

Comparison of clinical symptoms after *Helicobacter pylori* eradication in functional dyspepsia patients based on endoscopic view of antral gastropathy

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Abstract

Functional dyspepsia is a common gastric disease that can be associated with *Helicobacter pylori* infection. The aim of this study is to evaluate antral endoscopy of individuals who presented with functional dyspepsia, *H. pylori* infection status and the effects of eradication therapy on the symptoms. Following the diagnosis of dyspepsia as per Rome III criteria, 260 individuals who were eligible for the study underwent upper gastrointestinal endoscopy and were divided into four groups of 65 according to the endoscopic view, grades I, II, III and IV (negative). Stool antigen test was also performed for all patients to identify *H. pylori* infection. The early signs of dyspepsia were assessed by a standard questionnaire. In all groups, omeprazole, amoxicillin, clarithromycin and metronidazole were used for eradication treatment, and 1 month after the treatment, a faecal antigen test was repeated to evaluate the eradication of *H. pylori*. There was no statistically significant difference between the groups in terms of clinical symptoms before treatment. The highest response to eradication treatment was seen in individuals with antral gastropathy grade III (66.2%) and the lowest response was in patients without antral gastropathy Grade IV (32.3%). This difference was statistically significant. There was no statistically significant relationship between the participants in terms of family history, age, gender and response to treatment. Eradicating *H. pylori* reduces the symptoms of dyspepsia. The response of eradication therapy was greatest among the patients with grade III antral gastropathy.

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Introduction

Dyspepsia is one of the most common causes of referral to gastroenterology clinics, accounting for 40% of these visits [1]. According to Rome III criteria, dyspepsia is defined as pain or discomfort in the upper abdomen that has at least one of the following symptoms: early satiety, epigastric pain and burning sensation [2]. The onset of these symptoms should be at least 6

months before the time of diagnosis [3]. Dyspepsia is defined as both structural and functional dyspepsia [4]. Structural dyspepsia is associated with peptic ulcer, gastric cancer, oesophagitis and other structural abnormalities in the upper gastrointestinal tract. However, 50%–90% of patients suffer from functional dyspepsia or non-ulcer dyspepsia [5].

The prevalence of dyspepsia in the general population is 20%–40%, most of which are functional [6]. This rate is about 25% in the Asian population [7]. The prevalence of functional dyspepsia after endoscopy has been reported to be 12%–15% [5]. The annual incidence of dyspepsia in different communities is about 25%. Incidence varies according to age, sex, race and geographical area and most people experience it at least once in their lifetime [8]. On average, the incidence of dyspepsia is less than 1% within 3 months of the symptoms and more than 8.2% in 1 year following symptom appearance [9].

Dyspepsia reduces the quality of life and imposes a significant economic burden on the health system [10]. The exact pathophysiology of this disorder is unknown [11]; however, delayed bowel emptying, gastric dysfunction, increased sensitivity to gastric distention, *Helicobacter pylori* infection, altered metabolism of fats and duodenal acid, abnormal duodenal movement or central nervous system dysfunction, and psychological disorders are some reported causes [12]. *Helicobacter pylori* infection is one of the common causes of dyspepsia [13]. This infection is one of the most common chronic bacterial infections in humans and is present all over the world and in all age groups [14]. It is estimated that 50% of the world's population is infected with this microbe [15]. The high rate of *H. pylori* infection in patients with functional dyspepsia, which has been reported in some articles as 40%–70%, has led researchers to believe that *H. pylori* causes chronic gastritis and is one of the leading causes of functional dyspepsia [16]. A meta-analysis and systematic review of randomized control trials concluded that individual assessment is required for *H. pylori* eradication therapy among individuals with dyspepsia [13].

The aim of this study was to evaluate the endoscopic findings from individuals presenting with functional dyspepsia, the role of *H. pylori* infection in the disease and the effects of eradication therapy on the symptoms of functional dyspepsia.

Materials and methods

In this study, individuals referred to Shahid Rahimi Hospital, Khorramabad for upper gastrointestinal endoscopy from June 2019 to November 2019 were included. These individuals presented with symptomatic dyspepsia according to Roman III criteria. A detailed explanation of the study was given to all individuals and written consent for participation was obtained from all participants. The symptoms of dyspepsia evaluated included upper abdominal pain, bloating, fullness, chest pain or heartburn, acid reflux or sour-bitter taste, early satiety or lack of appetite, burping, nausea and epigastric pain during sleep. Individuals using histamine blockers or proton-pump inhibitors, or with anaemia, jaundice, suspicion of upper gastrointestinal bleeding, weight loss of more than 3 kg and those who did not consent to participate in the study were excluded.

All individuals underwent endoscopy and those with structural gastrointestinal disorders such as erosive lesions in the oesophagus or previously undiagnosed peptic ulcer disease were excluded. The gastric antrum was carefully examined by a physician for the appearance of antral gastropathy. Antral gastropathy that can be seen macroscopically was identified by a physician and was divided into three grades: grade I, erythema

with or without focal antrum atrophy; grade II, erythema with or without focal antrum atrophy with gastric trunk involvement; and grade III, grade I or grade II with nodularity or only nodularity. A sample was obtained from the gastric antrum for histological examination. Stool antigen test was also performed for all participants to identify those with *H. pylori* infection. The participants were divided into four groups: group I: *H. pylori*-positive patients with endoscopic view of grade I gastropathy; group II: *H. pylori*-positive patients with endoscopic view of antral grade II gastropathy; group III: *H. pylori*-positive patients with endoscopic view of antral gastropathy grade III; and group IV: *H. pylori*-positive patients with endoscopic antral gastropathy.

In all four groups, eradication treatment was prescribed by a physician for 10 days. This treatment comprised omeprazole 20 mg (twice daily), amoxicillin 1 g (twice daily), clarithromycin 500 mg (twice daily) and metronidazole 500 mg (twice daily). Four weeks after eradication treatment, participants from all groups were referred to a specialized laboratory for faecal antigen testing. For this test, patients must: not have taken antibiotics or bismuth for 4 weeks before the test, not be taking proton-pump inhibitors (such as omeprazole), antacids and histamine receptor inhibitors (such as ranitidine, famotidine and cimetidine) for at least 1 week before the test, and not be smoking an hour before the test [17].

Finally, participants in groups I, II, III and IV with the results of their eradication test were referred to the physician 4 weeks after the treatment. At this stage, the clinical symptoms of all four groups were evaluated by a standard questionnaire and the groups were compared in terms of clinical symptoms before and after treatment. Participants were re-evaluated 6 months after treatment and those with recurrent clinical symptoms were considered as treatment failure.

Data were computerized and statistically analysed using SPSS v22 (IBM, Armonk, NY, USA). Descriptive statistics was used to present the data and χ^2 -test was used to compare the parameters. A p value < 0.05 was considered statistically significant.

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>.

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Results

In this study, 260 individuals with dyspepsia were studied. Mean age of participants was 29.43 ± 6.46 years in group I, 31.8 ± 7.01

years in group II, 33.5 ± 6.7 years in group III and 32.21 ± 5.80 years in group IV, the group without antral gastropathy (Table I).

A χ^2 test was used to assess the gender distribution between the studied groups. As shown in Table I, the frequency of women with functional dyspepsia, whether with or without antral gastropathy, was higher than of men, especially for grade III (73.8% versus 26.2%) and this difference was statistically significant (p 0.001). There was a significant relationship between gender and the type of endoscopic view of patients (p < 0.05).

Analysis of variance showed that there was a significant difference between the study groups in terms of age (p 0.004). To examine the differences between the groups, post-hoc Tukey test was performed, which showed that the age difference between antral gastropathy grade I and grade II was significant (p 0.002), but this difference was not significant among the other groups (Fig. 1).

The χ^2 test was used to evaluate the differences in the symptoms of dyspepsia among the groups. The most common complaints among the patients in all four groups were abdominal fullness, early satiety and heartburn. However, the differences in the symptoms among the four groups were not statistically significant (p 0.851).

The χ^2 test was also used to investigate the correlation among family history within the groups. In all four study groups, a negative family history of dyspepsia was more common. There was no statistically significant relationship between family history and the endoscopic findings (p 0.811).

The highest response to treatment after eradication of *H. pylori* was seen in group III (66.2%) and the lowest response was found in the group without antral endoscopic view gastropathy (group IV, 32.3%) (Table 2). This difference was statistically significant (p 0.001). There was a significant correlation between the response to treatment and the type of endoscopic view (gastropathy) in patients (p < 0.05).

The response to eradication of *H. pylori* in groups with endoscopic antral gastropathy based on different age groups showed that the response to treatment was higher for all age groups in group III compared with groups I and II; the highest response to treatment was among participants aged over 35 years (72.4%). In group I, the highest response to treatment was in patients over 35 years old (57.1%) and in group II, the highest response was among patients aged 25 years and younger (62.5%). Age was not associated with the treatment response in the other groups (p > 0.05).

The highest treatment response was in women in groups I and III (Table 3) (72.9% and 45.5%, respectively), but this was not

TABLE I. Comparison of mean age between study groups

| | Antral view of gastropathy grade I | Antral view of gastropathy grade II | Antral view of gastropathy grade III | No antral gastropathy | p value |
|-----|------------------------------------|-------------------------------------|--------------------------------------|-----------------------|---------|
| Age | 29.43 ± 6.46 | 31.8 ± 7.01 | 33.5 ± 6.7 | 32.21 ± 5.80 | 0.004 |

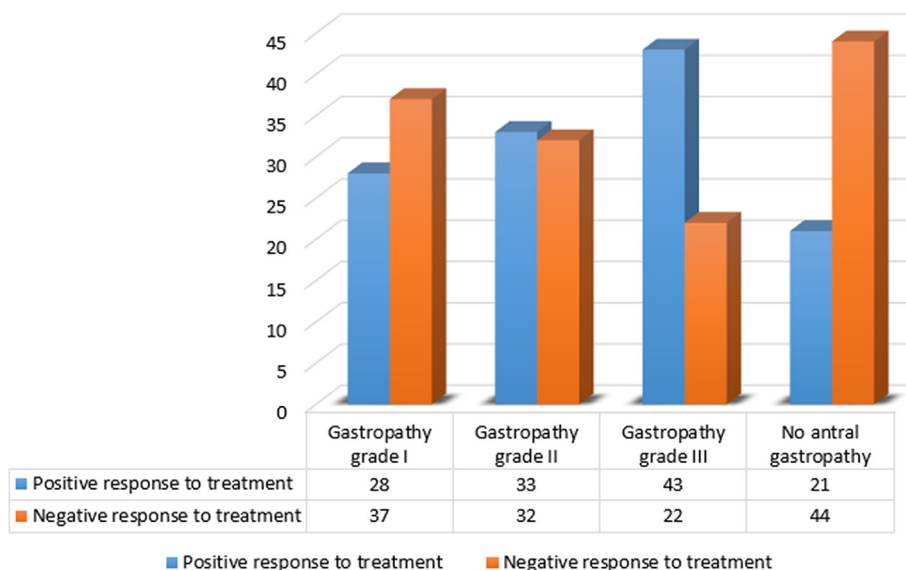


FIG. 1. Diagram of response to treatment after eradication of *Helicobacter pylori* in the study groups.

TABLE 2. Frequency distribution of response to treatment after eradication of *Helicobacter pylori* in the study groups

| Response to treatment | Groups | | | | p value |
|-----------------------|------------------------------------|-------------------------------------|--------------------------------------|-----------------------|---------|
| | Antral view of gastropathy grade I | Antral view of gastropathy grade II | Antral view of gastropathy grade III | No antral gastropathy | |
| Positive | 28 (43.1) | 33 (50.8) | 43 (66.2) | 21 (32.3) | 0.001 |
| Negative | 37 (56.9) | 32 (49.2) | 22 (33.8) | 44 (67.7) | |
| Total | 65 (100) | 65 (100) | 65 (100) | 65 (100) | |

TABLE 3. Frequency distribution by sex of response to treatment after eradication of *Helicobacter pylori* in groups with antral gastropathy

| Groups | Sex | Response to treatment | | | p value |
|--------------------------------------|--------|-----------------------|-----------|-----------|---------|
| | | Positive | Negative | Total | |
| Antral view of gastropathy grade I | Male | 13 (40.6) | 19 (59.4) | 32 (100) | 0.443 |
| | Female | 15 (45.5) | 18 (54.5) | 33 (100) | |
| | Total | 28 (43.1) | 37 (56.9) | 65 (100) | |
| Antral view of gastropathy grade II | Male | 20 (64.5) | 11 (35.5) | 31 (100) | 0.03 |
| | Female | 13 (38.2) | 21 (61.8) | 34 (100) | |
| | Total | 33 (50.8) | 32 (49.2) | 65 (100) | |
| Antral view of gastropathy grade III | Male | 8 (47.1) | 9 (52.9) | 17 (100) | 0.052 |
| | Female | 35 (72.9) | 13 (27.1) | 48 (100) | |
| | Total | 43 (66.2) | 22 (33.8) | 65 (100) | |
| Total | Male | 41 (51.2) | 39 (48.8) | 80 (100) | 0.367 |
| | Female | 63 (54.8) | 52 (42.5) | 115 (100) | |
| | Total | 104 (53.4) | 91 (46.7) | 195 (100) | |

statistically significant ($p > 0.05$). In group II, the highest response to treatment was in men (64.5%), which was statistically significant ($p 0.03$). The treatment response was not statistically significant among the two gender groups in group II ($p 0.367$).

Among participants with Grade I, II and III antral gastropathy, the response to treatment was greater in those with a family history of dyspepsia (Table 4). However, treatment was not significantly associated with family history ($p 0.18$).

Discussion

The results showed that the frequency of functional dyspepsia, whether with or without endoscopic view of antral gastropathy, was higher in women than men. There was no statistically significant relationship between family history and the type of endoscopic view observed. The highest response to treatment after eradication of *H. pylori* was in the group with grade III antral gastropathy and the lowest response was in group IV, without antral gastropathy. This difference was statistically significant. It can be said that there is a significant relationship between response to treatment and the type of endoscopic view observed.

Overall, 107 (41%) participants were men and 153 (59%) were women. In a study by Ünüsoy Aksu *et al.* [18], most of the

TABLE 4. Frequency distribution of response to treatment after eradication of *Helicobacter pylori* in groups with antral gastropathy in endoscopy based on family history

| Groups | Family history | Response to treatment | | | p value |
|--------------------------------------|----------------|-----------------------|-----------|-----------|---------|
| | | Positive | Negative | Total | |
| Antral view of gastropathy grade I | Male | 12 (44.4) | 15 (55.6) | 32 (100) | 0.526 |
| | Female | 16 (42.1) | 22 (57.9) | 38 (100) | |
| | Total | 28 (43.1) | 37 (56.9) | 65 (100) | |
| Antral view of gastropathy grade II | Male | 18 (58.1) | 13 (41.9) | 31 (100) | 0.191 |
| | Female | 15 (44.1) | 19 (55.9) | 34 (100) | |
| | Total | 33 (50.8) | 32 (49.2) | 65 (100) | |
| Antral view of gastropathy grade III | Male | 8 (47.1) | 9 (52.9) | 17 (100) | 0.052 |
| | Female | 35 (72.9) | 13 (27.1) | 48 (100) | |
| | Total | 43 (66.2) | 22 (33.8) | 65 (100) | |
| Total | Male | 41 (51.2) | 39 (48.8) | 80 (100) | 0.367 |
| | Female | 63 (54.8) | 52 (42.5) | 115 (100) | |
| | Total | 104 (53.4) | 91 (46.7) | 195 (100) | |

participants with dyspepsia were female (70%) [19]. Other studies have shown that there is no difference between men and women in the incidence of dyspepsia [20]. In our study, the highest frequency of grade III gastropathy was in women.

There was no statistically significant difference in the incidence of positive family history between the groups. Among 260 participants in this study, 148 (56.9%) had no family history of functional dyspepsia. Guariso *et al.* [21] reported that positive family history of functional dyspepsia and/or *H. pylori* infection is associated with positive endoscopic findings. In the study, Hyams *et al.* showed a positive correlation between functional dysplasia and a family history of irritable bowel syndrome [22]. Genetic factors might be associated with the incidence of functional dyspepsia. However, our study does not support such findings.

In this study, there was no statistically significant difference between the early symptoms of the disease between the groups. This indicates that the degree of gastropathy has no effect on the symptoms of the disease. In a study by Ünüsoy Aksu *et al.* [18], conducted on children presenting with dyspepsia, reported that dyspepsia score (based on the symptoms) was not significantly associated with *H. pylori* status. Overall, following the eradication therapy in individuals with *H. pylori* infection, their dyspepsia score improved. The most common pre-treatment symptoms were epigastric pain, heartburn and nausea in a study by Lan *et al.* [23].

There was a significant relationship between eradication of *H. pylori* and grade III antral gastropathy where the response of the treatment was also highest in this group. In a study evaluating gastric atrophy and symptoms of dyspepsia, it was found that gastric atrophy was more common in *H. pylori*-positive individuals. Therefore, eradicating *H. pylori* can greatly reduce the symptoms of gastropathy and dyspepsia [24]. Although a number of studies have indicated that *H. pylori* infection increases the risk of dyspepsia, the results of our study indicated that the grade of antral gastropathy in dyspeptic patients did not vary with *H. pylori* status. Recent studies of postinfection gastrointestinal dyspepsia suggest that postinfection immunity and inflammatory status may increase the symptoms of functional dyspepsia. In general, the cause of dyspepsia can be inflammation caused by *H. pylori* [25].

The results of our study indicated that the symptoms of dyspepsia and the severity of gastropathy are not significantly associated, but the response to treatment in antral gastropathy grade III was better compared with grades I and II. Few studies have been performed to evaluate the severity of gastropathy with symptoms of dyspepsia. In the study by Turkkan et al., it has been seen that patients with higher degrees of inflammatory diseases of the corpus and antrum have more severe symptoms of dyspepsia [26]. In two other studies, similar results were observed [27]. However, similar to the results of this study, there is no relationship between the severity of gastritis and the symptoms of dyspepsia [28,29].

Our study also reported that the response to treatment among the three groups with gastropathy was seen in 104 of the 195 patients. In a study by Mazzoleni et al., 94 out of 192 patients responded to treatment, compared with 72 out of 197 in the control group [30], and in the Lan et al. study, 36 of 84 patients in the treatment group responded to treatment, compared with 19 of 89 in the control group [31]. Overall, the symptoms of dyspepsia were lower in patients receiving *H. pylori* eradication treatment compared with the control group.

The response to *H. pylori* eradication treatment can vary with ethnicity [32], which could explain the differences in response to treatment in this study. In a meta-analysis, eradication of *H. pylori* in patients with dyspepsia improved symptoms 38.1 times compared with patients in the placebo group [33]. However, Gisbert et al. reported that eradicating *H. pylori* does not significantly improve symptoms in individuals with functional dyspepsia [34]. Ang et al. compared *H. pylori* eradication treatment and prokinetic treatment in individuals with functional dyspepsia and found that symptoms improved within 2 years in two-thirds of individuals in both groups [35].

It has been argued for many years that the management of dyspepsia should include awareness of the status of *H. pylori*, and

further diagnostic tests, including endoscopy, are necessary to assess an individual's gastropathy status [18].

Conclusion

In this study the management of dyspepsia according to the endoscopic view of antral gastropathy is described. The results show that eradicating *H. pylori* reduces the symptoms of dyspepsia. Reduction in symptoms was more noticeable in the group with grade III gastropathy on endoscopic view. The response to treatment based on endoscopic view of antral gastropathy varied but there was no difference in the response to treatment in terms of family history, gender and age.

Conflict of interest

The authors report no conflicts of interest.

Ethical approval and consent to participate

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Consent to participate for the under 16 year olds was given by a parent or legal guardian.

Availability of data and material

Data sharing is not applicable to this article as no data sets were generated or analysed during the current study.

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Authors' contribution

Saleh Azadbakht and Parisa Rahmani conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. Salehe Azadbakht designed the data collection instruments, collected data, carried out the initial analyses, and reviewed and revised the manuscript. Alireza Esmaili coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content.

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