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Original Research Article

Effect of *Helicobacter pylori* eradication on gastric histology and symptom resolution in functional dyspepsia: a preliminary follow-up study

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ABSTRACT

Background: Functional dyspepsia (FD) is a prevalent gastrointestinal condition with a multifactorial origin, in which *Helicobacter pylori* infection may play a contributory role. Although eradication therapy has been shown to offer symptomatic relief in a subset of patients, predictors of response remain inadequately defined. To evaluate the effect of *H. pylori* eradication on gastric histological parameters and symptom resolution in patients with functional dyspepsia and to identify histopathological predictors of treatment response.
Methods: This prospective observational study included 121 adult patients with functional dyspepsia and confirmed *H. pylori* infection. All patients underwent upper gastrointestinal endoscopy and gastric biopsies were obtained before initiating eradication therapy. Biopsy specimens were stained with H&E and Giemsa and histological assessment was performed by a blinded pathologist using the Modified Sydney System. Parameters assessed included chronic inflammation, neutrophilic activity, glandular atrophy, intestinal metaplasia and *H. pylori* density. A composite Sydney score was calculated. Follow-up was conducted at 3 months to assess symptom resolution. Patients were categorized into "Resolved" and "Non-improved" groups based on symptomatic outcomes.
Results: Out of 100 patients enrolled, follow-up data were available for 79. Symptom resolution was observed in 52 patients (51.5%), while 27 (26.7%) reported no improvement. Patients with symptom resolution had significantly higher pre-treatment scores for chronic inflammation (p=0.012), neutrophilic activity (p=0.021), *H. pylori* density (p=0.008) and composite Sydney score (p=0.002). Glandular atrophy (p=0.486) and intestinal metaplasia (p=0.671) showed no significant association with symptomatic improvement.
Conclusions: Symptomatic benefit following *H. pylori* eradication in functional dyspepsia appears to be associated with higher baseline levels of chronic and active gastric inflammation, as well as *H. pylori* density. Histopathological assessment using the Modified Sydney System may help predict treatment response and guide clinical decision-making.

Keywords: Functional dyspepsia, Gastric histopathology, *Helicobacter pylori* eradication, Modified Sydney system, Symptom resolution

INTRODUCTION

Functional dyspepsia (FD) is a prevalent gastrointestinal disorder characterized by chronic or recurrent upper abdominal discomfort without an identifiable structural cause. Its etiology is multifactorial, encompassing gastric motility disturbances, visceral hypersensitivity, psychosocial influences and *Helicobacter pylori* (*H. pylori)* infection.[1,2] Despite extensive research, the role of *H. pylori* in the pathogenesis of FD remains incompletely

understood. The bacterium, a well-known cause of peptic ulcer disease and gastric cancer, has been implicated in low-grade chronic gastritis that may overlap with functional symptoms.[3,4] The current Maastricht VI/Florence consensus supports testing and treating *H. pylori* in FD patients due to modest but significant symptom improvement post-eradication.[5] Several randomized controlled trials and meta-analyses have shown that *H. pylori* eradication can yield symptom relief in a subset of FD patients, although the precise mechanisms and predictors of response remain under investigation.[6,7]

Histopathologically, the modified Sydney system is a widely accepted grading tool for assessing gastritis. It includes parameters such as chronic inflammation, neutrophilic activity, glandular atrophy, intestinal metaplasia and *H. pylori* density.[8] Prior studies have focused on the role of *H. pylori* in modulating these parameters, but limited data exist on their predictive value in symptom resolution among FD patients undergoing eradication therapy.[9,10]

Furthermore, lifestyle and dietary habits, medication use and microbiota variations add to the complexity of FD pathophysiology.[11] Nonetheless, understanding the relationship between histological features of gastric mucosa and treatment outcomes may offer insight into underlying disease mechanisms and help stratify patients for therapy.

Objective

The present study aimed to assess the impact of *H. pylori* eradication on gastric histopathological alterations and the resolution of symptoms in patients with functional dyspepsia. Specifically, it sought to determine whether pre-treatment histological parameters such as chronic inflammation, neutrophilic activity, glandular atrophy, intestinal metaplasia and *H. pylori* density could predict clinical response to eradication therapy.

METHODS

This prospective observational study was conducted in the Department of General Surgery at Bhagwan Mahaveer Jain Hospital, Bengaluru, between March 2015 and February 2016. The primary objective was to evaluate the effect of Helicobacter pylori eradication on gastric histopathology and symptom resolution in patients diagnosed with functional dyspepsia.

Study population

Patients aged 18 years and above presenting with symptoms consistent with functional dyspepsia, based on Rome IV criteria, were considered eligible for inclusion. The dyspeptic symptoms evaluated included postprandial fullness, early satiety, epigastric pain and epigastric burning sensation. Only patients who tested positive for *H. pylori* on gastric biopsy were enrolled.

Patients were excluded if they had a history of prior *H. pylori* eradication therapy, endoscopic or histologic evidence of peptic ulcer disease, malignancy or gastrointestinal bleeding or had used proton pump inhibitors, antibiotics or non-steroidal anti-inflammatory drugs within the preceding four weeks. Those with significant comorbid conditions that could interfere with follow-up or symptom assessment were also excluded. All participants underwent a comprehensive clinical evaluation that included demographic data (age and sex) and dietary history (noting the consumption of spicy foods, tea or coffee). Dyspeptic symptoms were systematically recorded, detailing their presence and specific characteristics. Subsequently, all patients underwent upper gastrointestinal endoscopy. During the procedure, multiple biopsies were obtained from the antrum and body of the stomach.

Biopsy samples were fixed in 10% buffered formalin and stained with hematoxylin and eosin (H&E) as well as Giemsa stains. All slides were independently reviewed by a pathologist who was blinded to clinical outcomes. The histopathological parameters evaluated included chronic inflammation, neutrophilic activity (active inflammation), glandular atrophy, intestinal metaplasia and *H. pylori* density. Each parameter was graded on a 4-point scale (0=absent, 1=mild, 2=moderate, 3=severe) based on the Modified Sydney System. A composite Sydney score was calculated by summing the individual grades for all five parameters. All enrolled patients received standard first-line triple therapy for *H. pylori* eradication, consisting of a proton pump inhibitor (PPI), amoxicillin and clarithromycin administered over 14 days. Treatment adherence was monitored and patients were asked about the occurrence of any adverse effects.

Follow-up was conducted at 4 to 6 weeks following completion of therapy. Symptom resolution was assessed based on patient self-report. No repeat endoscopy was performed routinely. Based on follow-up, patients were categorized into three groups: Resolved (R) if there was complete resolution of symptoms, No Improvement (NI) if symptoms persisted and Incomplete (I) for those who were lost to follow-up or had inadequate outcome data.

Statistical analysis

Quantitative data were expressed as mean±standard deviation (SD). Independent t-tests or Mann–Whitney U tests were used for comparing histological parameters between the R and NI groups, depending on the distribution of the data. Categorical variables, such as the presence or absence of specific symptoms, were analyzed using Chi-square or Fisher's exact tests. Statistical analysis was conducted using appropriate software, with a p value<0.05 considered indicative of statistical significance.

RESULTS

A total of 100 patients diagnosed with functional dyspepsia and confirmed *H. pylori* infection on gastric biopsy were enrolled in the study. The mean age of the study population was 38.2±11.5 years, with a slight female predominance (58% female, 42% male). Dietary history revealed that 65% of patients regularly consumed spicy foods, while 72% reported frequent intake of tea or coffee. The most common presenting symptom was postprandial fullness (81%), followed by early satiety (55%), epigastric pain (47%) and epigastric burning (43%) (Table 1). Of the 100 patients, 52 (51.5%) experienced complete resolution of dyspeptic symptoms following *H. pylori* eradication therapy and were classified into the "Resolved" group. 27 patients (26.7%) had no improvement in symptoms (NI group), while 21 patients (21%) had incomplete or missing follow-up data and were excluded from the outcome analysis (Figure 1).

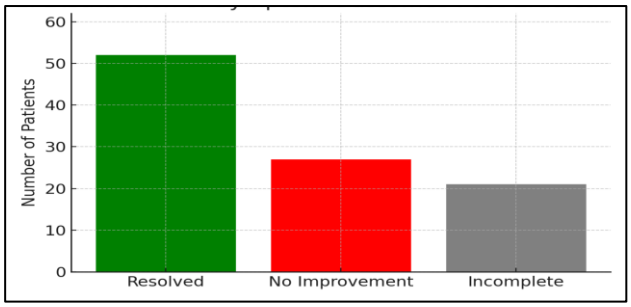

Figure 1: Distribution of symptom outcomes post-eradication therapy.

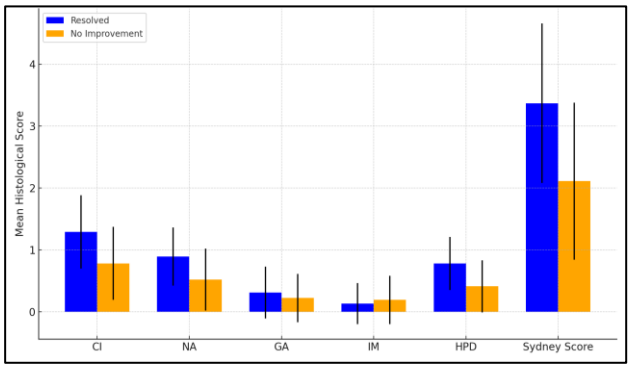

Figure 2: Mean histological scores in resolved vs. non-improved groups.

All patients underwent upper gastrointestinal endoscopy with gastric biopsies prior to the initiation of *Helicobacter pylori* eradication therapy. Histopathological evaluation was conducted using the modified Sydney system, which assesses five key parameters: chronic inflammation (CI), neutrophil activity (NA), glandular atrophy (GA), intestinal metaplasia (IM) and *H. pylori* density (HPD).

The mean pre-treatment histological scores across the study cohort were as follows: chronic inflammation was 1.09±0.65, neutrophil activity was 0.74±0.53, glandular atrophy was 0.28±0.41, intestinal metaplasia was 0.15±0.35 and *H. pylori* density was 0.64±0.46. The overall composite Sydney score averaged 2.91±1.42.

Comparison of histological parameters by outcome

Histological features were compared between the "Resolved" and "No Improvement" groups to evaluate predictive factors for symptom resolution. The results are summarized in Table 2.

Patients who experienced symptom resolution following *Helicobacter pylori* eradication demonstrated significantly higher pre-treatment levels of chronic inflammation (p=0.012), neutrophilic activity (p=0.021), *H. pylori* density (p=0.008) and the overall Sydney score (p=0.002) compared to those who did not improve.

However, no significant differences were observed between the groups in terms of glandular atrophy (p=0.486) or intestinal metaplasia (p=0.671). The Figure 2 visually demonstrates that patients who responded to therapy had significantly higher baseline inflammation and *H. pylori* colonization. Differences in glandular atrophy and metaplasia were minimal between the two groups.

Following eradication therapy, 51.5% of patients reported complete symptom resolution. Patients who responded to treatment exhibited higher levels of chronic inflammation, active (neutrophilic) inflammation and *H. pylori* density prior to therapy. Additionally, the overall modified Sydney score was significantly higher among responders compared to non-responders. In contrast, the presence of glandular atrophy and intestinal metaplasia did not appear to predict treatment response.

Table 1: Baseline demographics and clinical features of the study population (n=100).

Variable	Total
Age (mean±SD)	38.2±11.5 years
Sex	
Male	42 (42%)
Female	58 (58%)
Dietary habits	
Spicy food	65 (65%)
Coffee/Tea intake	72 (72%)

Continued.

Variable	Total
Dyspeptic symptoms	
Postprandial fullness (PPF)	81 (81%)
Early satiety (ES)	55 (55%)
Epigastric pain (EP)	47 (47%)
Epigastric burning (EBS)	43 (43%)

Table 2: Comparison of histopathological scores between outcome groups.

Parameter	Resolved (n=52)	No improvement (n=27)	P value
Chronic inflammation	1.23±0.68	0.84±0.52	0.012
Neutrophil activity	0.87±0.59	0.52±0.41	0.021
Glandular atrophy	0.25±0.38	0.30±0.45	0.486
Intestinal metaplasia	0.14±0.32	0.17±0.39	0.671
***H. pylori* density**	0.81±0.47	0.44±0.35	0.008
Sydney score	3.32±1.54	2.21±1.18	0.002

DISCUSSION

In our cohort of 100 *H. pylori* positive functional dyspepsia patients with follow-up data, 51.5% experienced complete symptom resolution following eradication therapy. Histologically, responders had significantly higher baseline scores of chronic inflammations, neutrophilic activity, *H. pylori* density and total Sydney score compared to non-responders. This suggests that patients with more intense gastric mucosal inflammation may derive greater benefit from *H. pylori* eradication.

These findings are in line with previous studies reporting modest but statistically significant symptom improvement in FD patients' post-eradication. A meta-analysis by Ford et al showed that *H. pylori* eradication resulted in a number needed to treat (NNT) of 14 for symptom relief in FD.[12] Similarly, Zhao et al found sustained benefit at 12-month follow-up in randomized controlled trials.[13] The study supports these findings and adds a histological dimension to predicting treatment response. The observation that glandular atrophy and intestinal metaplasia did not significantly differ between responders and non-responders aligns with the notion that these changes represent more chronic, possibly irreversible alterations that may not correlate with symptom generation.[14,15]

In contrast, active inflammation and *H. pylori* burden may directly influence gastric sensory function and mucosal cytokine profiles, thereby impacting symptomatology.[16] Georgopoulos and Papastergiou noted that advancements in pharmacotherapy, such as the use of vonoprazan-based regimens, have enhanced eradication rates and may influence FD symptom resolution.[1] While our study used conventional triple therapy, emerging regimens may further refine outcomes. Other studies have examined symptom response based on endoscopic appearance or antral gastropathy, with mixed results.[9] However, histology-based prediction has been less commonly explored, making our findings particularly relevant. Importantly, our study excluded patients with structural abnormalities or alarm symptoms, consistent with diagnostic criteria for FD and ensuring a homogenous population.[2,5] The baseline modified Sydney Scores in our cohort showed mild-to-moderate inflammation on average, consistent with previous findings in *H. pylori* infected individuals without ulcers.[8] Although the findings suggest a correlation between baseline histological inflammation and symptom response, it is worth noting that psychological, dietary and neuromotor factors also influence FD. Miftahussurur et al, highlighted the role of dietary intake in exacerbating dyspeptic symptoms, while Koloski et al associated lower physical activity with FD.[6,11] These unmeasured variables could partly account for non-response in patients without significant histological inflammation.

Strengths of our study include standardized histopathological grading using the modified Sydney System and a reasonably sized sample. However, limitations include lack of long-term follow-up, potential confounding by psychosocial factors and absence of a placebo control group.

CONCLUSION

Our data indicate that higher baseline levels of chronic and active gastric inflammation are associated with better symptom resolution following *H. pylori* eradication in functional dyspepsia. This suggests a potential role for histopathology in guiding therapeutic decisions in FD. Further large-scale prospective studies are warranted to validate these findings and explore integration with clinical and psychosocial predictors of treatment response.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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