

The Prevalence of Migraine in Inflammatory Bowel Disease, a Systematic Review and Meta-Analysis

Abstract

Background: Patients with inflammatory bowel disease (IBD) suffer from a wide range of comorbidities such as migraine. In studies, the prevalence of migraine in cases with IBD was reported differently. The goal of this systematic review and meta-analysis was to estimate the pooled prevalence of migraine in IBD cases. **Methods:** Two researchers independently and systematically searched PubMed, Scopus, EMBASE, Web of Science, and google scholar. They also searched the gray literature including references of the included studies and conference abstracts which were published up to May 2021. Cross-sectional studies were included. **Results:** The literature search revealed 840 articles, and after deleting duplicates, 650 remained. For the meta-analysis, 10 studies were included. Totally, 62,554 patients were evaluated. The pooled prevalence of migraine in patients with IBD was 19% (95% CI: 15–22%). The pooled prevalence of migraine in ulcerative colitis (UC) was 10% (95% CI: 4–15%) ($I^2 = 99.8\%$, $P < 0.001$). The pooled prevalence of migraine in the Crohn's disease (CD) group was 24% (95% CI: 17–30%) ($I^2 = 98.8\%$, $P < 0.001$). The pooled odds of developing migraine in IBD cases was 1.51 (95% CI: 1–2.27) ($I^2 = 90.8\%$, $P < 0.001$). **Conclusions:** The result of this systematic review and meta-analysis showed that the pooled prevalence of migraine in patients with IBD was 19% (95% CI: 15–22%).

Keywords: Inflammatory bowel disease, migraine disorders, prevalence

Introduction

Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), is a complex chronic disease affecting primarily the gastrointestinal tract along with other organs.^[1,2] The prevalence of IBD is reported as 0.4% in developed countries.^[1]

It is well known that IBD is associated with a number of extra-intestinal diseases. Some of them are complications of the disease process such as venous thromboembolism (VTE), whereas others are considered as extra-gastrointestinal (GI) manifestations.^[3]

Extra-GI manifestations include articular, cutaneous, neurological, and ocular involvement with prevalence of 40%.^[4,5]

Previous studies demonstrated that the prevalence of neurological manifestations in IBD cases ranges between 25 and 37.5%.^[6-8]

Migraine is a chronic disorder affecting women more than men and is the first

cause of disability under 50.^[9] Its origin is not clear as brain-gut interactions are considered as pathogenesis of the migraine in patients with IBD^[2] as well as side effects of immunosuppressive agents.

Previous studies demonstrate that the prevalence of migraine in patients with IBD is more than the general population and the odds are increased by 2.6-fold.^[10,11]

As the prevalence of migraine in cases with IBD is reported variously, we designed this systematic review and meta-analysis to estimate the pooled prevalence of migraine in IBD cases.

Methods

Literature search

Two researchers independently and systematically searched PubMed, Scopus, EMBASE, Web of Science, and google scholar. They also searched the gray literature including references of the included studies and conference abstracts which were published up to May 2021.

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Inclusion criteria

We included cross-sectional studies which had reported the number of patients with IBD who had migraine diagnosis.

Exclusion criteria

Letters to the editor, case-control, case reports, and cross-sectional studies which had no clear data regarding the prevalence of migraine in enrolled cases were excluded.

Data search and extraction

- The search strategy included the MeSH and text words as (“Migraine Disorder” OR (Migraine AND Disorder) OR “Migraine Disorders” OR (Migraine AND Disorders) OR “Migraine” OR “Migraines” OR “Migraine Headache” OR (Migraine AND Headache) OR “Migraine Headaches” OR (Migraine AND Headache)) AND (“Inflammatory Bowel Disease” OR “Inflammatory Bowel Diseases” OR (Inflammatory AND Bowel Disease) OR (Inflammatory AND Bowel Diseases) OR “Idiopathic Proctocolitis” OR (Idiopathic AND Proctocolitis) OR “Ulcerative Colitis” OR (Ulcerative AND Colitis) OR “Colitis Gravis” OR (Colitis AND Gravis) OR “Crohn’s Enteritis” OR (Crohn’s AND Enteritis) OR “Regional Enteritis” OR (Regional AND Enteritis) OR “Crohn’s Disease” OR (Crohn’s AND Disease) OR “Regional Ileitis” OR (Ileitis AND Regional) OR “Terminal Ileitis” OR (Terminal AND Ileitis) OR “Ileocolitis” OR “Granulomatous Colitis” OR (Granulomatous AND Colitis) OR “Granulomatous Enteritis” OR (Granulomatous AND Enteritis)). Two independent researchers independently evaluated the articles.

We extracted data regarding the total number of participants, first author, publication year, the country of origin, mean age, sex frequency, and number with migraine.

Risk of bias assessment

We evaluated the risk of potential bias using the NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE (adapted for cross-sectional studies).^[12,13] It is used for evaluating the quality of non-randomized studies including three sections (selection, comparability, and outcome). It has totally seven questions. The maximum total score could be 10 [Tables 2 & 3].

Statistical analysis

All statistical analyses were performed using STATA (Version 14.0; Stata Corp LP, College Station, TX, USA).

To determine heterogeneity, inconsistency (I^2) was calculated.

As the heterogeneity between results of included studies was more than 50%, we used the random effects model. Pooled prevalence of migraine in IBD cases as well as UC and Crohn’s subgroups is reported with 95% CI.

Results

The literature search revealed 840 articles, and after deleting duplicates, 650 remained. For the meta-analysis, 10 studies were included [Figure 1].

Totally, 62,554 patients were evaluated. The mean age ranged from 17 to 53 years [Table 1].

The pooled prevalence of migraine in patients with IBD was 19% (95% CI: 15–22%) ($I^2 = 99.2\%$, $P < 0.001$) [Figure 2].

The pooled prevalence of migraine in controls was 6% (95% CI: 4–8%) ($I^2 = 99.9\%$, $P < 0.001$) [Figure 3].

The pooled prevalence of migraine in UC was 10% (95% CI: 4–15%) ($I^2 = 99.8\%$, $P < 0.001$) [Figure 4].

The pooled prevalence of migraine in CD was 24% (95% CI: 17–30%) ($I^2 = 98.8\%$, $P < 0.001$) [Figure 5].

The pooled odds of developing migraine in IBD cases was 1.51 (95% CI: 1–2.27) ($I^2 = 90.8\%$, $P < 0.001$) [Figure 6].

Discussion

To our knowledge, this is the first systematic review and meta-analysis evaluating the prevalence of migraine in patients with IBD. The results of this study showed that the pooled prevalence of migraine in IBD cases is 19%, whereas the prevalence is higher in CD cases than UC ones (24% vs 10%). The results also show that the odds of developing migraine are significantly higher in IBD cases when compared with controls (1.5-fold).

In a study in Iran, Cheraghi *et al.*^[8] reported the prevalence of migraine in 21.3% of IBD cases compared to 8.8% of controls. In another study which was conducted by Dimitrova *et al.*,^[11] the prevalence of migraine was reported as 14% in IBD cases and 6% in controls.

Ghersin *et al.*^[17] assessed 295 UC and 595 CD cases and reported no association between migraine and IBD. In their study, none of the UC cases and only 8 CD cases had migraine.

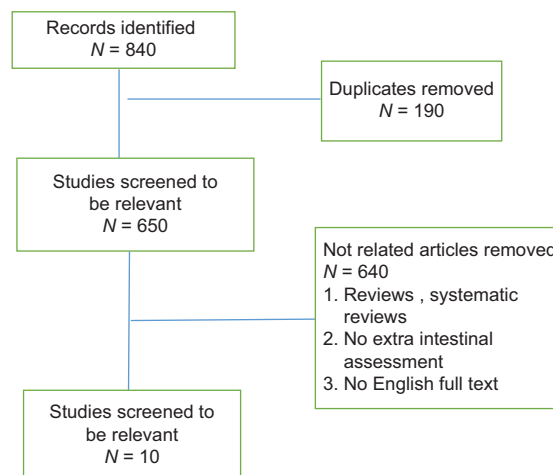


Figure 1: Flow diagram of including studies

Table 1: Basic characteristics of the included studies

Author	Country	Year of publication	Year of study	Type of article	Demographic features			Number of IBD patients			Number of migraine patients			IBD duration			Controls data			Number of Migraine in control	
					Age	Number		CD	UC	Total	In CD	In UC	In Total	Age	F	M	T	F	M		T
						F	M														
J. Tajti Jr	Hungary	2019	2005-2016	Retrospective abstract	NA	-	-	75	75	-	-	8	-	-	-	-	-	-	-	-	
Leitão et al. ^[14]	Brazil	2020	2015-2016	cross-sectional	43 (1)	83	72	155	75	80	155	30	23	53	46 (2)	35	66	101	21	21	
Bähler ^[15]	Switzerland	2017	2014	cross-sectional	56 (28)	2684	2107	4791	-	-	4791	-	-	105	-	44	575943	538695	1114638	12261	
Anadol Kelleci et al. ^[16]	Turkey	2016	2012	cross-sectional	35 (12)	26	25	51	51	-	51	35	-	9	29.17 (10.24)	27	24	51	21	21	
Card et al. ^[3]	United Kingdom	2016	1987-2011	cohort	47.2	29814	26283	56097	18204	27108	56097	1430	1892	4380	-	47.2	149030	131352	280,382	19376	
Dimitrova et al. ^[11]	United States	2013	2010-2011	Prospective	36.5	58	53	111	-	-	111	-	-	25	-	47.8	109	69	178	25	
Ford et al. ^[10]	United States	2009	2006	Prospective	40.3 (14.9)	77	23	100	66	27	100	24	4	28	12.11 (10.19)	-	-	-	-	-	
Ghersin et al. ^[17]	Israel	2019	2004-2016	cohort	17.1	318	573	891	595	296	891	8	0	8	-	-	-	-	1,141,841	37,576	
Cheraghi et al. ^[8]	Iran	2016	2014	Cross-sectional	35	33	47	80	18	62	80	-	-	17	-	34.69	36	44	80	7	
Moisset et al. ^[2]	France	2017	2014-2015	Cohort	40.1 (1)	113	90	203	129	73	203	-	-	83	10.5 (0.7)	-	-	-	-	-	

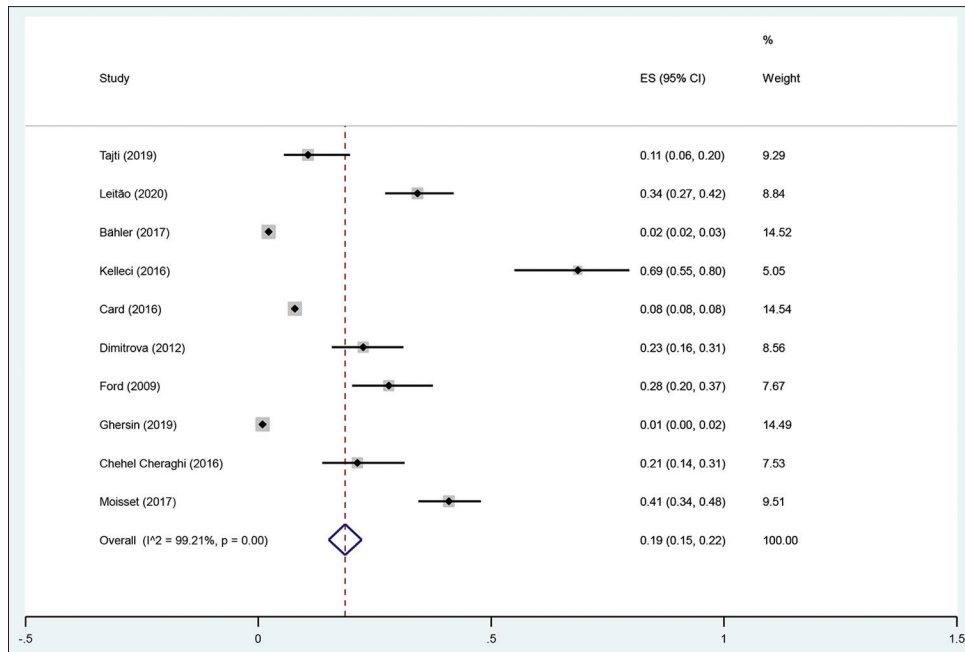


Figure 2: The pooled prevalence of migraine in patients with IBD

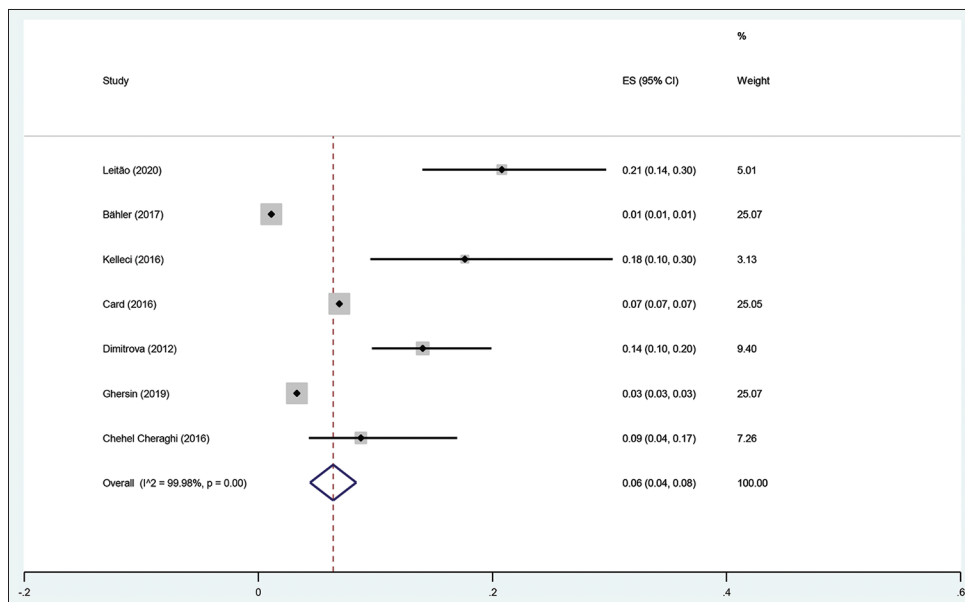


Figure 3: The pooled prevalence of migraine in controls

Table 2: Quality assessment of included studies

Name of the author	Questions									Total score
	Selection questions				Comparability questions			Outcome questions		
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q1	Q2	
Timothy R. Card	A*	B*	D	A*	A*	D	A*	A*		6
Sutapa Ford	B*	C	B*	A*	C	C	A*	A*		5
Itai Ghersin	A*	A*	D	A*	C	D	A*	A*		5

In a cross-sectional study which was conducted by Ford *et al.*,^[10] the prevalence of migraine in IBD was 30% and the prevalence was higher in CD cases than in UC ones (36 vs 14%).

Peripheral and central nervous systems could be affected in patients with IBD.^[18,19]

Migraine is a disabling disease affecting women more than men which interferes with daily activity and sexual life and

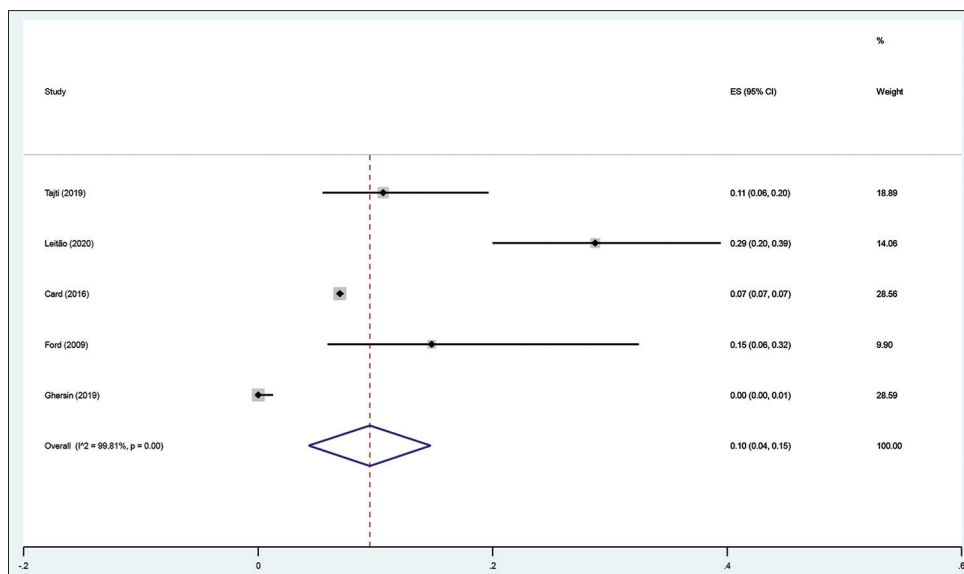


Figure 4: The pooled prevalence of migraine in UC

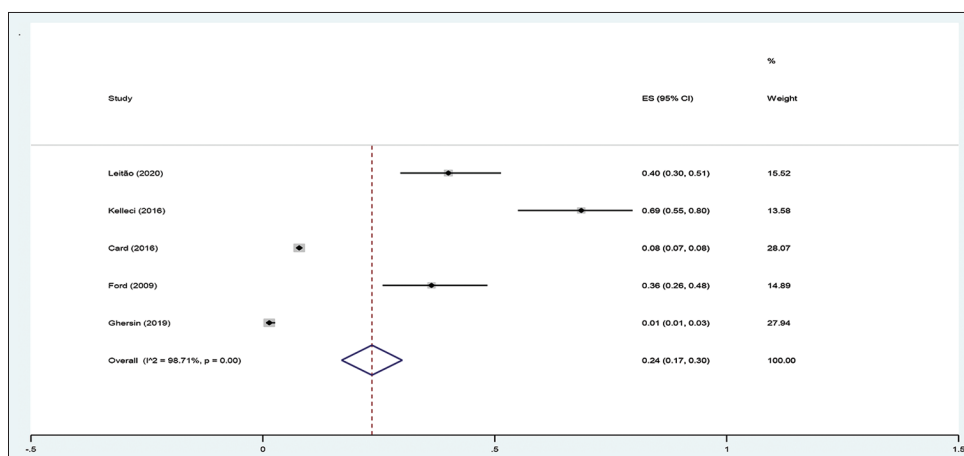


Figure 5: The pooled prevalence of migraine in CD

Table 3: Quality assessment of cross-sectional studies

Name of the author	Questions							Total score
	Selection				Comparability		Outcome	
	Q1	Q2	Q3	Q4	Q1	Q1	Q2	
Antônio M. F. Leitão	A*	A*	C	A**	-	C*	A*	6
Caroline Bähler	A*	A*	C	C	-	B**	A*	5
Ulker Anadol Kelleci	B*	A*	C	A**	B*	C*	A*	7
Alexandra K. Dimitrova	A*	A*	C	A**	-	C*	A*	6
Somaye Chehel Cheraghi	B*	A*	C	A**	A*	C*	A*	7
X. Moisset	A*	A*	C	A**	-	C*	A*	6

impairs the quality of sleep and life.^[20-22] Genetics plays an important role in developing migraine when there is a relationship between auto-immune disease and incidence of migraine, such as rheumatoid arthritis (RA), systemic lupus erythematosus, and multiple sclerosis.^[23-26] In a study which was conducted by Abdelaty ElSonbaty, the prevalence of migraine in patients with RA was estimated as 28%, and in a recent systematic review and meta-analysis, the pooled

prevalence of migraine in patients with multiple sclerosis was estimated as 31%.^[25,26]

The exact cause of migraine is unclear as neuronal and vascular mechanisms are involved.

The link between migraine and IBD could be clarified by the presence of systemic inflammation leading to neurogenic inflammation presenting with migraine.^[27]

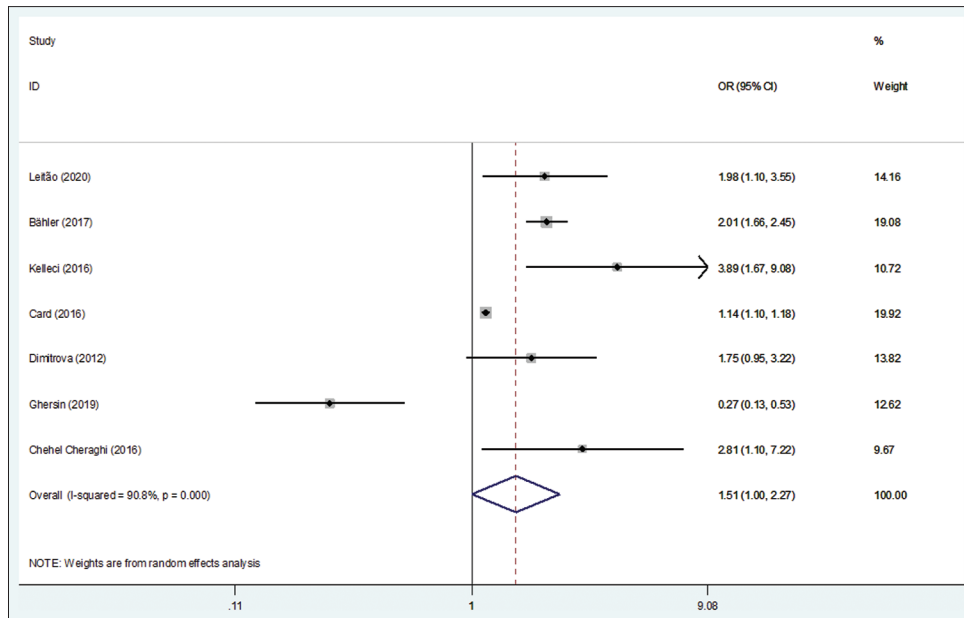


Figure 6: The pooled odds of developing migraine in IBD cases

Nowadays, the brain-gut axis is considered in the pathogenesis of some diseases. One of them is the serotonergic system.^[28] The level of serotonin is low between attacks and increases during migraine attacks, which shows a relationship between the low serotonin level and migraine incidence.^[29] It has been shown that in patients with UC, expression of the serotonin transporter in the gut epithelium is decreased and the level of serotonin is less than normal in the colon.^[30] Low serotonin levels could be the link between migraine and IBD.

Higher serum levels of cytokines in IBD cases than controls could flare headache. Moisset *et al.*^[2] showed that migraine is not associated with IBD clinical activity. They found that inflammatory activity is sufficient for migraine activity when there are no intestinal manifestations. The literature shows that C-reactive protein (CRP), matrix metalloproteinase 9 (MMP-9), cytokines, adhesion molecules, nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B), and inducible nitric oxide synthase (iNOS) have roles in developing migraine headache.^[31-33]

This systematic review and meta-analysis has some strength. It is the first study. Second, we estimated pooled prevalence in CD and UC separately.

Conclusions

The result of this systematic review and meta-analysis showed that the pooled prevalence of migraine in patients with IBD was 19% (95% CI: 15–22%).

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Nil.

Conflicts of interest

There are no conflicts of interest.

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References

1. Watts D, Satsangi J. The genetic jigsaw of inflammatory bowel disease. *Gut* 2002;50(Suppl 3):III31-6.
2. Moisset X, Bommelaer G, Boube M, Ouchchane L, Goutte M, Dapoigny M, *et al.* Migraine prevalence in inflammatory bowel disease patients: A tertiary-care centre cross-sectional study. *Eur J Pain* 2017;21:1550-60.
3. Card TR, Langan SM, Chu TP. Extra-gastrointestinal manifestations of inflammatory bowel disease may be less common than previously reported. *Dig Dis Sci* 2016;61:2619-26.
4. Vavricka SR, Schoepfer A, Scharl M, Lakatos PL, Navarini A, Rogler G. Extraintestinal manifestations of inflammatory bowel disease. *Inflamm Bowel Dis* 2015;21:1982-92.
5. Vavricka SR, Brun L, Ballabeni P, Pittet V, Vavricka BM, Zeitz J, *et al.* Frequency and risk factors for extraintestinal manifestations in the Swiss inflammatory bowel disease cohort. *Am J Gastroenterol* 2011;106:110-9.
6. Elsehety A, Bertorini TE. Neurologic and neuropsychiatric complications of Crohn's disease. *South Med J* 1997;90:606-10.
7. Greenstein AJ, Janowitz HD, Sachar DB. The extra-intestinal complications of Crohn's disease and ulcerative colitis: A study of 700 patients. *Medicine (Baltimore)* 1976;55:401-12.
8. Cheraghi SC, Daryani NE, Ghabae M. A survey on migraine prevalence in patients with inflammatory bowel disease-A single centre experience. *Middle East J Dig Dis* 2016;8:282-8.
9. Steiner TJ, Stovner LJ, Vos T, Jensen R, Katsarava Z. Migraine is first cause of disability in under 50s: Will health politicians now take notice? *J Headache Pain* 2018;19:17.
10. Ford S, Finkel AG, Isaacs KL. Migraine in patients with inflammatory bowel disorders. *J Clin Gastroenterol* 2009;43:499.

11. Dimitrova AK, Ungaro RC, Lebowitz B, Lewis SK, Tenmyson CA, Green MW, *et al.* Prevalence of migraine in patients with celiac disease and inflammatory bowel disease. *Headache* 2013;53:344-55.
12. Modesti PA, Reboldi G, Cappuccio FP, Agyemang C, Remuzzi G, Rapi S, *et al.* Panethnic differences in blood pressure in Europe: A systematic review and meta-analysis. *PLoS One* 2016;11:e0147601.
13. Peterson J, Welch V, Losos M, Tugwell PJ. The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-Analyses. Ottawa: Ottawa Hospital Research Institute; 2011. p. 1-12.
14. Leitão AM, Junior HL, Araújo DF, Braga LL, Souza MH, Barbosa AM, *et al.* Neuropathy and primary headaches affect different subgroups of inflammatory bowel disease patients. *Neurol Sci* 2021;42:935-42.
15. Bähler C, Schoepfer AM, Vavricka SR, Brüngger B, Reich O. Chronic comorbidities associated with inflammatory bowel disease: Prevalence and impact on healthcare costs in Switzerland. *Eur J Gastroenterol Hepatol* 2017;29:916-25.
16. Anadol Kelleci U, Calhan T, Sahin A, Kahraman R, Ozdil K, Sokmen HM, *et al.* The Prevalence of headache in Crohn's disease: Single-center experience. *Gastroenterol Res Pract* 2016;2016:6474651.
17. Ghersin I, Khateeb N, Katz LH, Daher S, Shamir R, Assa A. Comorbidities in adolescents with inflammatory bowel disease: Findings from a population-based cohort study. *Pediatr Res* 2020;87:1256-62.
18. Belkaid Y, Naik S. Compartmentalized and systemic control of tissue immunity by commensals. *Nat Immunol* 2013;14:646-53.
19. Vanmolkot FH, Van Bortel LM, de Hoon JN. Altered arterial function in migraine of recent onset. *Neurology* 2007;68:1563-70.
20. Sadeghniaat K, Rajabzadeh A, Ghajarzadeh M, Ghafarpour M. Sleep quality and depression among patients with migraine. *Acta Med Iran* 2013;51:784-8.
21. Mirmosayyeb O, Shaygannejad V, Ghajarzadeh M. Comparison of psychological difficulties in patients with migraine and epilepsy using PARADISE-24 questionnaire. *J Multidiscip Healthc* 2020;13:609-13.
22. Jalilian R, Ghajarzadeh M, Fateh R, Togha M, Sahraian MA, Azimi A. Comparison of sleep quality in women with migraine moreover, multiple sclerosis. *Acta Med Iran* 2014;52:690-3.
23. Cavestro C, Ferrero M. Migraine in systemic autoimmune diseases. *Endocr Metab Immune Disord Drug Targets* 2018;18:124-34.
24. Buse DC, Reed ML, Fanning KM, Bostic R, Dodick DW, Schwedt TJ, *et al.* Comorbid and co-occurring conditions in migraine and associated risk of increasing headache pain intensity and headache frequency: Results of the migraine in America symptoms and treatment (MAST) study. *J Headache Pain* 2020;21:1-16.
25. El-Sonbaty HA-E, Zarad CA, Mohamed MR, Elmaaty A, Ahmed A. Migraine in patients with rheumatoid arthritis and its relation to disease activity. *Egypt J Neurol Psychiatr Neurosurg* 2021;57:1-10.
26. Mirmosayyeb O, Barzegar M, Nehzat N, Shaygannejad V, Sahraian MA, Ghajarzadeh M. The prevalence of migraine in multiple sclerosis (MS): A systematic review and meta-analysis. *J Clin Neurosci* 2020;79:33-8.
27. Mathieu S, Couderc M, Pereira B, Dubost J-J, Malochet-Guinamand S, Tournadre A, *et al.* Prevalence of migraine and neuropathic pain in rheumatic diseases. *J Clin Med* 2020;9:1890.
28. O'Mahony SM, Clarke G, Borre Y, Dinan T, Cryan J. Serotonin, tryptophan metabolism and the brain-gut-microbiome axis. *Behav Brain Res* 2015;277:32-48.
29. Hamel E, Currents H. Serotonin and migraine: Biology and clinical implications. *Cephalalgia* 2007;27:1293-300.
30. Coates MD, Mahoney CR, Linden DR, Sampson JE, Chen J, Blaszyk H, *et al.* Molecular defects in mucosal serotonin content and decreased serotonin reuptake transporter in ulcerative colitis and irritable bowel syndrome. *Gastroenterology* 2004;126:1657-64.
31. Sarchielli P, Floridi A, Mancini M, Rossi C, Coppola F, Baldi A, *et al.* NF-κB activity and iNOS expression in monocytes from internal jugular blood of migraine without aura patients during attacks. *Cephalalgia* 2006;26:1071-9.
32. Leira R, Sobrino T, Rodríguez-Yáñez M, Blanco M, Arias S, Castillo J. Mmp-9 immunoreactivity in acute migraine. *Headache* 2007;47:698-702.
33. Vanmolkot F, Hoon JD. Increased C-reactive protein in young adult patients with migraine. *Cephalalgia* 2007;27:843-6.