathological examination and *H. pylori* staining. We took two biopsies for RUT using standard biopsy forceps, one from the antrum and the other from the corpus. Then, these two biopsies were embedded in the disc of RUT. We used the Pyloplus + RUT test, which is considered positive after the color change of the ring in the test disc from yellow to pink within a maximum of one hour of examination (Figure 1). The sensitivity and specificity of the 1-hour RUT are 89-98% and 89-93%, respectively (11), while for the histopathological test, we took four biopsies: two from the antrum and two from the corpus. The biopsies were then immersed in diluted formaldehyde-containing tubes and sent for histopathology to perform *H. pylori* staining using hematoxylin and eosin (H&E) and Giemsa stains. All patients included in this study should be off proton pump inhibitors (PPIs) for at least 2 weeks and off antibiotics and bismuth for at least 4 weeks, as recent use of these drugs may result in a false-negative result on RUT.

The nodularity of the gastric mucosa is recognized by white light, high-definition endoscopy (Olympus Evis Exera II and III), and by using narrow-band imaging from the Olympus company. Nodular mucosa is seen as a slight, few-millimeter elevation of the gastric mucosa (Figures 2a and b), and this nodularity can be documented histopathologically on gastric biopsy (Figures 3a, b, and c).

Statistical analysis:

Microsoft Excel version 2010 sheets summarised the data collected during the study. The statistical analysis was performed by using IBM SPSS version 26. The Pearson chi-square test and Fisher's exact test were chosen to determine the difference between the studied parameters in tables with more than two cells two. The chi-square test for goodness of fit was used to determine the difference in parameters between the two groups. A p-value ≤ 0.05 is considered significant.

Results:

*Note: All tables mentioned in this section are provided at the end of the article.

Three hundred fifty-three patients were included in our study. Of these, 78 patients had endoscopic findings of NG, and 275 had NNG. The patient population consisted of 124 males (35.1%) and 229 females (64.9%). The mean age of patients is 33.7±15.2 years; those with NG had a mean age of 23.6±7.9 years, and the 275 patients with NNG had a mean age of 36.7±15.5 years. The age distribution of our patients includes 190 (53.8%) patients between the ages of 20 and 40 years, 102 (28.9%) patients were above the age of 40 years, and just 61 (17.3%) were younger than 20 years. Two hundred fourteen (60.6%) patients were single, and 139 (39.3%) patients were married. In both the NG and NNG groups, only nine patients (2.54%) were smokers, while the remaining 344 patients (97.45%) were nonsmokers; specifically, only six out of 78 patients with NG were smokers. Two hundred and seventy (76.5%) patients had normal BMI or were just overweight, 32 (9%) patients were underweight, and 51 (14.4%) patients had a BMI over 30 (Table 1)

For those with NG, 67 (85.9%) out of 78 patients had no additional endoscopic findings besides NG, and 11 (14.1%) patients had duodenitis on endoscopy; 16 (20.5%) patients had a history of previous *H.pylori* infection and the remaining 62 (79.5%) were new cases; 19 (24.3%) patients received treatment for *H.pylori* before more than 30 days, and the remaining 59 patients (75.6%) were treatment-naïve.

H.pylori was present in 213 patients (60.3%), and 72 patients (33.8%) who were infected with *H.pylori* had NG on endoscopy compared to 141 patients (66.2%) with NNG with *H.pylori* infection. Seventy-two patients (99.3%) out of 72 patients with NG had *H. pylori* infection. NG had a sensitivity of 33.8%, specificity of 95.7%, positive predictive value (PPV) of 92.3%, and negative predictive value (NPV) of 48.7%, with an overall accuracy of 61.1% (Table 2). (*Chi-square test)

Discussion:

Our study reveals a predominance of female patients in both the NG and NNG groups, with 64.9% of patients being female and 35.1% male (p-value < 0.001), resulting in an F: M ratio of 1.84:1. A review of the literature confirms a female predominance among patients with NG. We found that females are more likely to have NG than male patients (17.9% vs. 82.1%) with an F: M ratio of 4.57:1. This may highlight that female gender plays a significant role regarding NG, which was in concordance with other studies from Kuwait and Turkey that showed females are more likely to have NG (12, 13). Most patients with *H.pylori* were young, less than 40 years (251 patients, 71.1%) in both NG (97.4%) and NNG (63.63%) groups, with a stronger association of young age and NG, as almost all patients with NG were less than 40 years of age (76 patients, 97.4%). The correlation between young age and nodular gastropathy was also evident in other research from Korea and Japan (14, 15, 16). The prevalence of NG decreases with age, likely due to a decrease in *H. pylori* infection with aging; this may explain our results of a lower prevalence of NG and *H. pylori* infection in patients over 40 years of age. There is a lower incidence of smoking among patients with NG; the negative association between smoking and NG was statistically significant ($p < 0.001$), as just six patients (7.7%) in the NG group, as well as three patients (1.1%) in the NNG group, were smokers. This can be explained by the lower incidence of *H.pylori* among smoker patients, as only nine patients (2.54%) were smokers. Some studies have documented that the prevalence of *H. pylori* infection is lower in smokers than in nonsmokers (17). After reviewing the literature, there is no precise data about the association between smoking and NG.

Regarding the relationship between body weight and Helicobacter pylori (H.pylori) infection, published papers from Iran (18,19) mentioned that *H.pylori* infection is more common in obese patients. Still, our study, contrary to these papers, showed that most patients with NG (68 patients, 87.2%) had a normal BMI or were only overweight, and only 10 patients (12.8%) were obese. We found no significant association between NG infection and body weight in our study. The association between the marital status of our patients and NG was not significant; 46 patients (58.9%) were single, and 32 patients (41.1%) were married. Upon reviewing the literature, no papers were found that specifically address the relationship between marital status and NG. However, a higher prevalence of *H. Pylori* Has Been Reported among married patients compared to single patients, as noted in papers from China and Iraq (20, 21). There is a strong association between NG and *H. pylori* infection ($p < 0.001$) in this study, as 72 patients (92.3%) with NG were found to have *H. pylori* infection. Just six patients (7.7%) with NG had no *H. pylori* infection. NG is considered a specific sign of *H. pylori* infection, as it has high specificity (95.7%) with a high positive predictive value (PPV) of 92.3%. The prevalence of *H. pylori* in the NG group is significantly higher than in the control group (92.3% vs. 51.3%). These results regarding the association between NG and H. pylori were in line with previous studies from Turkey and Hong Kong (13, 22).

Conclusion:

NG should be considered a strong indicator of H. pylori presence during EGD, particularly in young female patients.

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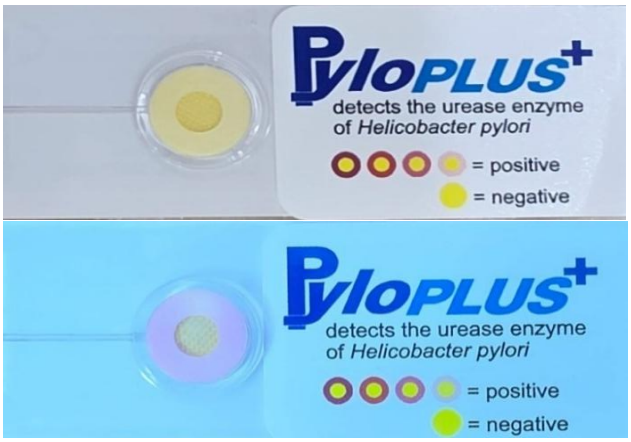

Figure 1: Pyloplus rapid Urease test (RUT), note the change of color of the test ring from yellow (1a) to pink color (1b); pink color indicates a positive test.

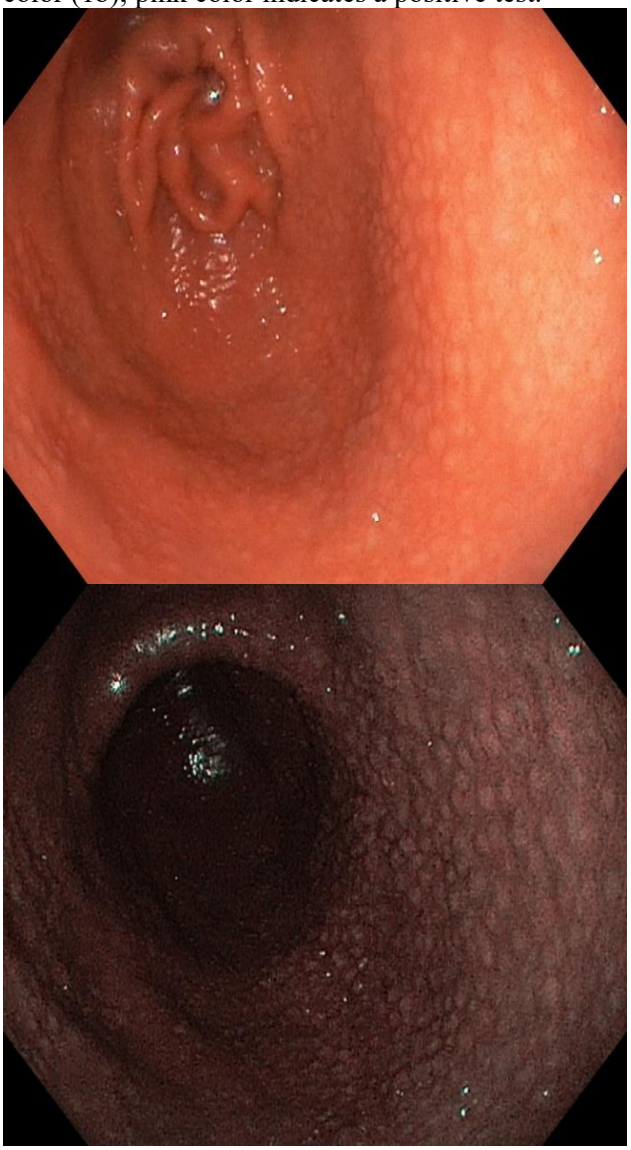

Figure 2: (a) Nodularity of gastric mucosa on white light endoscopy and (b) narrow band imaging (NBI).

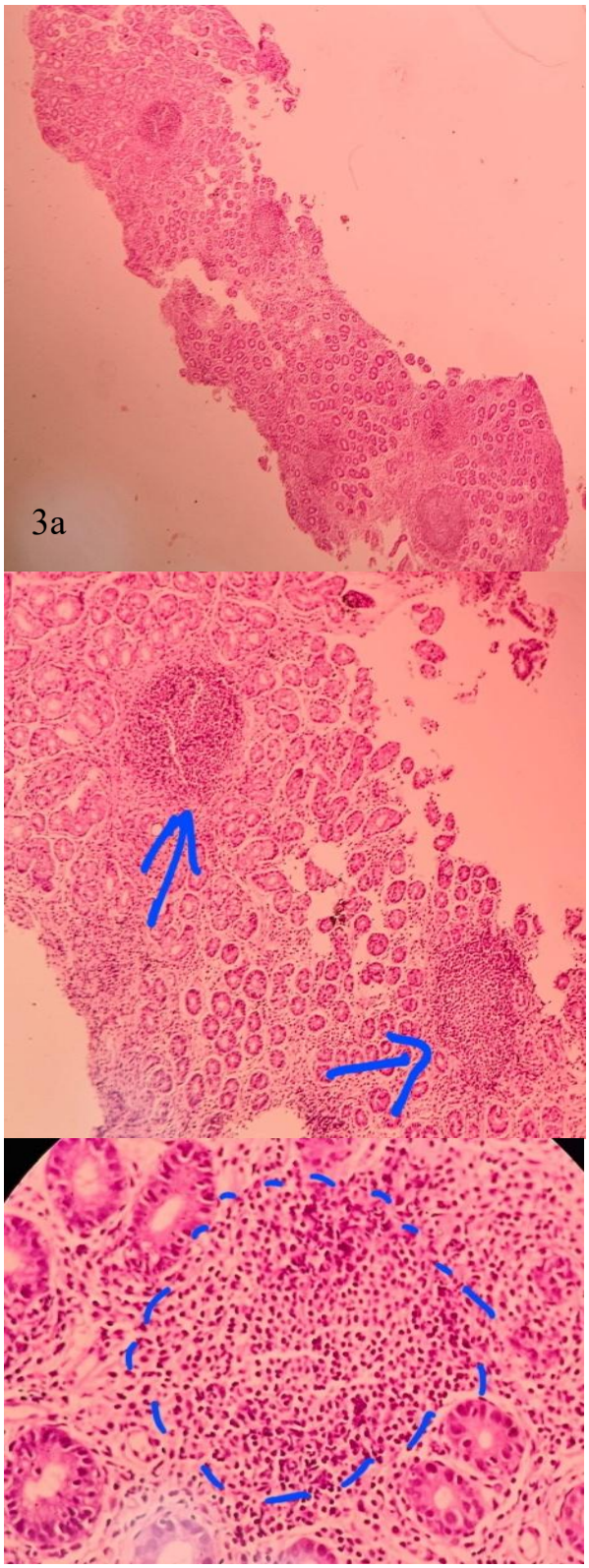

Figure 3: H&E slide: (a) Power 4x section shows gastric mucosal fragment with patchy lymphoid follicles. (b) Power 10x section shows gastric mucosal fragments with two lymphoid follicles (arrowed). (c) The Power 40x section shows a large lymphoid follicle with a pale, reactive germinal center (encircled).

Table 1: Different patients' demographic features in both nodular gastropathy (NG) and non-nodular gastropathy (NNG) groups

Variables		Studied groups		p-value
		NG (n=78)	NNG (n=275)	
		No.(%)	No.(%)	
Age groups in years	<20	28(35.9)	33(12.0)	<0.001*
	20-40	48(61.5)	142(51.6)	
	>40	2(2.6)	100(36.4)	
Sex	Males	14(17.9)	110(40.0)	<0.001*
	Females	64(82.1)	165(60.0)	
Residence	Urban	36(46.2)	116(42.2)	>0.05 *
	Rural	42(53.8)	159(57.8)	
Marital status	Single	46(59.0)	168(61.1)	>0.05 *
	Married	32(41.0)	107(38.9)	
Smoking	Yes	6(7.7)	3(1.1)	<0.001**
	No	72(92.3)	272(98.9)	
BMI	<18	10(12.8)	22(8.0)	>0.05 *
	18-25	36(46.2)	114(41.5)	
	25-30	22(28.2)	98(35.6)	
	≥30	10(12.8)	41(14.9)	

(*Chi square test; **Fisher Exact test).

Table 2: Association between nodular gastropathy (NG) with *H.pylori* infection

H.pylori test	Studied groups		p-value*
	NG (n=78)	NNG (n=275)	
	No. (%)	No. (%)	
Positive	72(92.3)	141(51.3)	p<0.001
Negative	6(7.7)	134(48.7)	

(*Chi square test).