RESEARCH ARTICLE

Merve Pozlu Cifci[1]
Ozden Gokdemir[2]
Olgu Aygün[3]
Ismail Cifci[4]
A. Dilek Guldal[5]

[1] Ege University Faculty of Medicine, Izmir, Türkiye
[2] Izmir University of Economics, Faculty of Medicine, Department of Family Medicine, Izmir, Türkiye
[3] İzmir Provıncıal Dırectorate of Health-Bozyaka Educatıon and Research Hospıtal Department of Family Medicine, Izmir, Türkiye
[4] Esenyalı Family Health Center, İzmir, Türkiye
[5] Dokuz Eylül University, Department of Family Medicine, Izmir, Türkiye

Corresponding Author:
Ozden Gokdemir
mail: gokdemirozden@gmail.com

Received: 03.10.2023
Acceptance: 29.11.2024
DOI: 10.18521/ktd.1370882

Konuralp Medical Journal
e-ISSN1309–3878
konuralptipdergi@duzce.edu.tr
konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

The Frequency of Gastroesophageal Reflux Disease (GERD) in Migraineurs and the Impact of GERD Treatment on Migraine Attacks

ABSTRACT

Objective: To determine the frequency of gastroesophageal reflux disease (GERD) in migraine patients and investigate the impact of adherence to gastroesophageal reflux treatment on migraine attack frequency.

Method: A total of 757 people aged 18-45 years who applied to the Dokuz Eylul University (DEU) Neurology-Headache Clinic and the DEU Family Health Centers and met the inclusion criteria were included in the study. Exclusion criteria were pregnancy, cancer or alarming findings, and any mental disability that would prevent understanding of the questionnaire. The Migraine Diagnostic Questionnaire, including International Headache Society (IHS) criteria, was used to diagnose migraine, the Gastroesophageal Reflux Disease Questionnaire (GERDQ) to diagnose GERD, and the Modified Morisky Scale to assess medication compliance. SPSS 22 package was used for statistical analysis. Chi-square, t-test and ANOVA were used for statistical evaluation of the data, and $p<0.05$ was considered significant.

Results: Of the 757 people who participated in the study, 428 patients were diagnosed with migraine and followed up in the neurology outpatient clinic. Of the 329 patients who applied for family health centers, 122 were diagnosed with migraine and 108 with non-migraine headaches. 99 did not complain of headache. When the GERDQ scores of the patients participating in the study were evaluated, there were 183 people (33.3%) with a GERDQ score of 8 and above among the migraineurs, 19 people (17.6%) with non-migraine headaches and 8 people (8.1%) without headaches. The GERDQ reflux score of migraineurs was found to be higher than in the other groups and this level was statistically significant ($p<0.001$). When the migraine attack frequency of migraine patients treated for GERD was evaluated, no significant relationship was found between treatment adherence and migraine attack frequency.

Conclusions: The incidence of GERD in patients with migraine was found to be higher than in patients without migraine, and the compliance of these patients with treatment was found to be lower. It may be useful to ask patients with migraine about GERD when they come to the outpatient clinic and to support their motivation for treatment.

Keywords: GERD, Migraine, Medication Adherence.

Migren Hastalarında Gastroözofageal Reflü Hastalığı (GÖRH) Sıklığı ve GÖRH Tedavisinin Migren Atakları Üzerindeki Etkisi

ÖZET

Amaç: Migren hastalarında gastroözofageal reflü hastalığı (GÖRH) sıklığını belirlemek ve GÖRH tedavisine uyumun migren atak sıklığı üzerindeki etkisini araştırmak.

Yöntem: Dokuz Eylül Üniversitesi (DEÜ) Nöroloji-Baş Ağrısı Kliniği ve DEÜ Aile Sağlığı Merkezlerine başvuran ve dahil etme kriterlerini karşılayan 18-45 yaş arası toplam 757 kişi çalışmaya dahil edildi. Dışlama kriterleri gebelik, kanser, alarm bulguları ve anketin anlaşılmasını engelleyecek herhangi bir zihinsel engeldi. Migreni teşhis etmek için Uluslararası Baş Ağrısı Derneği (IHS) kriterlerini içeren Migren Tanı Anketi, GÖRH' yi teşhis etmek için Gastroözofageal Reflü Hastalığı Anketi (GERDQ) ve ilaç uyumunu değerlendirmek için Modifiye Morisky Ölçeği kullanıldı. İstatistiksel analiz için SPSS 22 paketi kullanıldı. Verilerin istatistiksel değerlendirilmesinde ki-kare, t-testi ve ANOVA kullanıldı ve $p<0,05$ anlamlı kabul edildi.

Bulgular: Çalışmaya katılan 757 kişiden 428'i migren tanısı almış ve nöroloji polikliniğinde takip ediliyordu. Aile sağlığı merkezlerine başvuran 329 hastadan 122'si migren tanısı almış ve 108'i migren dışı baş ağrısı tanısı almıştı. 99'unun baş ağrısı şikâyeti yoktu. Çalışmaya katılan hastaların GERDQ skorları değerlendirildiğinde migren tanısı olanlarda GERDQ skoru 8 ve üzeri olan 183 kişi (%33,3), migren dışı baş ağrısı olan 19 kişi (%17,6) ve baş ağrısı olmayan 8 kişi (%8,1) vardı. Migren tanısı olanlarda GERDQ reflü skorunun diğer gruplara göre yüksek olduğu ve bu düzeyin istatistiksel olarak anlamlı olduğu bulundu ($p<0,001$). GÖRH tedavisi alan migren hastalarında tedaviye uyumun migren atak sıklığı ile anlamlı bir ilişkisinin olmadığı görüldü.

Sonuç: Migren tanısı olan hastalarda GÖRH insidansı migreni olmayan hastalara göre daha yüksek bulunmuş ve bu hastaların tedaviye uyumunun daha düşük olduğu görülmüştür. Migrenli hastalara poliklinik başvurularında GÖRH varlığı araştırılması ve tedavi motivasyonlarının desteklenmesi faydalı olabilir.

Anahtar Kelimeler: GÖRH, Migren, İlaç Uyumu.

INTRODUCTION

Migraine is described as a neurological disorder characterized by hyperexcitability of brain networks, sometimes due to metabolic imbalances (like magnesium deficiency) or genetic predispositions. It often involves central and peripheral nervous system dysfunction, and its comorbidities can include various metabolic, cardiovascular, and gastrointestinal disorders, such as GERD. GERD is a condition where stomach acid frequently flows back into the esophagus, causing irritation. It can be exacerbated by increased nitric oxide levels, which may also play a role in migraine pathophysiology by relaxing the lower esophageal sphincter, making reflux more likely. When examining the pathophysiology of both migraine and gastroesophageal reflux disease, some studies have found that migraines in patients are associated with brain hyperexcitability (due to from magnesium deficiency) and ion channel abnormalities due to chromosome 18 abnormalities. In addition, some studies have reported hypomagnesemia following the use of proton pump inhibitors in patients with gastroesophageal reflux patients. Plasma nitrate, nitrite, and total nitrite levels have been found to be high in both periods (interictal and attack period) in both aura-free and aura-present migraineurs. Nitric oxide (NO) at low concentrations is effective in maintaining the mucosal integrity of the stomach. Increased NO levels relax the lower esophageal sphincter. Impairment of the lower esophageal integrity also plays a role in the pathogenesis of reflux (1-5).

Although both of these conditions are frequently encountered in clinical practice, there is limited research in the literature on this topic. One study compared migraine patients, tension-type headache patients, and a control group to evaluate the incidence of gastroesophageal reflux disease, finding a significantly higher incidence of gastroesophageal reflux in migraine patients (6-9).,

The aim of this research is to determine the incidence of gastroesophageal reflux disease in migraineurs and to investigate the effect of adherence to gastroesophageal reflux treatment on migraine attack frequency.

MATERIAL AND METHODS

The study was designed as cross-sectional descriptive research. The necessary permissions were obtained from the Dokuz Eylul University Ethics Committee. It was conducted among individuals aged 18-45 years who presented to the Department of Family Medicine, the Department of Neurology Headache Clinic, and the Family Health Centre.

Individuals aged between 18 and 45 were included in the study, as the most common age range for migraine is reported to be 30 to 50 years in international studies and 30 to 39 years in Turkey.

The sample size was calculated to be minimum 632, with a minimum of 316 people in each group, assuming a 10% difference between the two groups, a 5% margin of error, 80% power, and a 95% confidence level.

The study was completed with a total of 757 individuals who applied to the Headache Clinic and Family Health Centers and who met the inclusion criteria, which were defined as being between 18 and 45 years of age, willing to participate in the study, and having no physical or mental problems that would interfere with understanding and answering the questionnaire. Exclusion criteria were pregnancy, dysphagia, odynophagia, iron deficiency anemia, weight loss, hematemesis or any condition that would make it difficult to understand and respond to the questionnaire.

Participants were verbally informed about the study before enrolment. The researcher then took anthropometric measurements (height and weight) and, using a face-to-face interview technique, completed a sociodemographic questionnaire (including age, education, alcohol consumption, smoking habits, and exercise status) and a health-related information form.

Participants completed the Migraine Diagnosis Questionnaire, which includes the criteria of the International Headache Society (IHS) criteria for migraines, the GERDQ questionnaire, and the Modified Morisky Scale for medication adherence.

Data Collection Tools

Sociodemographic questionnaire: The researcher prepared a questionnaire that included the following information about the participant: age, sex, weight, height, education level, exercise status in the past six months, and questions about smoking and alcohol consumption.

Migraine diagnosis questionnaire: A 15-item questionnaire was administered based on the criteria for migraine diagnosis according to the International Classification of Headache Disorders (ICHD-III) by the International Headache Society. The questionnaire items cover a range of topics including the age of onset, frequency, duration, headache characteristics, location, intensity, triggers, and associated symptoms (10).

GERDQ: Gastroesophageal Reflux Disease Questionnaire: The GERDQ is a patient-centered self-administered questionnaire used for the diagnosis and management of gastroesophageal reflux disease (GERD). It aims to differentiate between patients with frequent and occasional symptoms, and to guide treatment accordingly. It also allows the effects of treatment on patients' symptoms and daily life to be monitored.

The GERDQ questionnaire scores the frequency of six items experienced in the past seven days (heartburn, regurgitation, dyspepsia, nausea, need for non-prescription medication, and sleep

disturbance). Using a four-point scale ranging from zero to three, zero indicates zero days in a week, one indicates one day in a week, two indicates two days in a week, and three indicates 4-7 days in a week. Two items of the GERDQ questionnaire assess the impact of symptoms on the patient's daily life (need for non-prescription medication and sleep disturbance). The remaining four items (heartburn, regurgitation, need for non-prescription medication, and sleep disturbance) are used to monitor and evaluate the response to treatment.

During the administration of the questionnaire, a score of 2 or 3 on any item indicates the need to reassess the treatment (11). In the GERDQ questionnaire, complaints experienced in the past week are assessed, and scores are assigned for each item, which are then summed to obtain a total score [0-18]. Additionally, the sum of scores from the 5th and 6th questions provides an impact score [0-6]. An impact score of 3 or higher indicates a significant impact of reflux. The validity and reliability studies for the GERDQ were conducted by Hançerlioğlu and Bor, and it is recognized as a practical tool for assessing reflux symptoms in the Turkish population (12).

The Modified Morisky Medication Adherence Scale: The Modified Morisky Medication Adherence Scale is a 6-item scale with response options of "yes" and "no." In the participant's responses, in the 2nd and 5th questions, a score of 1 is assigned for "yes", and 0 for "no." In the 1st, 3rd, 4th, and 6th questions, a score of 0 is given for "yes," and 1 for "no." The total score obtained from the 1st, 2nd, and 6th questions indicates low motivation if 0 or 1, and high motivation if >1. The total score obtained from the 3rd, 4th, and 5th questions indicates low knowledge if 0 or 1, and high knowledge if >1.

The Turkish validity and reliability of the Modified Morisky Medication Adherence Scale were conducted by Bekir Vural and colleagues (13,14).

RESULTS

A total of 757 people were included in the study, consisting of whom 481 (63.5%) were women and 276 (36.5%) were men. The age range of the participants was between 18 and 45 years, with a mean age of 32.67 (std=6.61) for females and 32.48 (std=6.22) for males. Regarding the participants' educational status of the participants, 33.8% had completed high school education, while 29.2% had completed university or higher education (Table 1).

Regarding health care utilization, after being diagnosed with migraine, 43.5% of the patients went to the family health center (FHC) and 56.5% to the headache clinic (Table 1).

Among our participants: 35.7% smoked and 22.5% consumed alcohol, while 31.3% reported regular exercise in the previous six months. The mean body mass index (BMI) was 24.96 kg/m2.

Table 1. Demographic characteristics of the participants

Demographic characteristics of the participants	**Total (n=757)**	
	Number (n)	Percentage (%)
Age Groups		
18-20	23	3.0
21-25	93	12.3
26-30	158	20.9
31-35	227	30.0
36-40	161	21.3
41-45	95	12.5
Sex		
Women	481	63.5
Men	276	36.5
Education Status		
Illiterate	7	0.9
Literate	20	2.6
Primary School	89	11.8
Secondary School	164	21.7
High School	256	33.8
University and higher	221	29.2
Application places of patients		
Family Health Center	329	43.5
Headache treatment clinic	428	56.5

50.6% of individuals were classified as underweight or normal weight, while 9.6% were classified as obese or morbidly obese. Of the 757 participants, 193 (29.3%) reported having a good/regular sleep pattern and 124 (18.8%) reported early morning awakening/tiredness (Table 2).

Table 2. Typical behaviors of the participants

Typical behaviors of the participants	**Total (n=757)**	
	Number (n)	%
Tobacco usage		
Yes	270	35.7
No	487	64.3
Alcohol usage		
Yes	170	22.5
No	587	77.5
Exercise		
Yes	237	31.3
No	520	68.7
Classification according to body mass index		
Underweight and Normal Weight	383	50.6
Overweight	301	39.8
Obese and Morbid Obese	73	9.6
Sleep behaviors		
Good/regular	193	29.3
Insomnia/difficulty falling asleep	105	16.0
Frequent waking / difficulty falling back asleep	114	17.3
Early morning waking / exhaustion after waking	124	18.8
Difficulty waking up in the morning/ excessive sleepiness	122	18.5

The most commonly reported chronic conditions were as follows 4.8% had hypothyroidism, 3% had hypertension, 2.6% had diabetes mellitus, 2.5% had asthma and 0.9% had allergies (Table 3).

Table 3. The chronic disease status of the participants

The chronic disease status of the participants	**Total (n=757)**	
	Number (n)	%
Chronic diseases		
+	157	20.7
-	600	79.3
Top 5 Chronic Diseases		
Hypothyroid	37	4.8
Hypertension	23	3.0
Diabetes Mellitus	20	2.6
Asthma	19	2.5
Allergy	7	0.9

Of the 757 participants in the study, 428 were diagnosed with migraine and were patients in the neurological headache clinic. Of the patients attending the FHC, 122 were diagnosed with migraine and 108 with non-migraine headaches. 99 had no headache complaints. Of the 658 respondents with headache complaints, 404 (61.4%) had sought medical advice. The most common diagnoses were migraine in 274 (41.6%) and tension-type headache in 27 (4.1%) (Table 4).

When asked about the frequency of headache episodes, 193 people (29.3%) reported having headaches once a month, 192 (29.2%) 1-3 days a week and 183 (27.8%) every other week (Table 4).

Regarding the type of headache onset, 212 (32.2%) reported sudden onset and 446 (67.8%) reported gradual onset and progression. Regarding the characteristics of the headache, 596 individuals (90.6%) reported throbbing pain, 114 individuals (17.3%) reported dull pain and 213 (32.4%) reported a feeling of heaviness associated with the headache (Table 4).

The most common pattern of headache onset was irregular, reported by 298 respondents (45.3%). When asked about the duration of the headache, 369 (56.1%) reported that it lasted from 4 to 12 hours and 112 (17%) that it lasted from 12 to 24 hours. The intensity was severe in 321 people (48.8%) and moderate in 243 people (36.9%) (Table 4).

Aura symptoms were present in 293 people (44.5%) with headaches. The most common accompanying symptoms of headache were sensitivity to sound, reported by 617 individuals (93.8%), sensitivity to light, by 596 individuals (90.6%), and nausea, by 559 individuals (85%) (Table 4).

The location of the headache was unilateral in 532 patients (80.9%). The most common headache onset was in the afternoon, reported by 295 patients (44.8%). Regarding the use of medication for headache, 470 patients (71.4%) reported the use of analgesics and 172 (26.1%) reported the use of headache prophylaxis (Table 4).

Of the patients with headaches, 293 had aura symptoms. These symptoms began before the headache in 150 (51.2%), were visual in 233 (79.5%) and lasted between 5 and 20 minutes in 173 (59%). Of the 431 female headache sufferers, 223 (51.7%) reported an association between their headache and menstruation. When the relationship between gender and headache type was evaluated, the number of women in the headache groups was statistically significantly higher than in the non-headache group ($p=0.13$). Looking at mean age, the mean age of migraineurs was 33.68 years, non-migraineurs 29.28 years and non-headaches 30.25 years ($p<0.001$).

The proportion of participants in each category with a GERDQ score of 8 or higher was as follows: 183 (33.3%) in migraineurs, 19 (17.6%) in non-migraineurs and 8 (8.1%) in non-headaches. Migraineurs had higher GERDQ reflux scores, and this increase was statistically significant compared with both migraineurs and non-headaches ($p<0.001$) (Table 5).

Table 4. Headache characteristics of the participating patients

Headache characteristics of the participants	Total (n=658)	
	Number (n)	Percentage (%)
Age of headache onset		
5-15	212	32.2
16-25	340	51.7
26-35	96	14.6
36-45	10	1.5
Headache-related medical consultations		
Yes	404	61.4
No	254	38.6
Frequency of headaches		
Everyday	17	2.6
4-6 day/week	55	8.4
1-3 day/week	192	29.2
Once every two weeks	183	27.8
Once a month	193	29.3
Once every two months	17	2.6
A few days per year	1	0.2
Onset pattern of headaches		
Suddenly	212	32.2
Slow progressing	446	67.8
Characteristics of headaches		
Throbbing	596	90.6
Dull	114	17.3
Exploding	69	10.5
Heaviness	213	32.4
Pulsating	95	14.4
Tingling, burning, numbness	49	7.4
Features of headaches		
Always	187	28.4
Episodic (coming in attacks)	173	26.3
Intermittent (occurring at irregular intervals)	298	45.3
Duration of headache		
Less than 1 hour	33	5.0
1-3,59 hours	60	9.1
4-11,59 hours	369	56.1
12-23,59 hours	112	17.0
More than 24 hours	84	12.8
Severity of headache		
Mild	22	3.3
Moderate	243	36.9
Severe	321	48.8
Very severe	72	10.9
Headache with aura		
Yes	293	44.5
No	365	55.5
Symptoms accompanying headache		
Nausea	559	85.0
Vomiting	237	36.0
Light sensitivity	596	90.6
Sound sensitivity	617	93.8
Odor sensitivity	410	62.3
Loss of appetite	442	67.2
Increase in pain with physical activity	550	83.6
The site of the headache		
Unilateral	532	80.9
Bilateral	71	10.8
Sometimes unilateral, sometimes bilateral	47	7.1
Others	8	1.2
Onset time of headache during the day		
Morning	146	22.2
Afternoon	295	44.8
Evening	198	30.1
During sleeping	19	2.9
Use of painkillers for headache		
Yes	470	71.4
No	188	28.6
Prophylactic treatment for headache		
Yes	172	26.1
No	486	73.9

Headache patients were assessed using the GERDQ and scored according to their impact score. An evaluation of those who scored 8 or more on the GERDQ showed that 31 (16.9%) of the migraineurs were significantly affected by reflux disease, 4 (21.1%) of the non-migraineurs and 2 (25%) of the non-headaches. However, this difference was not statistically significant ($p = 0.774$).

The headache patients were asked about their use of medication for stomach complaints. The Modified Morisky Treatment Adherence Scale (MMTAS) was used to assess the use of proton pump inhibitors for gastric symptoms in 226 patients. Among patients with migraine headaches, 69.5% (n=132) were found to be poorly motivated to adhere to treatment, a significantly higher proportion than both migraine-free patients and those without headaches ($p=0.017$). Among those with non-migraine headaches, 50% (n=18) had low motivation to adhere to treatment (Table 6).

Table 5. The relationship between headache and GERDQ

The relationship between headache and GERDQ	Evaluation based on GERDQ score (n=757)				p value
	0-7 point		≥8 points		
	n	%	n	%	
Headache type					
Migraine headache	367	66.7	183	33.3	
Non-migraine headache	89	82.4	19	17.6	**<0.001**
No headache	91	91.9	8	8.1	

GERDQ: Gastroesophageal Reflux Disease Questionnaire

Table 6. Evaluation of those receiving treatment for GERD according to the MMMAS

Headache type	Evaluation according to The Modified Morisky Medication Adherence Scale				p value
	Poor medication adherence		High medication adherence		
	n	%	n	%	
Migraine headache	132	69.5	58	30.5	
Non-migraine headache	18	50	18	50	**0.017**
No headache	5	41.7	7	58.3	

MMMAS: Morisky Medication Adherence Scale

DISCUSSION

According to the literature, migraine is described as a recurrent primary headache disorder characterized by unilateral, pulsating pain of moderate to severe intensity, with pathophysiological mechanisms that are not fully understood. In our study, when examining the pain characteristics of patients, we found them to be consistent with the literature. There is no definitive laboratory test for diagnosing migraines. The diagnosis is based on the criteria established by the International Headache Society (IHS), which we also adhered to in our study (10,15).

Epidemiological studies conducted in our country have found that the prevalence of migraine is 16.4%. In general, 21.8% of women and 10.9% of men are affected. Migraines can occur at any age, but they are most seen between the ages of 30 and 50 (16,19). The prevalence of migraine varies by age and sex, with higher rates observed in males before adolescence, but a marked increase in females after puberty. The prevalence continues to rise until the age of 40 and then begins to decline. The most common onset of migraines is in the second and third decades of life. People who experience their first migraine attack after the age of 50 represent only about 2% of cases. All studies show a higher incidence of migraine in women, with a male-to-female ratio of 1:2-3. While the exact reason for this is unknown, it is thought to be related to female sex hormones. The higher proportion of female participants in our study may be because migraines tend to be more severe in women, leading to a higher rate of hospital admissions. Possible reasons for this imbalance include the effects of sex hormones, genetic factors, differential exposure to environmental stressors, and differences in pain perception and response to stress (20,21).

In one study, the incidence of gastroesophageal reflux disease (GERD) was reported to be about 27% in the migraine group and 10% in the control group. Gastric ulcers were also found to be more common in the migraine and tension-type headache groups compared to the control group (11.9% in the migraine group, 11.9% in the tension-type headache group, and 5.65% in the control group) (22). In our study, the prevalence of GERD was found to be 33.3% in migraine patients, 17.6% in the non-migraine group, and 8.1% in the group without headaches. Another clinic-based study found no significant difference in the prevalence of gastritis and peptic ulcers between migraineurs and non-migraineurs. However, like our study, they reported a higher frequency of gastroesophageal reflux disease (GERD) in migraineurs compared with those without migraines (42% in migraineurs and 18% in those without migraines) (23). While the exact mechanism underlying the increased incidence of GERD in migraine patients is not fully understood, it is known that these two conditions share common pathophysiological mechanisms. Autonomic nervous system dysfunction has been associated with both types of headaches, particularly migraine, and with gastrointestinal disorders (24-26). Therefore, it is likely that autonomic nervous system dysfunction plays a role in the pathogenesis of these disorders and may explain the co-occurrence of gastroesophageal reflux disease

(GERD) and migraine. Additionally, patients with dyspeptic symptoms have been reported to have abnormal visceral mechanics, sensory functions, and vagal function, and migraine is also associated with visceral nerve dysfunction (27).

Both epidemiological data and pathophysiological evaluations have reported an association between migraine and gastrointestinal disorders. These studies suggest that gastrointestinal symptoms in migraine patients may be a consequence of migraine attacks. The cross-sectional design of this study, however, does not allow us to determine whether migraine attacks cause gastrointestinal symptoms or if other common risk factors contribute to the relationship between these two conditions. Gastrointestinal symptoms may also be a side effect of medications used to treat migraines. Opioid analgesics can cause constipation and nausea, and various gastrointestinal complaints are known to be common side effects of non-steroidal anti-inflammatory drugs (NSAIDs). Additionally, psychological factors may have a common basis for both conditions, as both are strongly associated with anxiety and depression (28). In our study, no significant association was found between the use of analgesics and GERD. One possible explanation for this is that some patients using NSAIDs also use proton pump inhibitors (PPIs), which may delay the onset of NSAID-induced gastric erosion or suppress symptoms. This may explain the lack of significance in the incidence of reflux disease among patients using NSAIDs in our study.

A review of the current literature reveals a lack of studies specifically investigating the impact of gastroesophageal reflux disease (GERD) treatment on the frequency of migraine attacks. In our study, no significant effect of GERD treatment on migraine attack frequency was observed. A potential explanation for this finding could be that proton pump inhibitor (PPI) therapy in GERD patients provides symptomatic relief rather than a definitive cure in many cases. Additionally, a significant proportion of patients may use PPIs intermittently, primarily during symptom exacerbation, rather than following a consistent and prescribed treatment regimen. Further research is required to elucidate this issue. In analyzing other data, we found that according to the Modified Morisky Medication Adherence Scale, medication adherence motivation in the migraine group was significantly lower compared to the group without headaches. To our knowledge, no other study has examined the relationship between treatment adherence in gastroesophageal reflux disease and the frequency of migraine attacks. While previous studies have explored the relationship between reflux and migraines, which is also included in our study, this study's strength lies in its evaluation of treatment adherence (8,29,30). Another strength is that the data were collected through face-to-face interviews conducted by a physician.

However, several limitations must be considered. The number of individuals with non-migraine headaches or without headache symptoms was lower than that of migraineurs, which might have contributed to the differing observed rates of reflux disease. Additionally, the inclusion of patients undergoing long-term PPI therapy, who experienced a reduction or disappearance of symptoms, could have influenced the reported prevalence of reflux disease. There may also have been some data loss due to inconsistent PPI usage, as some patients may not have been able to provide clear information. When designing the study, it might have been more appropriate to include patients in the migraine group, the other headache group, and a control group without headaches, provided that they had not taken proton pump inhibitors or similar reflux treatments for at least the last 6-8 weeks. Especially in the control group, treatments for conditions like gastritis or peptic ulcers may have masked GERD symptoms, potentially reducing the prevalence in this group.

CONCLUSION

Our study results indicate that gastroesophageal reflux disease (GERD) is significantly more prevalent among migraineurs compared to those with non-migraine headaches or without headache symptoms. Consistent with the literature, migraine prevalence was significantly higher among women than men in our participant group.

When assessing the impact of headaches and the results of the GERDQ questionnaire regarding the influence of GERD, no significant differences were found in impact scores between migraineurs, individuals with non-migraine headaches, and those without headache symptoms. Among GERD-treated patients, a significant association was observed between poor medication adherence and the presence of migraine headaches. However, no significant link was found between medication knowledge and migraine. Although these findings are intriguing, they require further research for validation.

No significant association was found between medication adherence and migraine attack frequency in GERD-treated patients. These findings provide valuable insights into the relationship between migraine, GERD, medication adherence, and the impact of GERD on migraine sufferers. However, more research is necessary to confirm and expand upon these findings. To better understand the relationship between migraine and GERD, future studies should explore the impact of the duration and severity of PPI treatment on migraine attack frequency. Additionally, intervention studies aimed at improving medication adherence and awareness could be beneficial.

It would also be useful to investigate the effectiveness of different treatment strategies in managing migraine attacks during GERD therapy.

Acknowledgement: All the authors would like to thank Simon Edward Mumford, MSc. TESOL, Writing Centre Advisor at the Izmir University of Economics for his great contribution in editing the language of the manuscript.

REFERENCES

1. Altamura C, Corbelli I, de Tommaso M, Di Lorenzo C, Di Lorenzo G, Di Renzo A, et al. Pathophysiological bases of comorbidity in migraine. Front Hum Neurosci. 2021;15:1-12.
2. Domitrz I, Cegielska J. Magnesium as an important factor in the pathogenesis and treatment of migraine-From theory to practice. Nutrients. 2022;14(5):1-16.
3. Gallai V, Sarchielli P, Albeni A, Floridi A. Nitrites, prostaglandins, and trigeminal vasoactive peptides in internal jugular venous blood in migraine patients during spontaneous attacks. Neurol Sci. 2000;21.
4. Goadsby PJ, Karsan N. Molecular mechanisms of migraine: Nitric oxide synthase and neuropeptides. Int J Mol Sci. 2023;24(15):11993.
5. Mauskop A, Varughese J. Why all migraine patients should be treated with magnesium. J Neural Transm. 2012;119(5):575-9.
6. Cámara-Lemarroy CR, Rodriguez-Gutierrez R, Monreal-Robles R, Marfil-Rivera A. Gastrointestinal disorders associated with migraine: A comprehensive review. World J Gastroenterol. 2016;22(36):8149-60.
7. Ponce J, Garrigues V, Agréus L, Tabaglio E, Gschwantler M, Guallar E, et al. Structured management strategy based on the Gastro-oesophageal Reflux Disease (GERD) Questionnaire (GerdQ) vs. usual primary care for GERD: Pooled analysis of five cluster-randomised European studies. Int J Clin Pract. 2012;66(9):897-905.
8. Shen Z, Bian Y, Huang Y, Zhou W, Chen H, Zhou X, et al. Migraine and gastroesophageal reflux disease: disentangling the complex connection with depression as a mediator. PLOS ONE. 2024;19(7)
9. Hormati A, Bian Y, Huang Y, Zhou W, Chen H, Zhou X, et al. Higher risk of migraines among patients with GERD. PLOS ONE. 2023;18(5).
10. Headache Classification Committee of the International Headache Society (IHS). The international classification of headache disorders, 3rd edition (beta version). Cephalalgia. 2013;33(9):629-808.
11. Jones R, Junghard O, Dent J, Wiklund I. Development of the GerdQ, a tool for the diagnosis and management of gastro-oesophageal reflux disease in primary care. Aliment Pharmacol Ther. 2009;30(10):1030-8.
12. Hançerlioğlu S, Bor S. Turkish validation of the reflux disease questionnaire. J Gastrointest Liver Dis. 2021;30(2):193-7.
13. Vural UB, Özgür U, Acar T, Topsever DP, Filiz DTM. Modifiye Morisky Ölçeğinin Türkçe Geçerlilik Güvenilirlik Çalışması. Turkish Fam Physician. 2012;4:17-20.
14. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. J Clin Hypertens (Greenwich). 2008;10(5):348-54.
15. Pescador Ruschel MA, De Jesus O. Migraine headache. NCBI Bookshelf [Internet]. National Library of Medicine; 2023. [cited:2024 Nov 13] Available from: https://www.ncbi.nlm.nih.gov/books/NBK582491/
16. Bıçakçı Ş, Bozdemir N, Over F, Saatçi E, Sarıca Y. Prevalence of migraine diagnosis using ID Migraine among university students in southern Turkey. J Headache Pain. 2008;9:159-63.
17. Wacogne C, Lacoste JP, Guillibert E, Hugues FC, Le Jeunne C. Stress, anxiety, depression and migraine. J Headache Pain. 2003;4:451-5.
18. Ertas M, Baykan B, Orhan EK, Zarifoglu M, Karli N, Saip S, et al. One-year prevalence and the impact of migraine and tension-type headache in Turkey: A nationwide home-based study in adults. J Headache Pain. 2012;13:147-57.
19. Aamodt AH, Stovner LJ, Hagen K, Zwart JA. Comorbidity of headache and gastrointestinal complaints. The Head-HUNT Study. Cephalalgia. 2008;28(2):144-51.
20. Al-Hassany L, Haas J, Piccininni M, Kurth T, Maassen Van Den Brink A, Rohmann JL. Giving researchers a headache – Sex and gender differences in migraine. Front Neurol. 2020;11:1-16.
21. Chalmer MA, Kogelman LJA, Callesen I, Christensen CG, Techlo TR, Møller PL, et al. Sex differences in clinical characteristics of migraine and its burden: A population-based study. Eur J Neurol. 2023;30(7):1774-84.
22. Lee SH, Lee JJ, Kwon Y, Kim JH, Sohn JH. Clinical implications of associations between headache and gastrointestinal disorders: A study using the Hallym smart clinical data warehouse. Front Neurol. 2017;8:1-8.
23. Peşkersoy C, Peker Ş, Kaya A, Ünalp A, Gökay N. Evaluation of the relationship between migraine disorder and oral comorbidities: Multicenter randomized clinical trial. Turk J Med Sci. 2016;46(3):712-8.
24. Peroutka SJ. What turns on a migraine? A systematic review of migraine precipitating factors. Curr Pain Headache Rep. 2014;18(10):454.
25. Heitkemper M, Jarrett M, Cain KC, Burr R, Levy RL, Feld A, et al. Autonomic nervous system function in women with irritable bowel syndrome. Dig Dis Sci. 2001;46(6):1276-84.

26. Shechter A, Stewart WF, Silberstein SD, Lipton RB. Migraine and autonomic nervous system function: A population-based, case-control study. Neurology. 2002;58(3):422-7.
27. Kurth T, Holtmann G, Neufang-Hüber J, Gerken G, Diener HC. Prevalence of unexplained upper abdominal symptoms in patients with migraine. Cephalalgia. 2006;26(5):506-10.
28. Craske MG, Wolitzky-Taylor KB, Labus J, Wu S, Frese M, Mayer EA, et al. A cognitive-behavioral treatment for irritable bowel syndrome using interoceptive exposure to visceral sensations. Behav Res Ther. 2011;49(6-7):413-21.
29. Katić BJ, Golden W, Cady RK, Hu XH. GERD prevalence in migraine patients and the implication for acute migraine treatment. J Headache Pain. 2009;10(1):35-43.
30. Basavannaiah S. A comparative study of laryngopharyngeal reflux disease and migraine: Insights from a hospital-based analysis. Tr-ENT. 2024;34(1):13-7.