

## Comparative cross-sectional study of comorbid depression in patients with irritable bowel syndrome and chronic gastritis at an urban outpatient clinic

Akaki Burkadze <sup>1</sup>, Eka Burkadze <sup>2,\*</sup>, Tamar Kandashvili <sup>3</sup> and Teimuraz Silagadze <sup>4</sup>

<sup>1</sup> Department of Psychiatry, Tbilisi State Medical University, Tbilisi, Georgia.

<sup>2</sup> Department of Scientific Research, Mental Health Clinic "Mental Hub", Tbilisi, Georgia.

<sup>3</sup> Department of Internal Medicine, Tbilisi State Medical University, Tbilisi, Georgia.

<sup>4</sup> Department of Psychiatry, Tbilisi State Medical University, Tbilisi, Georgia.

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### Abstract

This comparative cross-sectional study evaluates the prevalence of comorbid depression in patients with Irritable Bowel Syndrome (IBS) and chronic gastritis (CG) at an urban outpatient clinic. A total of 178 patients—89 diagnosed with IBS and 89 with CG—were assessed for depressive symptoms using the Beck Depression Inventory-II (BDI-II) and the 21-item Hamilton Depression Rating Scale (HDRS-21). Our findings indicate a significantly higher prevalence of depression in IBS patients, with 71.9% meeting criteria for depression based on the BDI-II and 70.8% based on the HDRS-21, compared to 10.1% in CG patients. The study highlights that retardation symptoms, including depressed mood and loss of interest, are central to depression and contribute to substantial impairment in daily activities and quality of life. Additionally, anxiety and somatization were prominent in the IBS cohort. This study emphasizes the need for integrated care approaches that address both gastrointestinal and psychological symptoms, fostering improved patient management and outcomes. Our results underscore the importance of regular psychological assessments in IBS patients, particularly those without overt depressive symptoms, to enhance their overall well-being.

**Keywords:** Irritable Bowel Syndrome; Depression; Gastrointestinal Disorders; Chronic Gastritis; Hamilton Depression Rating Scale; Beck Depression Inventory.

### 1 Introduction

There has been ongoing interest in the connection between gastrointestinal disorders and mood and anxiety disorders. Numerous clinical and epidemiological studies have identified significant associations between mood disorders and various common gastrointestinal conditions, including Irritable Bowel Syndrome (IBS) (1–4).

IBS is a complex biopsychosocial disorder with an incompletely defined etiology and diverse pathogenesis (5). It is one of the most common gastrointestinal disorders, with a prevalence ranging from 4% to 22% in the general population (6–8). Although the exact pathophysiology of IBS remains unclear, several physiological triggers have been proposed for its onset, including abnormal motility, visceral hypersensitivity, inflammation, autonomic dysfunction, and central nervous system modulation (4,5). Additionally, psychological factors—particularly those related to somatization—are believed to play a significant role and may serve as indicators of IBS onset (8–10).

Because the pathophysiology and causes of IBS are poorly understood, medical management has historically focused on alleviating the most distressing gastrointestinal symptoms, yet, evidence has shown that psychological therapies and

\* Corresponding author: Eka Burkadze

dietary modifications can significantly improve overall symptoms (7–9). Consequently, an integrated care model delivered by a multidisciplinary team is now considered best practice for managing IBS (11–13).

A limited number of clinical studies have reported increased levels of depressive symptoms in specific samples of patients with chronic gastritis (CG). However, several important questions about the relationship between gastritis and mental disorders remain unanswered. First, to the best of our knowledge, no prior epidemiological studies have compared depression levels between patients with IBS and those with chronic gastritis (CG). Furthermore, most existing evidence on IBS and chronic gastritis with comorbid depression originates from high-income countries, with limited research exploring the manifestations of depression in these groups in the South Caucasus region. Therefore, this study aimed to evaluate the prevalence of depression in patients with IBS compared to those with chronic gastritis. Additionally, it sought to explore the relationships between demographic factors, depression severity, and IBS subtypes within the Georgian population.

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## 2 Materials and Methods

The data presented here were collected as part of a comparative cross-sectional study conducted in the Gastroenterology Department of the V. Iverieli Endocrinology, Metabology, and Dietology Center "ENMEDIC" in Tbilisi, capital city of Georgia (population: 1,175,200). This center provides outpatient services to a national population of 3,716,900. All patients aged 18 years and older with IBS who visited the outpatient department between January 1, 2020, and December 31, 2023, were eligible to participate in the study. The study approval was obtained from the Ethics Review Committee.

The minimum sample size for the study was calculated using prevalence data from the literature and the formula:  $N = \frac{Z^2 * P * (1-P)}{d^2}$ , where N is the minimum sample size, P is the estimated prevalence of IBS from the literature (8% or 0.08),  $Z(1-\alpha/2)$  is the constant for a 95% confidence interval in a two-tailed study (1.96), and d is the absolute precision required (0.05 for this study). The calculation yielded a minimum sample size of 86.

Eighty-nine patients with IBS were enrolled in the study after providing informed consent. The control group consisted of 89 age- and sex-matched patients with confirmed chronic gastritis, ensuring comparability between the groups. IBS diagnoses were made using the Rome IV criteria, and the Bristol Stool Scale was employed to assess the clinical form of IBS.

Patients with IBS were further classified according to the Rome IV criteria into the following subtypes: IBS-C (constipation predominant), IBS-D (diarrhea predominant), IBS-M (mixed symptoms), and IBS-U (unsubtyped).

Depression was assessed using the 21-item Hamilton Depression Rating Scale (HDRS-21) and the Beck Depression Inventory-II (BDI-II). The HDRS-21 was administered by trained medical professionals, with depression severity categorized as follows: normal (HDRS score  $\leq 7$ ), mild (8–13), moderate (14–18), severe (19–22), and very severe ( $> 23$ ). The first 17 items of the HDRS were grouped into five factors: "anxiety/somatization" (including items of psychic anxiety, somatic anxiety, gastrointestinal symptoms, general somatic symptoms, hypochondriasis and insight), "mental disorders" (including items of guilt, suicide and agitation), "retardation symptoms" (including items of depressed mood, work and interests, retardation, and genital symptoms), "sleep disturbances" (including items of initial insomnia, middle insomnia, and delayed insomnia) and "weight loss" (14,15).

Patients completed the self-administered Beck Depression Inventory-II (BDI-II) questionnaire, which consists of 21 groups of statements designed to assess depressive symptoms over the past two weeks. Each item was scored from 0 to 3, resulting in total scores that range from 0 to 63. Scores of 14–19 indicated mild depression, 20–28 indicated moderate depression, and 29–63 indicated severe depression.

Data were entered into Microsoft Excel and analyzed using the Statistical Package for Social Sciences (SPSS) software, version 28.0. Results were presented in tables, with categorical data expressed as frequencies and percentages. The Pearson chi-square and Fisher's exact tests were used to compare categorical variables between groups. Independent samples t-test was used to compare the means between IBS and CG patients. A confidence level of 95%, i.e., p-value of less than 0.05 (two-tailed) was considered statistically significant.

### 3 Results

During the study period, a total of 178 patients were recruited. The mean age of the case group was  $51.4 \pm 14.67$  years, while the mean age of the control group was  $43.89 \pm 10.98$  years. Women comprised 59.6% (n = 53) of the study group and 64% (n = 57) of the control group. As shown in Table 1, the 25-44 age group was the most prevalent in both the IBS and CG groups, comprising 42.7% and 62.9%, respectively ( $p < 0.05$ ). Although women were more likely to be diagnosed with IBS, no statistically significant relationship was found ( $\chi^2 = 0.381$ ,  $p = 0.644$ ). In terms of IBS subtype, 7 patients (7.9%) had IBS-D while 82 patients (92.1%) had IBS-C. However, there was no significant difference between the IBS-C and IBS-D groups in terms of HDRS-21 and BDI-II scores.

**Table 1** Sociodemographic characteristics of patients with IBS and patients with CG

Characteristics	IBS (n=89)		CG (n=89)		Total		$\chi^2$	P value
	n	%	n	%	n	%		
Age (years)								
25-44	38	42.70%	56	62.90%	94	52.80%	14.30	0.001*‡
45-64	33	37.10%	30	33.70%	63	35.40%		
65+	18	20.20%	3	3.40%	21	11.80%		
Total (within diagnosis)	89	100.00%	89	100.00%	178	100.00%		
Gender								
Male	36	40.40%	32	36.00%	68	38.20%	0.38	0.644‡
Female	53	59.60%	57	64.00%	110	61.80%		
Total (within diagnosis)	89	100.00%	89	100.00%	178	100.00%		

\*Statistically significant at  $p < 0.05$ ; † $\chi^2$  test; ‡Fisher's exact test.

An independent samples t-test was conducted to compare the BDI-II and HDRS-21 scores between IBS and non-IBS patients. The results indicated a significant difference in scores for both instruments between the two groups ( $p < 0.001$ ). The effect sizes were calculated using Cohen's d, which were 2.06 and 2.03, respectively, indicating a large effect. The results suggest that patients with IBS scored significantly higher than the control group (see Table 2).

**Table 2** Differences between IBS cases and patients with chronic gastritis in terms of BDI-II and HDRS-21 scores

	Group	N	Mean	Std. Deviation	t	df	p	Cohen's d
BDI_II	IBS	89	24.31	14.93	13.79	176	<0.001*	2.06
	CG	89	2.21	2.37				
HDRS-21	IBS	89	17.38	8.92	13.54	176	<0.001*	2.03
	CG	89	4.13	2.38				

\*Statistically significant at  $p < 0.05$ .

The prevalence of depression was calculated in patients with IBS as well as in controls using HDRS (>7) and BDI (>13) cutoff scores. Among patients with IBS, the prevalence was 71.9% according to the BDI-II and 70.8% according to the HDRS. In patients with chronic gastritis, the prevalence was 0% according to the BDI-II score and 10.1% according to the HDRS score.

The mean HDRS-21 score for all patients was  $10.76 \pm 9.29$ . When comparing structural factors, there were no significant differences between patients with and without depression ( $p > 0.05$ ). In all patient groups, the anxiety/somatization score was the highest among the structural factors of the HDRS (see Table 3).

**Table 3** Scores of Hamilton Depression Rating Scale and structural factors of patients with IBS and chronic gastritis

HDRS and Structural Factors	All Patients (n=178)	Patients with Depression (n=143)	Patients without Depression (n=34)
HDRS	10.76 ± 9.29	18.03 ± 8.38	3.80 ± 1.70
Anxiety/Somatization	4.91 ± 3.25	7.49 ± 2.93	2.44 ± 1.08
Mental Disorders	0.98 ± 1.36	1.98 ± 1.35	0.04 ± 0.21
Retardation Symptoms	2.92 ± 3.17	5.29 ± 3.01	0.65 ± 0.67
Sleep Disturbances	1.69 ± 1.76	2.78 ± 1.80	0.65 ± 0.86
Weight Loss	0.25 ± 0.46	0.49 ± 0.55	0.02 ± 0.15

Data present as mean ± SD;  $p > 0.05$

#### 4 Discussion

We evaluated eighty-nine consecutive patients with IBS for the presence of depression and compared the results to those of patients with chronic gastritis. Depression was assessed using the Beck depression Inventory (BDI-II) and Hamilton Depression Rating Scale (HDRS-21) respectively.

The BDI-II is a widely utilized tool for assessing depression, but it has encountered several criticisms. As a self-report instrument, responses can be affected by an individual's current mood or viewpoint, which may result in biased outcomes. Additionally, some individuals might downplay their symptoms due to social stigma or a desire to seem "normal" (16). The BDI primarily targets cognitive and emotional symptoms, which may not encompass the entire spectrum of depressive experiences, including behavioral and social dimensions. It's important to note that while the BDI can signal the presence of depressive symptoms, it is not designed to serve as a diagnostic tool for clinical depression and should be complemented by clinical evaluations. Despite its limitations, the BDI-II is one of the most widely used self-report measures for depression and has shown strong psychometric properties, including validity and reliability.

On the other hand, the HDRS-21 contains items that focus on physical symptoms (such as sleep disturbances and fatigue), potentially skewing results towards the somatic aspects of depression rather than purely psychological factors. Scoring can vary based on the clinician's interpretation of responses, leading to inconsistencies and potential bias. Moreover, it has been criticized for not adequately addressing cognitive components of depression, like hopelessness and self-esteem issues, which are essential for a thorough assessment. Furthermore, the 21-item format can be lengthy and time-consuming for both clinicians and patients, which may hinder its practicality in busy clinical environments. Despite these critiques, the HAMD-21 continues to be a valuable tool for measuring depression severity, particularly when used in conjunction with other assessment methods for a more holistic understanding of a patient's mental health.

The most prevalent age group for IBS was 25-44 years, accounting for 42.7%, with no significant differences observed in the frequency of IBS subtypes by age. This finding is consistent with studies by Maxwell et al. and Tang et al., which noted that IBS can affect individuals across all age groups, including children and the elderly, with no significant differences observed in the frequency of subtypes based on age. Additionally, 50% of patients with IBS report experiencing their first symptoms before the age of 35 (6, 17–19). Furthermore, the prevalence of IBS is approximately 25% lower in individuals over 50 compared to younger individuals (20). This suggests that symptoms may improve over time, challenging the notion that IBS is a chronic lifelong condition. If it were truly chronic, one would expect the prevalence to remain stable or increase with age.

In our study, 59.6% of patients with IBS were female, which aligns with findings from systematic review and meta analyses evaluating 390 papers, involving 188,229 subjects, all of which consistently demonstrated that women are at greater risk for IBS (21). It is important to note that women with IBS typically report more severe symptoms than men (22). The underlying mechanisms contributing to this increased vulnerability related to gender/sex are still largely unclear. Various factors, including mood, stress, gender roles, hormones, and inflammatory mediators, may influence the brain-gut axis. Consequently, the reasons for gender-related differences in IBS are likely multifaceted, involving a combination of environmental, psychological, and biological (sex-based) influences (23).

Our study reveals that 37.1% (n = 33) of IBS patients experienced severe depression, 7.9% (n = 7) had moderate depression, and 27% (n = 24) had mild depression, resulting in an overall prevalence of 71.9%. This rate of depression is significantly higher with significantly higher than that observed in the general population. These findings are consistent with the study by Tomic-Golubovic et al., which reported a depression prevalence of 83.3% among IBS patients (24).

The prevalence rates of depression in patients with chronic gastritis varies across studies, ranging from approximately 20% to 50%, with some studies report even higher rates. In our study, we found that 10.1% of patients with CG experienced depression, which is lower than the findings reported by Goodwin et al. (25).

Anxiety/somatization includes six items: psychic anxiety, somatic anxiety, gastrointestinal symptoms, general somatic symptoms, hypochondriasis, and insight. A cross-sectional study on major depressive disorder (MDD) found that patients with an anxiety/somatization score of 7 or higher experienced more pain symptoms, functional impairments, and a lower quality of life (26). Our study showed IBS patients with depression also have higher anxiety/somatization score ( $7.49 \pm 2.93$ ). Hypochondriasis is a key component of the anxiety/somatization factor in the HDRS scale. Research using the Minnesota Multiphasic Personality Inventory has shown that hypochondriasis is associated with abdominal pain and significantly impairs the quality of life in patients with IBS (27, 28). Patients with IBS who exhibit hypochondriasis may mistakenly believe they have serious organic diseases, leading them to seek frequent medical examinations and wasting valuable healthcare resources (29). Consequently, clinical practice should emphasize the psychological traits associated with hypochondriasis on the HDRS scale in IBS patients, particularly for those who do not display signs of depression, through regular assessments (29).

The second highest scored factor among patients with and without depression was retardation (scores:  $5.29 \pm 3.01$  and  $0.65 \pm 0.67$ , respectively). Retardation symptoms are a core component of depression and include four items: depressed mood, loss of interest in work and activities, psychomotor retardation, and genital symptoms. These symptoms are particularly significant because they often lead to substantial impairment in daily activities, affecting work, relationships, and overall quality of life. By emphasizing these symptoms, healthcare providers can better support patients in managing their depression and improving their overall well-being.

Despite limitations such as a small sample size, hospital-based samples that may represent more severe cases, and a cross-sectional design that restricts the generalizability of our findings, our study results were prospectively collected using two standardized and validated psychiatric tools: the Beck Depression Inventory (BDI-II) and the 21-item Hamilton Depression Rating Scale (HDRS-21). This dual approach provided a more comprehensive assessment of depression for several reasons.

The BDI is a self-report measure that captures the patient's subjective experience of depressive symptoms, while the HDRS is clinician-rated, offering an objective evaluation. This combination allows for a fuller understanding of the patient's condition. Each tool emphasizes different aspects of depression; the BDI focuses more on cognitive and affective symptoms, whereas the HDRS includes physical symptoms. Using both ensures that all relevant symptom domains are assessed.

Combining these measures can also improve diagnostic accuracy by cross-validating findings. Discrepancies between self-reported and clinician-rated symptoms may highlight areas that require further exploration. In research settings, employing both instruments creates a richer data set, facilitating the examination of the nuances of depression across different populations.

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## 5 Conclusion

This study highlights the significant prevalence of depression in patients with Irritable Bowel Syndrome compared with those with chronic gastritis, emphasizing the complex relationship between IBS and mental health. The findings support an integrated care model that combines psychological therapies and dietary changes with traditional treatments. Recognizing demographic factors and the severity of depression in relation to IBS subtypes is essential, especially in under-researched regions like the South Caucasus. There is a critical need for healthcare providers to routinely screen for depression in IBS patients to enhance care and outcomes. Future studies should further explore these relationships across diverse populations to improve treatment decisions.

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## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

### *Statement of ethical approval*

The study protocol was approved by the Ethics Review Committee (N1267251. 25/11/2021). The present research work does not contain any studies performed on animals/humans subjects by any of the authors.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

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## References

- [1] Dunlop DD, Song J, Lyons JS, Manheim LM, Chang RW. Racial/Ethnic Differences in Rates of Depression Among Preretirement Adults. *Am J Public Health*. 2003;93(11):1945-1952. doi:10.2105/AJPH.93.11.1945
- [2] Mawdsley JE. Psychological stress in IBD: new insights into pathogenic and therapeutic implications. *Gut*. 2005;54(10):1481-1491. doi:10.1136/gut.2005.064261
- [3] Whitehead WE, Palsson O, Jones KR. Systematic review of the comorbidity of irritable bowel syndrome with other disorders: What are the causes and implications? *Gastroenterology*. 2002;122(4):1140-1156. doi:10.1053/gast.2002.32392
- [4] Goodwin RD, Cowles RA, Galea S, Jacobi F. Gastritis and mental disorders. *J Psychiatr Res*. 2013;47(1):128-132. doi:10.1016/j.jpsychires.2012.09.016
- [5] Zhang QE, Wang F, Qin G, et al. Depressive symptoms in patients with irritable bowel syndrome: a meta-analysis of comparative studies. *Int J Biol Sci*. 2018;14(11):1504-1512. doi:10.7150/ijbs.25001
- [6] Card T, Canavan C, West J. The epidemiology of irritable bowel syndrome. *Clin Epidemiol*. Published online February 2014:71. doi:10.2147/CLEP.S40245
- [7] Grundmann O, Yoon SL. Irritable bowel syndrome: Epidemiology, diagnosis and treatment: An update for health-care practitioners. *J Gastroenterol Hepatol*. 2010;25(4):691-699. doi:10.1111/j.1440-1746.2009.06120.x
- [8] Choung RS, Locke GR. Epidemiology of IBS. *Gastroenterol Clin North Am*. 2011;40(1):1-10. doi:10.1016/j.gtc.2010.12.006
- [9] Malinen E, Rinttilä T, Kajander K, et al. Analysis of the fecal microbiota of irritable bowel syndrome patients and healthy controls with real-time PCR. *Am J Gastroenterol*. 2005;100(2):373-382. doi:10.1111/j.1572-0241.2005.40312.x
- [10] Cho HS, Park JM, Lim CH, et al. Anxiety, Depression and Quality of Life in Patients with Irritable Bowel Syndrome. *Gut Liver*. 2011;5(1):29-36. doi:10.5009/gnl.2011.5.1.29
- [11] Chey WD, Keefer L, Whelan K, Gibson PR. Behavioral and Diet Therapies in Integrated Care for Patients With Irritable Bowel Syndrome. *Gastroenterology*. 2021;160(1):47-62. doi:10.1053/j.gastro.2020.06.099
- [12] Satylganova A. *Integrated Care Models: An Overview*. Copenhagen: WHO Regional Office for Europe; 2016.; 2016.
- [13] Staudacher HM, Black CJ, Teasdale SB, Mikocka-Walus A, Keefer L. Irritable bowel syndrome and mental health comorbidity — approach to multidisciplinary management. *Nat Rev Gastroenterol Hepatol*. Published online June 2, 2023:1-15. doi:10.1038/s41575-023-00794-z
- [14] Hamilton M. A RATING SCALE FOR DEPRESSION. *J Neurol Neurosurg Psychiatry*. 1960;23(1):56-62. doi:10.1136/jnnp.23.1.56
- [15] Williams JBW. A Structured Interview Guide for the Hamilton Depression Rating Scale. *Arch Gen Psychiatry*. 1988;45(8):742. doi:10.1001/archpsyc.1988.01800320058007
- [16] Stuart H. Reducing the stigma of mental illness. *Glob Ment Health*. 2016;3:e17. doi:10.1017/gmh.2016.11

- [17] Maxwell P, Mendall M, Kumar D. Irritable bowel syndrome. *The Lancet*. 1997;350(9092):1691-1695. doi:10.1016/S0140-6736(97)05276-8
- [18] Tang YR. Age-related symptom and life quality changes in women with irritable bowel syndrome. *World J Gastroenterol*. 2012;18(48):7175. doi:10.3748/wjg.v18.i48.7175
- [19] Seemüller F, Schennach R, Musil R, et al. A factor analytic comparison of three commonly used depression scales (HAMD, MADRS, BDI) in a large sample of depressed inpatients. *BMC Psychiatry*. 2023;23(1):548. doi:10.1186/s12888-023-05038-7
- [20] Lovell RM, Ford AC. Global Prevalence of and Risk Factors for Irritable Bowel Syndrome: A Meta-analysis. *Clin Gastroenterol Hepatol*. 2012;10(7):712-721.e4. doi:10.1016/j.cgh.2012.02.029
- [21] Lovell RM, Ford AC. Effect of Gender on Prevalence of Irritable Bowel Syndrome in the Community: Systematic Review and Meta-Analysis. *Am J Gastroenterol*. 2012;107(7):991-1000. doi:10.1038/ajg.2012.131
- [22] John Britto JS, Di Ciaula A, Noto A, et al. Gender-specific insights into the irritable bowel syndrome pathophysiology. Focus on gut dysbiosis and permeability. *Eur J Intern Med*. 2024;125:10-18. doi:10.1016/j.ejim.2024.03.011
- [23] Heitkemper M, Jarrett M. Irritable bowel syndrome: Does gender matter? *J Psychosom Res*. 2008;64(6):583-587. doi:10.1016/j.jpsychores.2008.02.020
- [24] Tomic-Golubovic S, Miljkovic S, Nagorni A, Lazarevic D, Nikolic G. IRRITABLE BOWEL SYNDROME, ANXIETY, DEPRESSION AND PERSONALITY CHARACTERISTICS. *Irrit BOWEL Syndr*. 22(3).
- [25] Goodwin RD, Cowles RA, Galea S, Jacobi F. Gastritis and mental disorders. *J Psychiatr Res*. 2013;47(1):128-132. doi:10.1016/j.jpsychires.2012.09.016
- [26] Lin CH, Wang FC, Lin SC, Chen CC, Huang CJ. A comparison of inpatients with anxious depression to those with nonanxious depression. *Psychiatry Res*. 2014;220(3):855-860. doi:10.1016/j.psychres.2014.08.048
- [27] Talley NJ, Phillips SF, Bruce B, Twomey CK, Zinsmeister AR, Melton LJ. Relation among personality and symptoms in nonulcer dyspepsia and the irritable bowel syndrome. *Gastroenterology*. 1990;99(2):327-333. doi:10.1016/0016-5085(90)91012-U
- [28] Rey E, García-Alonso MO, Moreno-Ortega M, Alvarez-Sanchez A, Diaz-Rubio M. Determinants of Quality of Life in Irritable Bowel Syndrome. *J Clin Gastroenterol*. 2008;42(9):1003-1009. doi:10.1097/MCG.0b013e31815af9f1
- [29] Lu J, Shi L, Huang D, et al. Depression and Structural Factors Are Associated With Symptoms in Patients of Irritable Bowel Syndrome With Diarrhea. *J Neurogastroenterol Motil*. 2020;26(4):505-513. doi:10.5056/jnm19166