Original Article

Relative Frequency of Gastrointestinal Functional Disorders in Patients with Inflammatory Bowel Disease Based on Rome IV: A Case-Control Study

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Abstract

Background: Inflammatory bowel disease (IBD) is a digestive system ailment that causes significant bodily disruption. This problem may coexist with other digestive system illnesses. One of the diseases that reduces the quality of life and other disorders is functional dyspepsia (FD), the diagnosis of which is associated with unique limitations. In this study, we aim to investigate the relative frequency of FD in IBD patients and compare it with a healthy control group.

Materials and Methods: In a case-control study, we selected a group of IBD patients and healthy controls, and all participants were prepared for a diagnosis of FD symptoms using ROME IV criteria. Data were analyzed and compared using Chi-square and *t*-test, and $P \leq 0.05$ was considered significant.

Results: There were 100 IBD patients, including 91 with ulcerative colitis and 9 with Crohn's disease (mean age, 41.37 ± 13; 39 males, 61 females). Furthermore, 100 healthy control subjects (mean age, 44.23 ± 14; 38 males, 62 females) were analyzed. 10% of IBD patients met the criteria of FD, which was comparable with the controls (5, 5%) ($P > 0.05$). Some of the symptoms of irritable bowel syndrome (IBS) including abdominal pain ($P = 0.01$) and bowel movement ($P = 0.02$) were significantly higher in IBD patients than in non-IBD subjects.

Conclusions: The symptoms of FD were not significantly greater in IBD patients compared to the control group, while IBS symptoms were significantly higher in IBD individuals, indicating a possible overlap of Rome IV IBS and FD.

Keywords: Dyspepsias, functional gastrointestinal disorders, inflammatory bowel diseases

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Introduction

IBD, or inflammatory bowel disease, is a term used to describe a collection of recurring, chronic digestive ailments that include Crohn's disease (CD) and ulcerative colitis (UC). Because of their intricate pathophysiology, which has been connected to changes in the microbiota, intestinal nervous system abnormalities, and innate immune system disorders, these diseases require long-term research and therapy.[1,2]

IBD can overlap with other diseases of the digestive system. Functional dyspepsia (FD) is an illness that reduces the quality of life and is related to mental disorders, irritable bowel syndrome (IBS), heartburn, and somatization. The diagnosis of FD comes with unique limitations.[3-6] FD, along with IBD, causes many complications for the patient and the treatment system, which has been investigated in a limited way until now.[7,8]

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FD is a group of symptoms of the upper digestive system related to the digestive tract. According to reports, FD affects 10%–30% of adults and 3.5%–27% of children.[9] Recent studies have shown that the symptoms of FD include postprandial filling, epigastric distension, pain and burning, early satiety, nausea, and vomiting.[10]

The Rome IV criteria for gastrointestinal illnesses were introduced in 2016 and replaced the Rome III standards created in 2006. In light of recent discoveries in the literature, including new data on microenvironments and interactions between the gut and the brain, the aim of the Rome IV method changed to replace diagnostic tools. The ROME IV criteria's definition of dyspepsia includes the four symptoms of feeling full after eating, feeling full before you are full, experiencing epigastric discomfort, and experiencing epigastric burning. The severity of these symptoms makes daily activities difficult.[11]

Previous studies have assessed the prevalence of FD in specific groups using the ROME I, II, and III criteria. The results of this study cannot be applied to the prevalence of this disease in other populations. It is increasingly important to consider FD in patients with IBD in the Iranian patient population because of inadequate previous evaluation criteria, the need for further study, inconsistent results, and indications for ROME IV included. In this study, the incidence of FD in patients with IBD was assessed and compared with the incidence of FD in a healthy control (HC) group.

Materials and Methods

Study design and participants

This prospective case-control study was conducted between 2021 and 2022 in the gastrointestinal clinic of Al-Zahra Hospital in Isfahan, Iran. In this case-control study, participants were selected for the study based on having IBD or not. The cases included selected patients with IBD in remission. Inclusion criteria included Isfahan residents, no history of gastrointestinal surgery, and no gastrointestinal cancers. Organic gastrointestinal problems, the requirement for surgery, and the refusal to submit to the trial were all exclusion factors. The HC group of participants included healthcare staff and visitors to patients. Citizens of the Isfahan province, no prior gastrointestinal surgery, no IBD, no gastrointestinal diseases, permission to participate in the trial, and age and gender comparable to the patients were the inclusion criteria for HC. Exclusion criteria were comparable to those used in cases of IBD remission. Face-to-face interviews are conducted by a trained interviewer who uses a standardized interview protocol and a standardized set of responses for recording participants' responses. Demographic information (gender, age) for each case and control and anthropometric measurements (height, weight, and BMI) were gathered. IBD patients were also questioned about how long they had it and what medications they took.

Rome IV criteria for this study

According to ROME IV criteria,[11] all participants were prepared for a diagnosis of FD and its subtypes based on epigastric pain, postprandial distress, and also other symptoms of the upper gastrointestinal tract, including belching disorders, heartburn, nausea, vomiting, and IBS symptoms.

Sample size

According to the value of alpha 0.05, the value of beta 0.84, the proportion of controls with exposure (p0) 6.7%, and the proportion of cases with exposure (p1) 5.6%, the sample size has been calculated as 100 in each group (cases and controls).

Statistical analysis

Categorical variables for the characteristics of participants were computed as frequencies (%) for statistical analysis, and continuous variables for the results were given as mean SD. We assessed statistical differences in proportions between patients with IBD in remission and non-IBD illnesses using the appropriate Chi-square and Fisher's exact tests. To compare the mean proportions of the two groups (those with and without IBD), use the Student's *t*-test or the Mann-Whitney U test. The difference was considered statistically significant if the *P* value was less than 0.05. All analyses were carried out using the SPSS version 25.0 statistical software package.

Ethical considerations

Before participating in the study, all subjects provided written informed consent. This work was approved by the Research Ethics Committee of Isfahan University of Medical Sciences in Isfahan, Iran (ethical code: IR.ARI.MUI.REC.1401.023).

Results

Of 100 IBD patients who participated in this study, 91 had UC and 9 had CD. The mean duration of disease in IBD patients was 8.7 ± 7.2 years, and the mean length of using medication was 8 ± 6.7 years. The demographic characteristics of the participants are demonstrated in Table 1. There were no statistically significant differences in age, gender, or BMI between the case and control subjects. The frequency of FD, derived from the ROME IV questionnaire, was not significantly different between IBD patients and the control group (10% vs. 5.5%, $P = 0.3$). Five patients with positive symptoms of dyspepsia had a history of taking mesalamine drug [Table 2]. Statistical analysis showed no relationship between the frequency of FD and IBD characteristics, including the type of disease (UC/CD), injury site, medications, and surgical

Table 1: Comparison of demographic characteristics in patients with IBD (cases) and non-IBD subjects (controls)

Variable	Group		*P*
	Case (*n*=100)	Control (*n*=100)	
Gender			
Female	61	62	0.5
Male	39	38	
Age (mean±SD)	41.37±13	44.23±14	0.13
BMI (kg/m^2)	25.15±4.5	25.67±3.8	0.08

BMI=Body mass index. Derived from Chi-square or Student's *t*-tests

Table 2: The frequency of FD associated with IBD characteristics

IBD characteristics	FD+*	FD-*	*P***
IBD type			
UC	10	81	0.37
CD	0	9	
Injury site			
Pancolitis	4	36	0.91
Left colitis	1	14	
proctosigmoiditis	5	38	
Proctotitis	0	2	
Medication-5ASA			
Mesalamine	5	20	0.15
Asacol	0	1	
Medication-Cytotoxic			
Azathioprine	0	7	0.08
Tacrolimus	4	10	
Cellcept	0	1	
Medication-Biologic			
Remicade	0	6	0.24
Cinnora	3	11	
Surgical history			
Yes	0	17	0.14
No	10	73	

*FD+/-: with or without functional dyspepsia. **Derived from Chi-square

history in patients with IBD [Table 2]. IBS symptoms were reported in 24 IBD patients and six non-IBD subjects. For these participants, the irritable bowel severity scoring system (IBSSS) questionnaire was completed. Among the IBS characteristics during the last 10 days, the frequency of abdominal pain and bowel movement satisfaction was significantly higher in IBD patients than in the non-IBD subjects [Table 3].

Table 3: The comparison of IBS characteristics in IBD (case) and non-IBD (control) subjects in the last 10 days

IBS characteristics	Group		*P*
	Case (100)	Control (100)	
Intensity of abdominal pain			
Without pain	1	2	0.26
Slightly pain	2	3	
Relatively intensive pain	8	1	
Intensive pain	2	0	
Very intensive pain	1	0	
Frequency of abdominal pain			
1 day	3	5	0.01*
2 days	10	1	
3 days	4	0	
4 days	5	0	
7 days	2	0	
Belching			
Nothing	8	0	0.07
Slightly	12	6	
Relatively intensive	1	0	
Intensive	3	0	
Bowel movement satisfaction			
Very satisfied	16	0	0.02*
Relatively satisfied	6	5	
Unsatisfied	1	1	
Very unsatisfied	1	0	
Impact of IBS in life			
No impact	15	3	0.26
Low impact	5	3	
Relatively much impact	4	0	

Derived from IBSSS questionnaire. *Statistically significant

Discussion

This study has established the relative frequency of FD in IBD subjects according to the new Rome IV criteria. The frequency of FD was not significantly different between IBD patients and the control group (10% vs. 5.5%, $P = 0.3$), and none of the patients with CD had FD symptoms ($P = 0.05 \geq 0$). This study is the first report on the prevalence of FD symptoms in individuals with IBD.

The ROME criteria are used to classify functional digestive system disorders and have changed through time and by more contemporary scientific discoveries. Compared to its predecessors, criterion ROME IV was drastically different when it was launched in May 2016. The illnesses affecting the communication between the brain and the intestine are how this version describes the functional diseases of the digestive system. Instead of merely considering the citizens of Western countries, this criterion was developed with the nature of multinational organizations in mind.[12-14]

There are limitations to research on FD. Past research to investigate the prevalence of this disease according to the criteria introduced by ROME in different countries has yet to be investigated simultaneously. Previous studies have examined ROME I, II, and III criteria separately in separate medical centers and specific communities, which have been reported with different prevalence in these studies. The results of these studies cannot be generalized to other diseases and even societies. On the other hand, the various indicators examined in the ROME studies were different. According to the studies conducted according to the ROME III indicators, only seven were found, of which six were conducted in Asia and one was conducted in the United States. The reported prevalence is between 1.8% and 17.5%, which is a vast and unconformable range, which, on the other hand, indicates racial differences in epidemiological and clinical studies.[15-17]

Kotani *et al*. demonstrate that of the 172 UC subjects, 9 (5.2%) met the criteria of FD, which was comparable with the controls (22/330, 6.7%). Also, IBS-like syndromes were more prevalent in patients with UC.[16] In our study, the prevalence of FD was non-significantly low in the IBD patients, and the symptoms of IBS in IBD patients were more severe compared to the control group. However, in the sub-group of IBD patients, such as CD, none were positive for FD. In a systematic review by Ford *et al*., patients with dyspepsia had

a significant increase in prevalence of IBS compared with the control population[6]. Barberi*o et al*.[7] discovered a connection between FD and Rome IV irritable bowel syndrome in other investigations. In this research, 807 people satisfied the Rome IV criteria for IBS at baseline and supplied complete data. The overlap of FD occurred in 446 (55.3%) patients who satisfied Rome IV criteria for IBS at the time of study enrollment. At 12 months, 451 (55.9%) people had been effectively followed up. Individuals with an overlap of IBS and FD were much more likely to contact their primary care physician ($P = 0.001$) or a gastroenterologist ($P = 0.001$) for IBS, and the number of new IBS therapies started was significantly greater ($P = 0.007$). Those with IBS and FD overlap reported considerably more severe IBS symptoms ($P = 0.001$), constant abdominal discomfort, and that their IBS symptoms impeded normal daily activities 50% of the time.[18] In Wang *et al*. study, 3014 patients (52.8% female, 89% response rate) completed questionnaires based on Rome III criteria. 5.0% of the patients had FD-IBS overlap, while 15.2% and 10.9% were classified as FD alone and IBS alone, respectively. The odds ratio of FD among IBS patients was 2.09 (95% CI: 1.68-2.59) compared to non-IBS patients. Patients with FD-IBS overlap showed more outstanding severity scores for the postprandial fullness symptom (2.35 1.49 vs. 1.72 1.59, $P = 0.001$) and overall FD symptom (6.65 2.88 vs. 5.82 2.76, $P = 0.002$).[19]

Conclusion

According to ROME IV criteria, people with IBD were more likely to have FD, while IBS symptoms, such as abdominal discomfort and satisfaction with bowel movements, were much more common in IBD patients. More research is needed to determine whether the worsening of FD and IBS symptoms at the same time contributes to the exacerbation of IBD in patients.

Availability of data and materials

The datasets used or analyzed during the current study are available from the corresponding author upon reasonable request.

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Conflicts of interest

The authors declare no conflicts of interest.

References

1. Torres J, Mehandru S, Colombel JF, Peyrin-Biroulet L. Crohn's disease. Lancet 2017;389:1741-55.
2. de Souza HS, Fiocchi C. Immunopathogenesis of IBD: Current state of the art. Nat Rev Gastroenterol Hepatol 2016;13:13-27.
3. Brook RA, Kleinman NL, Choung RS, Melkonian AK, Smeeding JE, Talley NJ. Functional dyspepsia impacts absenteeism and direct and indirect costs. Clin Gastroenterol Hepatol 2010;8:498-503.
4. Lacy BE, Weiser KT, Kennedy AT, Crowell MD, Talley NJ. Functional dyspepsia: The economic impact to patients. Aliment Pharmacol Ther 2013;38:170-7.
5. Gracie DJ, Bercik P, Morgan DG, Bolino C, Pintos-Sanchez MI, Moayyedi P, *et al*. No increase in prevalence of somatization in functional vs organic dyspepsia: A cross-sectional survey. Neurogastroenterol Motil 2015;27:1024-31.
6. Ford AC, Marwaha A, Lim A, Moayyedi P. Systematic review and meta-analysis of the prevalence of irritable bowel syndrome in individuals with dyspepsia. Clin Gastroenterol Hepatol 2010;8:401-9.
7. Barros LL, Farias AQ, Rezaie A. Gastrointestinal motility and absorptive disorders in patients with inflammatory bowel diseases: Prevalence, diagnosis and treatment. World J Gastroenterol 2019;25:4414-26.
8. Teruel C, Garrido E, Mesonero F. Diagnosis and management of functional symptoms in inflammatory bowel disease in remission. World J Gastrointest Pharmacol Ther 2016;7:78-90.
9. Zhou L, Zeng Y, Zhang H, Ma Y. The role of gastrointestinal microbiota in functional dyspepsia: A review. Front Physiol 2022;13:910568.
10. Drago L, Meroni G, Pistone D, Pasquale L, Milazzo G, Monica F, *et al*. Gastrobiota Group. Evaluation of main functional dyspepsia symptoms after probiotic administration in patients receiving conventional pharmacological therapies. J Int Med Res 2021;49:300060520982657.
11. Drossman DA. Functional gastrointestinal disorders: History, pathophysiology, clinical features and Rome IV. Gastroenterology 2016;150:1262-79.
12. Kamiya T, Osaga S, Kubota E, Fukudo S, Motoya S, Murakami K, *et al*. Questionnaire-based survey on epidemiology of functional gastrointestinal disorders and current status of gastrointestinal motility testing in Asian countries. Digestion 2020;102:73-89.
13. Schmulson MJ, Drossman DA. What is new in Rome IV. J Neurogastroenterol Motil 2017;23:151-63.
14. Ford AC, Mahadeva S, Carbone MF, Lacy BE, Talley NJ. Functional dyspepsia. Lancet 2020;396:1689-702.
15. Aziz I, Palsson OS, Törnblom H, Sperber AD, Whitehead WE, Simrén M. Epidemiology, clinical characteristics, and associations for symptom-based Rome IV functional dyspepsia in adults in the USA, Canada, and the UK: A cross-sectional population-based study. Lancet Gastroenterol Hepatol 2018;3:252-62.
16. Kotani S, Fukuba N, Kawashima K, Mishima Y, Sonoyama H, Okimoto E, *et al*. Prevalence of functional dyspepsia-like symptoms in ulcerative colitis patients in clinical remission and overlap with irritable bowel syndrome-like symptoms. Scand J Gastroenterol 2020;55:560-4.
17. Fang YJ, Liou JM, Chen CC, Lee JY, Hsu YC, Chen MJ, *et al*. Distinct aetiopathogenesis in subgroups of functional dyspepsia according to the Rome III criteria. Gut 2015;64:1517-28.
18. Barberio B, Yiannakou Y, Houghton LA, Black CJ, Savarino EV, Ford AC. Overlap of Rome IV irritable bowel syndrome and functional dyspepsia and effect on natural history: A longitudinal follow-up study. Clin Gastroenterol Hepatol 2022;20:e89-101.
19. Wang A, Liao X, Xiong L, Peng S, Xiao Y, Liu S, *et al*. The clinical overlap between functional dyspepsia and irritable bowel syndrome based on Rome III criteria. BMC Gastroenterol 2008;8:43.