

Migraine and gastric disorders: Are they associated?

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Background: Migraine is a common disorder which affects quality of life. There has been an increasing interest for discovering the association of gastrointestinal (GI) disorders with migraine during past years. This study aims to evaluate the association of *Helicobacter pylori* contamination, gastroesophageal reflux disease (GERD), gastric ulcer (GU), and duodenal ulcer (DU) with migraine in patients who underwent upper GI endoscopy due to refractory dyspepsia. **Materials and Methods:** In this observational cross-sectional study, 341 dyspeptic patients who underwent upper GI endoscopy in Shahid Beheshti Hospital, Qom, Iran, included during 2016–2018. A checklist was used for collecting demographics, symptoms, and results from endoscopy and *H. pylori* testing. Diagnosis of migraine was made according to the International Headache Society criteria in patients who had headache. Data were analyzed using Chi-square and independent samples *t*-tests in SPSS 16 (SPSS Inc., Chicago, IL, USA) with $P < 0.05$ as significance level. **Results:** Among 341 patients, 141 (41.3%) were male and 200 (58.7%) were female. 149 (43.7%) patients were diagnosed with migraine, from which 48 (32.2%) were male and 101 (67.8%) were female. The observed difference in migraine prevalence among male and female was statistically significant ($P = 0.003$). 198 (58.06%) patients were *H. pylori* contaminated, among these 138 (69.7%) suffered from migraine. Among 143 *H. pylori*-negative patients, there were 11 (7.7%) migraineurs. The difference in the prevalence of migraine among *H. pylori* positive and negative patients was significant. *H. pylori* and GERD were associated with migraine with $P < 0.001$. Patients with DU were more commonly suffering from migraine ($P = 0.001$). The association in patients with GU was not statistically significant ($P = 0.863$). **Conclusion:** Migraine might be associated with GERD, *H. pylori* infection, and DU, and the treatment of the underlying GI disorder may control headaches.

Key words: Gastrointestinal diseases, headache disorders, *Helicobacter pylori*, migraine, peptic ulcer

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INTRODUCTION

Among primary headache syndromes, migraine is the most common complication with a prevalence of 8.6% and 17.5% in American males and females, respectively. The overall prevalence is estimated to be 14% in the Iranian population.^[1]

Migraine is characterized by recurrent episodes of usually unilateral headache with pulsatile quality, which may accompany nausea, vomiting, photophobia,

and phonophobia. Attacks may be triggered by diet, hormones, sensory stimuli (e.g., strong light, odors, and sounds), stress, and changes in environment or habits. Due to the chronic nature of the disease, it can affect the quality of life and interfere with daily activities.

Many theories explain the pathophysiology of migraine headaches. One of the mechanisms is known as sensitization, which is due to an increase in neuronal responsiveness to stimuli. It can be responsible for many symptoms including worsening of the pain

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following cough, sudden movement of the head or bending, hyperalgesia defined as an increased sensitivity to a normally painful stimuli, and allodynia defined as pain due to a stimuli that is not normally noxious.^[2,3]

Another mechanism involved in migraine pathogenesis is related to serotonin levels. Migraine is known as a chronic low serotonin syndrome, but the serotonin synthesis in the brain significantly increases during migraine attacks.^[4]

Many gastrointestinal (GI) disorders, including dyspepsia, constipation, inflammatory bowel syndrome, celiac disease, and *Helicobacter pylori* infection, are associated with primary headache syndromes, particularly migraine.^[5-7]

According to some literature, dyspepsia, which is a common GI disorder with different etiologies, and *H. pylori* infection are associated with migraine headaches. Some studies reported that dyspepsia was more common among migraineurs than the general population. There is a growing interest to evaluate the association between migraine headaches and *H. pylori* infection since 2002. Despite numerous studies, the results are controversial and the association of migraine with *H. pylori* infection and dyspepsia is not completely understood yet.^[8-12]

With respect to high prevalence of both disorders, dyspepsia and migraine, the current study aimed at clarifying the association of migraine headaches with GI findings in dyspeptic patients undergoing upper GI endoscopy due to refractory symptoms in a 21-month period in Qom, Iran.

MATERIALS AND METHODS

The current monocentric, observational, cross-sectional study conducted at Gastroenterology and Hepatology Disease Research Center of Qom University of Medical Sciences aimed at determining the association of *H. pylori* infection, gastroesophageal reflux disease (GERD), and peptic ulcer disease with migraine in patients undergoing upper GI endoscopy in Shahid Beheshti Hospital, Qom, Iran.

The current study was conducted on 341 patients with symptoms of refractory dyspepsia undergoing upper GI endoscopy from 2016 to 2018. Patients taking antibiotics or proton pump inhibitor (PPI) drugs within the past 2 weeks were excluded.

A checklist was used to collect data including patient's demographics, symptoms, findings of upper GI endoscopy, and the result of *H. pylori* infection testing. In case of a positive history of headache, a questionnaire to diagnose migraine according to the International Headache Society (IHS) guidelines was filled. All endoscopies were performed using an Olympus® cv-180 endoscope. Rapid urease test (RUT) was implicated to diagnose *H. pylori* infection with respect to its sensitivity. Diagnosis of gastric ulcer (GU) and duodenal ulcer (DU) was made based on the opinion of gastroenterologist performing the endoscopy.

Data were analyzed with SPSS 16 (SPSS Inc., Chicago, IL, USA) using descriptive statistics including frequency, mean, and standard deviation to interpret the findings. Chi-square test was used to compare two groups based on sex, family history, and GI disorders. Moreover, the independent samples *t*-test was used to compare two groups based on age and body mass index (BMI). *P* < 0.05 was considered statistically significant.

The protocol of the current study was approved by the Ethics Committee of Qom University of Medical Sciences, Qom, Iran, (ethical code: IR.MUQ.REC.1395.22).

RESULTS

A total of 341 patients were included within a 21-month period from June 2016 to March 2018. Of which, 141 (41.3%) patients were male and 200 (58.7%) female. Table 1 summarizes patients' demographics.

Evaluation of headache

Among the participants, 146 (42.8%) had a positive family history of migraine headaches. According to the questionnaire, 149 patients (43.7%) fulfilled the IHS criteria

Table 1: The association of patient's demographics with migraine and *Helicobacter pylori* contamination

	Migraine		<i>P</i>	<i>Helicobacter pylori</i>		<i>P</i>
	Positive	Negative		Positive	Negative	
Sex						
Male	48	93	0.003*	81	60	0.846*
Female	101	99		117	83	
Family history of headache						
Positive	97	49	<0.001*	105	41	<0.001*
Negative	52	143		93	102	
Age (years)	42.4±11.9	44.8±16.3	0.131 [§]	43.9±13.7	42.8±15.3	0.487 [§]
BMI (kg/m ²)	26.5±4.3	25.9±4.7	0.226 [§]	25.7±5.1	26.3±4.9	0.277 [§]

*Chi-square test; [§]Independent samples *t*-test. BMI=Body mass index

for migraine diagnosis, of which 48 (32.2%) were male and 101 (67.8%) female. The mean age of this group was 42.4 ± 11.9 years and the mean BMI was 26.5 ± 4.3 kg/m². These values were 44.8 ± 16.3 years and 25.9 ± 4.7 , respectively, for nonmigraineurs. The higher prevalence of migraine among female was statistically significant ($P = 0.003$). The difference in the mean age and BMI between the migraineurs and nonmigraineurs was not significant.

None of the migraineurs were using nonsteroidal anti-inflammatory drugs (NSAIDs) to relieve pain during attacks. Table 2 summarizes the features of the headache among migraineurs.

Gastrointestinal findings

The results of RUT on gastric biopsy specimens revealed that 198 (58.06%) patients were infected with *H. pylori*, of which 81 (40.9%) were male and 117 (59.1%) female. There was no significant difference in the prevalence of *H. pylori* infection between males and females.

Among the patients with *H. pylori* infection, 138 (69.7%) had migraine and 60 (30.3%) had no headache; the difference in the frequencies was statistically significant ($P < 0.001$). Evaluation of the association between endoscopic findings and *H. pylori* infection revealed an association between DU and *H. pylori* infection ($P < 0.001$), but GU had no significant relationship with infection ($P = 0.472$). A total of 109 patients were diagnosed with GERD, of which 78 (71.56%) had migraine as well; therefore, there was an association between migraine and GERD symptoms ($P < 0.001$). Table 3 summarizes the correlation between migraine and GI disorders.

Statistical analysis revealed a significant relationship between family history of migraine and the presence of the disease. Among endoscopic findings, DU had a significant association with migraine ($P = 0.001$), but GU showed no significant relationship with migraine ($P = 0.863$).

Based on multiple logistic regression, the family history of migraine was the most important variables that remained in the model (odds ratio = 5.49, confidence interval 95%: 3.34–9.01; $P > 0.001$). However, age, sex, and BMI were excluded from model and have not a significant effect.

DISCUSSION

Some previous studies showed that many GI diseases were related to primary headache syndromes including migraine, to such an extent that Noghani *et al.* conducted a narrative review study entitled “Gastrointestinal Headache.”^[13]

The results of the current study revealed a significant association between *H. pylori* infection and migraine. *H.*

Table 2: Severity and duration of headaches

Characteristic of the headache	Mean±SD
Duration* (hours)	8.4±12.7
History of disease** (years)	3.7±4.2
Severity*** (pain score 1–10)	4.3±3.9
Interfering with daily activity (days per month)	0.4±0.8

*Duration of each migraine attack; **Determines for how many years they have been suffering from migraine; ***Determines severity of headache according to patient's scoring in a 1–10 scale

Table 3: Association of migraine with gastroesophageal reflux disease, *Helicobacter pylori* contamination and peptic ulcer disease

	Migraine		P
	Positive	Negative	
GERD			
Positive	78	31	<0.001
Negative	71	161	
<i>Helicobacter pylori</i>			
Positive	138	60	<0.001
Negative	11	132	
Duodenal ulcer			
Positive	37	21	0.001
Negative	112	171	
Gastric ulcer			
Positive	10	12	0.863
Negative	139	180	

GERD=Gastroesophageal reflux disease

pylori infection was approved by RUT with respect to its sensitivity and cost-effectiveness.

Some previous studies showed a correlation of *H. pylori* infection with migraine headaches. Gasbarrini *et al.* demonstrated the association of *H. pylori* infection with migraine and concluded that *H. pylori* eradication may lead to improvement in headaches.^[14,15] Faraji *et al.* reported the efficacy of *H. pylori* eradication in the management of migraine headaches in a double-blind, controlled, clinical trial. These findings support the results of the current study.^[16]

H. pylori produces platelet activating factor, which results in releasing serotonin from platelets. Previous studies demonstrated the elevation of serotonin level during migraine attacks in the affected patients. This mechanism may be the underlying pathophysiology that explains the prevalence of *H. pylori* infection among patients with migraine.^[8-10]

With respect to aforementioned results, it may be reasonable to check migraineurs for *H. pylori* infection routinely by noninvasive means and eradicate positive cases to prevent migraine attacks.

GERD, a common upper GI complaint defined as reflux of the gastric contents into the esophagus leading to mucosal

damage, was diagnosed in 78 (52%) of 149 migraineurs and 31 (16%) of 192 nonmigraineurs. There was a significant difference between frequencies as well as a significant association between migraine and GERD ($P < 0.001$).

In the Head-HUNT study, Aamodt *et al.*^[17] reported that GERD was the most common complication among 43,000 participants. They also reported that headache was more prevalent among patients with reflux. In another study, Katić *et al.*^[18] evaluated the prevalence of GERD among 1800 patients with migraine and found out that about half of the migraineurs had GERD, heartburn, or related symptoms. The latter patients also experienced more severe headaches than the ones with no complaint of reflux.

Mavromichalis demonstrated the association of GI inflammation with migraine and declared that treatment of GI complications leads to improvement of headache.^[7] Another study by Meucci *et al.*^[6] revealed that migraine was more common among dyspeptic patients than the control group. However, in the current study, upper GI endoscopy was normal in 90% of the cases.

The results of the current study revealed that DU was significantly more prevalent among migraineurs. This difference was not significant among patients diagnosed with GU in upper GI endoscopy. As already mentioned, none of the participants took NSAIDs to relieve pain; therefore, NSAIDs could not be the underlying etiology for peptic ulcer diseases.

It is evident that *H. pylori* infection is associated with DU, but not GUs. Most of the patients presenting DU with a negative history of taking NSAIDs have *H. pylori* infection. Besides, the infection occurs before DU, and *H. pylori* eradication prevents relapse of the ulcer.

Pathogenesis of DU is an increase in acid secretion due to elevated gastrin level along with gastric metaplasia caused by excessive acid exposure. Metaplasia usually occurs when the luminal pH is < 2.5 .

H. pylori can induce elevation of acid secretion and reduce bicarbonate secretion, which leads to a decrease in luminal pH. Besides, *H. pylori* infection weakens the mucosa in sites of gastric metaplasia and makes the mucosa more susceptible to acid secretion.

Because DU and *H. pylori* infection, which are both accompanied by a high gastric acidity situation, are associated with migraine, it can be hypothesized that a low gastric pH can trigger migraine, and acid suppression treatment with PPI drugs may reduce severity and frequency of attacks.

On the other hand, sleep disorders are more prevalent among patients with DU. The typical pain of DU is triggered when acid secrets in the absence of a food buffer and when sleeping, from 11 p.m. to 2 a.m. With respect to this fact that sleep disorders can trigger migraine attacks, another hypothesis to explain the association of DU with migraine is sleep disorder.^[19]

CONCLUSION

According to the comparison between the results of the current study and those of previous similar ones, and with regard to the association of dyspepsia and *H. pylori* infection with migraine headache, it can be concluded that evaluation of *H. pylori* infection in patients with migraine could be reasonable. Besides, treatment of underlying GI disorders may help relieve headaches. With respect to the design of the current study, only the association of these disorders could be clarified. Assessment of the effect of peptic ulcer treatment and acid suppression therapy on the sleep quality and the intensity and frequency of headache attacks needs further interventional controlled studies. Besides, the current study was monocentric; multicentric case-control studies can have more conclusive results in this regard.

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Conflicts of interest

There are no conflicts of interest.

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