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Article

# Association of Migraine and Irritable bowel Syndrome in Saudi Arabia: a nationwide survey.

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**Abstract:** Migraine is a primary headache disorder with a prevalence of 11.6% globally and 27% in Saudi Arabia. Irritable bowel syndrome has a prevalence of 9.2% worldwide. The prevalence of IBS has not been established nationally. However, provincial studies for both migraine and IBS have been conducted across the nation. There is a significant link between migraines and IBS globally. This identifies an association that needs to be investigated in a nationwide manner. This study aims to observe the association and the relationship between migraine and irritable bowel syndrome in Saudi Arabia. A cross-sectional study was conducted between March 2021 to June 2021 among the general population of Saudi Arabia, whose ages are 15 years old or greater. The data collection tools included MS-Q for migraine symptoms, MIGSEV scale for severity of migraine, and The IBS module of the Rome IV Diagnostic Questionnaire (R4DQ) for IBS symptoms and its subtype. With a total of 2802 participants, the majority of the study sample were males, who constituted 52.5%. Among the study's sample, the prevalence of migraine consisted of 27.4%, and the prevalence of IBS was 16.4%. The odds of having IBS in migraineurs were much higher than in those without migraines (OR 4.127; 95% CI 3.325-5.121), and the association was statistically significant ( $P<0.001$ ). In conclusion, there is a strong association between migraine and irritable bowel syndrome in Saudi Arabia.

**Keywords:** *Migraine, Headache, Irritable Bowel Syndrome, Chronic Pain, Saudi Arabia*

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## 1. Introduction

Migraine is a common primary headache disorder with recurrent attacks lasting between 4 to 72 hours, causing moderate to severe unilateral throbbing pain, worsened by physical activity, and can be associated, photophobia, and phonophobia [1]. With a prevalence of 11.6 percent, migraine is the third most common disease in adults worldwide and the third leading cause of disability in those under the age of 50 [2,3]. In Saudi Arabia, migraineurs accounted for 27% of the population, with an adjusted 1-year prevalence of 25% [4,5].

Four studies were conducted on the general public of different regions of Saudi Arabia, three to assess the prevalence of migraine headaches, and a fourth study to assess migraine awareness. The first paper provides historical evidence of migraine prevalence. It was carried out in 1997 in Thuqbah, Saudi Arabia, using a modified version of the WHO criteria to screen for headaches in 23,227 participants. Their findings revealed that 5% of their participants suffered from migraine headaches [6]. Nevertheless, the study population for this article was only the residents of the Thuqbah neighborhood in Khobar city. An article undertaken in the southern part of Saudi Arabia, Aseer, aimed to determine the prevalence of migraine based on the ICHD-III criteria; they concluded that 12.3 percent of their sample had migraine headaches [7]. Furthermore, according to a study performed in Taif, located in the western part of Saudi Arabia, 78.5 percent of their sample experienced

migraine headaches classified by the IHS migraine criteria [8]. However, this astronomical percentage of migraineurs is inconsistent with the rest of the study reporting. In the final paper, nearly 40% of a study sample in Saudi Arabia's Eastern province were found to experience migraine headaches; However, the article directly asked if the participants had migraines without using any measuring tools [9]. A common disadvantage of these studies is that each one utilized a different methodology of evaluating migraine headaches, emphasizing the need for a large-scale study that presents migraine prevalence in various regions of Saudi Arabia using consistent criteria.

Irritable Bowel Syndrome (IBS) is a chronic idiopathic gastrointestinal condition characterized by abdominal pain that persists for more than one day per week in the previous three months and begins more than six months before diagnosis [10]. IBS can present as different subtypes, those with predominant constipation (IBS-C), diarrhea (IBS-D), mixed (IBS-M), or unsubtyped (IBS-U) [11]. IBS has long been known to have a serious impact on people's quality of life. It is one of the most common gut-brain connection disorders, affecting approximately one out of every ten people worldwide [12]. When evaluated using ROME-III criteria, the global prevalence of IBS was 9.2 percent, while it was 3.8 percent when assessed using ROME-IV criteria [13].

The prevalence of IBS has not been established nationally, with many cross-sectional studies only reporting the prevalence in a limited selection of the general populace. A study conducted in the central region investigated the prevalence of IBS using ROME III criteria and found it to be 30.5 percent [14]. Additionally, two recent studies were conducted using ROME IV criteria to measure the prevalence of IBS. The first was done in the southern region of Saudi Arabia, Jazan, which showed a total IBS prevalence of 16%. In contrast, the second study, conducted in Hail, located in the northern region of Saudi Arabia, discovered that 11.8 percent of participants had IBS [15,16]. Overall, the literature on IBS prevalence in Saudi Arabia is higher than the worldwide estimates. Nonetheless, they did not reflect a national prevalence of IBS in the general population and resulted in greater variability in prevalence rates; thus, a nationwide prevalence investigation of IBS is required.

In terms of high prevalence, female preponderance, chronic and recurrent symptoms, pathogenesis, and burden to social and financial costs, migraine and IBS share many similar attributes [17]. Both illnesses are diagnosed using symptom-based criteria. Because various disorders have been related to both the central nervous system and the enteric nervous system, the brain-gut axis is thought to substantially affect how neuronal disorders affect the GI tract [18].

Globally, various studies have shown a significant link established between migraine and IBS. A cohort study that looked at the prevalence of migraine in IBS patients using data from a major US health plan discovered that those with IBS had a 60% higher risk of migraine than people without IBS (POR= 1.6, 95% CI 1.4 – 1.7) [19]. Additionally, a retrospective cohort based on Taiwan's National Health Insurance Research Database also observed that IBS incidence was nearly two times greater in the migraine cohort than in the comparator cohort [20]. Furthermore, according to a 2020 systematic review and meta-analysis, migraineurs had a considerably greater prevalence of IBS than non-migraineurs (OR= 2.49, 95 % CI 2.22-2.78) [21]. Nationally, the link has not been studied thoroughly; therefore, a large-scale nationwide study must fill this gap in the literature.

This study aims to observe the association and the relationship between migraine and irritable bowel syndrome in Saudi Arabia; this includes measuring the prevalence of migraine and irritable bowel syndrome, evaluating and comparing the severity of migraine, and finally, assessing the link between migraine and irritable bowel syndrome. We hypothesize irritable bowel syndrome and migraine to have a direct relationship, increasing the odds of having irritable bowel syndrome in migraine patients.

## 2. Materials and Methods

### 2.1. Study design

This is an observational cross-sectional analytical study aiming to observe the association and the relationship between migraine and irritable bowel syndrome in Saudi Arabia over a period from March 2021 to June 2021. The study population consisted of Saudi Arabia's general population, aged 15 and older. Participants filled an online self-administered survey. Data collectors were recruited from each of the five geographical regions of Saudi Arabia (Central, Eastern, Western, Northern, and Southern).

### 2.2. Data collection tools

The survey was divided into three sections; The first section focuses on the participants' demographic and personal information. The second section discusses migraine symptoms using the Migraine Screen Questionnaire (MS-Q) and their severity measured by the MIGSEV scale. Irritable bowel syndrome manifestations are evaluated in the third section by utilizing the IBS module of the Rome IV Diagnostic Questionnaire (R4DQ).

The MS-Q is a five-question survey used in research and health care settings to test for migraines in the general population. Each "YES" on the questionnaire is equal to one point, whereas each "NO" equals zero points. With a maximum score of 5, if the total score is equal to four or more, this indicates having migraine symptoms [22]. MS-Q has a sensitivity of 0.82 and a specificity of 0.97 [23]. Furthermore, The MIGSEV scale is a 4-item migraine severity questionnaire that categorizes people as having a low, moderate, or high overall migraine severity. MIGSEV is a reliable scale, with a Cronbach's coefficient of 0.84 for physician evaluation and 0.86 for patient review [24].

The R4DQ was developed and published in 2016 by the Rome Foundation [25]. In IBS, the questionnaire showed a sensitivity of 62.7% and specificity at 97.1% [10]. Six questions make up the IBS module of the questionnaire. When a participant answers "Once a week" or a greater frequency for the first question, "30%" or higher for the second to the fourth question, and "Yes" for the fifth question, they are labeled IBS-positive. The sixth question classifies participants into IBS subgroups.

### 2.3. Statistical analysis

For data analysis, IBM's SPSS v21 was used. Continuously measured variables were described using the mean and standard deviation, while categorically measured variables were described using frequency and percentages. The normality assumption of the continuous variables was assessed using the histogram and the statistical Kolmogorov-Smirnov K-S test. In contrast, the equality of statistical variance assumption was evaluated using Levene's homogeneity of variance. The correlations between categorically measured variables were assessed using the chi-squared ( $\chi^2$ )-test of independence. The statistical significance of mean differences in metric variables across levels of binary outcomes was evaluated using the independent samples t-test. When the statistical assumptions of the chi-square test expected counts were violated, a corrected Likelihood Ratio chi-squared test was utilized. A multivariate logistic regression model was used to analyze the significance of the participants' odds of migraine and IBS. The link between Migraine and IBS odds and other important

## 3. Results

Two thousand eight hundred two participants submitted the survey, 52.5% were males, and 47.5 % were females. The majority of replies (46.7%) came from people aged 20 to 29. In terms of marital status, 54.9% had never married, compared to 45.1 % who had ever been married (married, divorced, or widowed). The percentage of the responses from different geographical regions in Saudi Arabia was close, with the majority from the

western geographical area 23.7%, followed by southern 22.1%, and eastern 21.2%. A complete listing of the samples' sociodemographic characteristics is presented in Table 1.

Seven hundred sixty-seven were found to be migraine positive, showing a prevalence

**Table 1: Descriptive analysis of people's sociodemographic characteristics.**

of	N=2802	n (%)
<b>Sex</b>		
Female		1332 (47.5)
Male		1470 (52.5)
<b>Age group</b>		
15-19 years		342 (12.2)
20-29 years		1308 (46.7)
30-39 years		431 (15.4)
40-49 years		503 (18)
50-59 years or older		218 (7.8)
<b>Marital state</b>		
Never married		1538 (54.9)
Ever married		1264 (45.1)
<b>Nationality</b>		
Saudi		2715 (96.9)
Non-Saudi		87 (3.1)
<b>Residence</b>		
Central region		514 (18.3)
Eastern region		593 (21.2)
Northern region		412 (14.7)
Southern region		618 (22.1)
Western region		665 (23.7)
<b>Occupation</b>		
Unemployed/Retired		501 (17.9)
Student		1147 (40.9)
Private sector employed		181 (6.5)
Military sector		88 (3.1)
Health sector		104 (3.7)
Governmental Job		428 (15.3)
Education		274 (9.8)
Freelance Job/Charitable business		79 (2.8)

27.4%. Females had a considerably higher prevalence of migraine, with 37.5%, compared to 18.2% in males. 333 constituting the bulk of migraineurs (43.4 %) experienced moderate migraine attacks, followed by 237 with mild migraine attacks (30.9%), and just 197 had severe migraine attacks (25.7 %). IBS was found to be less common than migraine in our sample, with 460 subjects fulfilling the Rome-IV criteria for IBS, showing a prevalence of 16.4%. Females also had a higher percentage, with 20.9% compared to 12.4% for males. Figure 1 depicts the prevalence of migraine and IBS in each geographical region of Saudi Arabia. To classify their IBS, subjects were asked to identify their stool form in the past three months, and the results revealed that the majority (160) had IBS-M, followed by IBS-C (152), IBS-D (113), and IBS-U was the least common (35).

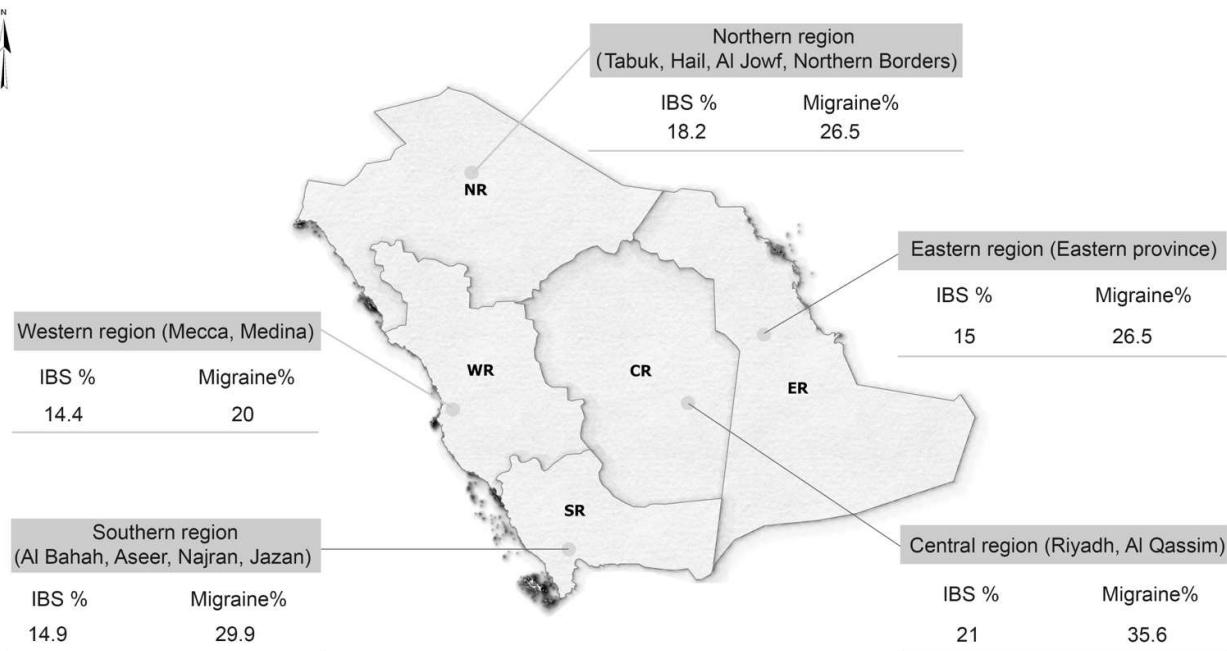


Figure 1: Prevalence of Migraine and IBS in each geographic region of Saudi Arabia

Females were shown to be significantly more likely to have both migraine and IBS in the bivariate analysis ( $p<0.001$ ), and in the multivariate regression analysis, the same result is seen for migraine and IBS, with males having 55.9% less probability of having migraine than females (OR 0.441; 95% CI 0.364-0.534;  $p<0.001$ ), and showing less chance of having IBS (OR 0.689; 95% CI 0.547-0.868;  $p=0.002$ ).

In the bivariate analysis, age groups differed in their chance of having a migraine. Individuals aged 40-49 years were shown to be substantially more likely than others to suffer from migraines, compared to those old 20-29 years, which were significantly less predisposed ( $p<0.001$ ). In IBS, age did not correlate significantly.

People residing in central Saudi Arabia were significantly more likely to have migraines ( $p<0.001$ ) and IBS ( $p=0.013$ ). Those living in the western region were considerably less likely to have migraines ( $p<0.001$ ). However, none of those relations is established in the multivariate regression analysis. Types of occupation converge significantly with migraines ( $p<0.001$ ), people working in education, freelance/charitable business, and those unemployed/retired were more likely to have migraines. In comparison, those working in the military were found to be significantly less inclined to migraines. In the regression analysis, people working in freelance jobs and charitable works were still found to be significantly more inclined (2.22 times more) to be migraineurs compared to people in other employment or those unemployed (OR 2.223; 95% CI 1.339-3.693;  $p=0.002$ ). Students were found to be significantly less predicted (39.1% times less) for migraines compared to people who have other occupations (OR 0.609; 95% CI 0.467-0.794;  $P<0.001$ ). Table 2 presents a detailed bivariate analysis of migraine and IBS with participants' sociodemographic characteristics and an analysis of the association between migraine and IBS.

**Table 2:** Descriptive bivariate analysis of migraine and IBS with participants' sociodemographic characteristics and the association between migraine and IBS.

	Migraine		test statistic p-value	Irritable Bowel Syndrome		test statistic p-value
	No=2035	Yes=767		No=2342	Yes=460	
<b>Sex</b>						
Female	832 (40.9)	500 (65.2)	$\chi^2 (1)=131.94$	1054 (45)	278 (60.4)	$\chi^2 (1)=36.7$
Male	1203 (59.1)	267 (34.8)	p<0.001	1288 (55)	182 (39.6)	p<0.001
<b>Age group</b>						
15-19 years	253 (12.4)	89 (11.6)	$\chi^2 (4)=36.99$	291 (12.4)	51 (11.1)	$\chi^2 (4)=2.034$
20-29 years	1011 (49.7)	297 (38.7)	p<0.001	1100 (47)	208 (45.2)	p=0.729
30-39 years	300 (14.7)	131 (17.1)		359 (15.3)	72 (15.7)	
40-49 years	323 (15.9)	180 (23.5)		412 (17.6)	91 (19.8)	
50+ years	148 (7.3)	70 (9.1)		180 (7.7)	38 (8.3)	
<b>Marital state</b>						
Never married	1183 (58.1)	355 (46.3)	$\chi^2 (1)=31.58$	1289 (55)	249 (54.1)	$\chi^2 (1)=0.13$
Ever married	852 (41.9)	412 (53.7)	p<0.001	1053 (45)	211 (45.9)	p=0.72
<b>Nationality</b>						
Non-Saudi	54 (2.7)	33 (4.30)	$\chi^2 (1)=5.03$	73 (3.1)	14 (3)	$\chi^2 (1)=0.007$
Saudi	1981 (97.3)	734 (95.7)	p=0.025	2269 (96.9)	446 (97)	p=0.934
<b>Residence</b>						
Central region	331 (16.3)	183 (23.9)	$\chi^2 (1)=38.15$	406 (17.3)	108 (23.5)	$\chi^2 (1)=12.70$
Eastern region	436 (21.4)	157 (20.5)	p<0.001	504 (21.5)	89 (19.3)	p=0.013
Northern region	303 (14.9)	109 (14.2)		337 (14.4)	75 (16.3)	
Southern region	433 (21.3)	185 (24.1)		526 (22.5)	92 (20)	
Western region	532 (26.1)	133 (17.3)		569 (24.3)	96 (20.9)	
<b>Occupation type</b>						
Unemployed/Retired	329 (16.2)	172 (22.4)	$\chi^2 (7)=58.54$	415 (17.7)	86 (18.7)	$\chi^2 (7)=9.19$
Student	902 (44.3)	245 (31.9)	p<0.001	956 (40.8)	191 (41.5)	p=0.239
Private sector employed	139 (6.8)	42 (5.5)		165 (7)	16 (3.5)	
Military sector	72 (3.5)	16 (2.1)		73 (3.1)	15 (3.3)	
Health sector	74 (3.6)	30 (3.9)		85 (3.6)	19 (4.1)	
Governmental Job	295 (14.5)	133 (17.3)		356 (15.2)	72 (15.7)	
Education	179 (8.8)	95 (12.4)		224 (9.6)	50 (10.9)	
Freelance Job/charitable business	45 (2.2)	34 (4.4)		68 (2.9)	11 (2.4)	
<b>Irritable bowel syndrome (IBS)</b>						
Negative	1829 (89.9)	513 (66.9)	$\chi^2 (1)=214.63$	-	-	
Positive	206 (10.1)	254 (33.1)	p<0.001	-	-	

Participants with migraines were found to be significantly more likely to have IBS (p<0.001); also, those with IBS showed a significant probability of having a migraine (p<0.001), as shown in Table 2. This was also confirmed in our regression analysis, as those with migraines had higher odds (OR 4.127) of having IBS (95% CI 3.325-5.121; p<0.001). In addition to those with IBS having an increased likelihood of having migraines (OR 3.304; 95% CI 2.632-4.147; p<0.001). Migraineurs with severe symptoms were more likely to have IBS than migraineurs with moderate or lower migraine symptoms (P=0.015). The analysis showed no correlation between IBS subtypes and migraines.

#### 4. Discussion

This article aims to assess the association between migraines and IBS in Saudi Arabia. The prevalence of migraine and IBS was found to be 27.4% and 16.4%, respectively. In both conditions, females outnumbered males in terms of prevalence. The highest prevalence of both migraine and IBS was seen in the central region. Both migraine and IBS were found to be substantially linked.

We found the prevalence of migraine similar to the prevalence of 27% reported in a previous study conducted in Saudi Arabia that used an independently developed questionnaire structured on ICHD-III criteria [5]. This is notably higher than the worldwide prevalence [2]. Up to our knowledge, this is the first nationwide study conducted in the kingdom of Saudi Arabia to assess IBS prevalence. Even though the prevalence of IBS reported in this study is considerably higher than the global prevalence reported in a meta-analysis of articles using the Rome-IV criteria, this number is comparable to some worldwide reports [13,26–28].

Various studies have been conducted to determine the prevalence of migraine and IBS in the general public. However, those studies were often conducted in Saudi Arabia's 13 provinces rather than geographical regions, making the comparison with our findings challenging. Additionally, different methodologies were utilized in the literature, complicating the comparison even more. A study conducted in Asser, located in the southern part of Saudi Arabia, found the prevalence of migraine to be 12.3%, which is lower than the prevalence of migraine we measured in the southern region (29.9%) [7]. This could be due to other provinces in the southern part having a higher prevalence of migraine, increasing the prevalence for the whole geographical area. The southern region had a comparable IBS prevalence (14.9%) to a research conducted in Jazan (16%), which employed the same data collection tool for IBS symptoms measurement [15]. Using the same data collection method, a study in Hail city reported a lower prevalence of IBS (11.8%) than our findings in the northern region (18.2%). This could be due to the fact that their study results were limited to Hail city, compared to our result, which pertains to the entirety of the northern region [16]. Our report of IBS prevalence in the central region (21%) is lower than an article that utilized the old Rome-III criteria, which found a prevalence of 30.5%. This result is expected, as a systematic review showed papers that used Rome-III criteria scored a higher prevalence compared to those using Rome-IV criteria [13,14].

In this study, females had a higher prevalence of migraine and IBS than males. This observation has been thoroughly established in the literature pertaining to Arab nations as well as globally [2,13,29,30]. Females showed not only a higher prevalence of migraine and IBS, but also the bivariate and regression analysis demonstrated that females had a higher probability of having migraine and IBS. A standard theory for the sex discrepancy in migraine and IBS is due to hormonal factors, especially sex hormones [31,32]. Ultimately, more research is needed to investigate sex-related vulnerability to migraine headaches and IBS, including genetic and biological determinants and other environmental factors that influence migraine and IBS prevalence in females.

Migraine and IBS showed a strong association, as the presence of one disease increased the chance for the other. Migraineurs had 4.13 times the possibility of having IBS than those without migraine, which is higher than results shown by a recently published meta-analysis done on this subject (OR 2.49) [21]. The opposite is also true, as IBS-positive participants had a higher risk for migraines. This link is also seen in current literature [17,19]. The cause of this relation is not yet fully understood. However, it is hypothesized that the brain-gut axis, serotonin, central and visceral hypersensitivity, and hereditary factors are common pathogenesis pathways for migraine and IBS [17,33]. Additionally, we found migraineurs to have more severe migraine symptoms when they were comorbid with IBS. This finding may be comparable to one reported in a recent article, which found that headache-related disability was more significant in participants with IBS symptoms than those without IBS, as measured by HIT-6 [34].

As hypothesized, migraineurs showed higher odds of having IBS compared to non-migraineurs, showing a significant positive relationship between the two variables.

There are a few limitations to this paper that should be highlighted. For starters, no causal effects can be determined due to the study being cross-sectional. Since this paper is based on the information given by respondents, there is a risk of recall bias. Even though migraine and IBS screening were done using validated questionnaires, the diagnosis was not confirmed clinically. Also, the study did not use the 13 provincial categorizations, and the five geographical regions were chosen based on ease of measurement and data comparability. The sensitivity and specificity of the MIGSEV migraine severity scale have yet to be established to reflect validity. Moreover, the prevalence of IBS may vary depending on the criteria used, as evidenced by prior research. [35–37].

## 5. Conclusion

There is evidence of a high prevalence of migraine headaches in the Saudi population (27.4%) and irritable bowel syndrome (16.4%). In terms of prevalence, females are much more likely than males to experience migraine and irritable bowel syndrome. Migraineurs who are IBS positive are far more likely to have severe migraine symptoms than migraineurs without IBS. Our investigation observed a significant link between migraine and irritable bowel syndrome nationwide, which confirms our hypothesis. However, more research is needed to determine the prevalence of migraine and IBS in each of Saudi Arabia's 13 provinces using consistent methodologies. In addition, while migraine is associated with IBS, there is no clear pathophysiological explanation for the correlation, and extensive research on overlapping factors in the migraine-IBS relationship is required to fill gaps in the literature.

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**Informed Consent Statement:** Participants were told consent is given by filling the survey. consent of all participants and data were gathered in complete confidence.

**Conflicts of Interest:** The authors declare no conflict of interest

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