

## Examining the Impact of Anxiety and Depression on Irritable Bowel Syndrome Patients

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### Abstract:

**Background and Aim:** Irritable bowel syndrome (IBS) patients commonly experience psychiatric disorders, such as depression and anxiety. This study aimed to assess the various subtypes of IBS according to the Rome IV criteria, assess anxiety and depressive symptoms in patients with IBS at baseline and also at various phases of follow-up over one year, and see the impact of the treatment of both IBS and associated anxiety and depressive symptoms if present, in the severity of IBS and other psychiatric symptoms.

**Material and Methods:** Seventy patients were recruited in the initial 6 months of the study. Of them, 50 patients continued their follow-ups till the end of the study. A thorough history taking was performed followed by a mental status examination and clinical examination. The Bristol stool chart was used to classify the form of human fecal material. The classification of IBS patients according to the Rome IV criteria was performed as follows: IBS with predominant constipation (IBS-C), IBS with predominant diarrhea (IBS-D), IBS with mixed bowel habits (IBS-M), and IBS unclassified (IBS-U). The patients were then assessed on the Hamilton Rating Scale for Depression (HAM-D)<sup>9</sup> and the Hamilton Rating Scale for Anxiety (HAM-A).

**Results:** The most common physical comorbidity was diabetes mellitus (38%). It was seen that the scores significantly decreased over the time frame, thus showing that adequately treating not only the IBS symptoms but also the concomitant anxiety and depressive symptoms helps in a significant decrease in the IBS severity score and thus improvement in all baseline symptoms. It was seen that there was a significant positive correlation between the IBS severity score and HAM-A and HAM-D scores at most of the time frames, showing that the more severe the symptoms of IBS are, there are more depressive and anxiety symptoms.

**Conclusion:** The presence of anxiety and depressive symptoms in patients of IBS shows the importance of their screening in both psychiatry and GI clinics. The association of the severity of IBS symptoms and HAM-D and HAM-A scores points to a common ground and thus the need for adequate treatment of all domains for a better recovery and improved quality of life.

**Keywords:** Diabetes mellitus, Gastrointestinal disorder, Hamilton Rating Scale for Depression, Irritable bowel syndrome.

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### Introduction

Irritable bowel syndrome (IBS) is a common functional gastrointestinal (GI) disorder that is characterized by alteration of bowel habits, abdominal pain and discomfort, and bloating sensation. The main hypothesis behind IBS is that it is a disorder of the interaction between the GI tract and the brain. It may occur after an infection or after stressful life events. The inflammation caused by these processes may lead to altered bowel habits. [1] The global prevalence ranges from 1.1 to 45% with the female gender being more affected. The interaction between the gut and the brain is a major basis for the co-existence or

causation role of psychological disorders in IBS. The biopsychosocial model explains that psychological factors influence gut physiology by altering sensory threshold, stress reactivity, and gut motility via vagus innervation (top-down model) and in turn abdominal symptoms do have an influence on anxiety and depression (bottom-up model). [2] The role of stressful life events and chronic stressor also plays a role in the pathogenesis of IBS. The research on IBS and psychiatric disorders has shown some interesting light on its clinical picture, genetic basis, and treatment protocols. The Rome criteria that are

used to diagnose IBS are majorly gut restricted and overlook the fact that a majority of patients suffering from anxiety and depressive disorder have symptoms of IBS and vice versa that the majority of IBS patients meet diagnostic criteria for anxiety or depressive disorder.

Several recently published studies have mapped IBS's relationship with psychological disorders and compared depression and anxiety levels in IBS-subtypes. [3-6] However, the relationship between IBS and psychological disorders (depression or anxiety) was inconsistent, even in a recent meta-analysis entailing eight studies. [7] The heterogeneity of the results was too high, with no further analysis of its cause. A systematic review and meta-analysis have shown higher anxiety and depressive symptoms in patients with IBS as compared to controls, [8] but a consideration of a common model where anxiety-depressive symptoms and IBS can be thought of as a single construct is not yet validated. IBS research focusing on symptoms and clinical description is present, but a biology-derived definition and thus its implication on treatment protocols are still scanty.

The major pharmacological treatments indicated by the Food and Drug Administration are majorly targeting the physical symptoms of intestinal secretion and motility and include antispasmodics to treat abdominal pain, peppermint oil, and agents targeting altered bowel habits. The second-line agents include antidepressants such as tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs). It has been seen that these agents mainly decrease the pain component. It has also been seen that treating the associated anxiety and depressive features indeed causes an improvement in the IBS symptoms too, [9] but research focusing on following up these patients prospectively and seeing the impact of conventional treatment strategies over a considerable amount of time is lacking. The trend of anxiety and depressive symptoms vis-à-vis IBS symptoms needs follow-up studies. Therefore, our current study aimed to assess the various subtypes of IBS according to the Rome IV criteria, assess anxiety and depressive symptoms in patients with IBS at baseline and also at various phases of follow-up over 1 year, and see the impact of the treatment of both IBS and associated anxiety and depressive symptoms, if present, in the severity of IBS and other psychiatric symptoms. The uniqueness of the study was that the patients were followed up over a long period of 1 year, and studies in India with such prospective analysis of IBS symptoms are lacking.

## Material and Methods

The study was conducted at the Department of Psychiatry of a tertiary care medical college and hospital in India. Patients aged between 18 years and 65 years and diagnosed with IBS according to the Rome IV criteria were taken for the study after obtaining written informed consent. Patients with other pre-existing GI disorders, patients with GI surgery, and abnormal upper and lower GI endoscopy; patients of chronic medical illness such as chronic kidney disease and diabetes mellitus (DM); and patients taking drugs producing GI symptoms or affecting GI motility were excluded from the study. All patients fulfilling these selection criteria and attending the IBS clinic during the recruitment phase were taken up for the study by purposive consecutive sampling.

A thorough history taking was performed followed by a mental status examination and clinical examination. The Bristol stool chart was used to classify the form of human fecal material. The following investigations were performed at baseline for a comprehensive assessment: complete hemogram, fasting sugar (FBS), urea, and creatinine, liver function tests (LFTs), prothrombin time, international normalized ratio (INR), ultrasonography (USG) of the whole abdomen, upper GI endoscopy (UGIE), and colonoscopy. The classification of IBS patients according to the Rome IV criteria was performed as follows: IBS with predominant constipation (IBS-C), IBS with predominant diarrhea (IBS-D), IBS with mixed bowel habits (IBS-M), and IBS unclassified (IBS-U). The patients were then assessed on the Hamilton Rating Scale for Depression (HAM-D) [9] and the Hamilton Rating Scale for Anxiety (HAM-A) [10] for depressive and anxiety symptoms, respectively. The patients were treated with conventional pharmacotherapy for IBS with concomitant treatment of anxiety and depressive symptoms, as indicated by both pharmacological and non-pharmacological measures. IBS treatment protocol was performed by the gastroenterologist as per symptoms and type of IBS. Anxiety and depressive symptoms were treated by the psychiatrist with SSRIs and/ or TCAs as deemed appropriate. All the patients were then followed up at 4 weeks after the first visit, then at weeks 10, 18, and 30, and then at every 3 months (week 42 and week 54). In every follow-up visit, IBS severity, HAM-A, and HAM-D scores were assessed by trained psychiatrists.

**Statistical analysis:** The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2019) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). Quantitative variables were described as means and standard deviations or median and interquartile range based on their

distribution. Qualitative variables were presented as count and percentages. For all tests, confidence level and level of significance were set at 95% and 5% respectively.

## Results

Seventy patients were recruited in the initial 6 months of the study. Of them, 50 patients continued their follow-ups till the end of the study. This population was taken up for analysis. The age of the patients ranged from 18 years to 65 years with a mean of  $37.5 \pm 12.9$  years. The majority of the study population were male ( $n = 40$ , 80%). Of the total 50 patients, 42 had IBS- (84%), 7 had IBS-C (14%), and 1 of them had IBS-U (2%). Of the 40 males, 32 had IBS-D, and of 10 females, nine had IBS-D. The sociodemographic and clinical characteristics are described in Table 1. The most common physical comorbidity was diabetes mellitus (38%). The majority of the population had stressful life events (68%) and chronic stressors

(64%). The IBS severity, HAM-D, and HAM-A scores were assessed at baseline and subsequently at 4, 10, 18, 30, 42, and 54 weeks. The Kolmogorov-Smirnov test was applied to test normality, and the data were found to be normal. It was seen that the scores significantly decreased over the time frame, thus showing that adequately treating not only the IBS symptoms but also the concomitant anxiety and depressive symptoms helps in a significant decrease in the IBS severity score and thus improvement in all baseline symptoms. Pearson's correlation was used to correlate the various scores at various time frames and is described in Table 2. It was seen that there was a significant positive correlation between the IBS severity score and HAM-A and HAM-D scores at most of the time frames, showing that the more severe the symptoms of IBS are, there are more depressive and anxiety symptoms. IBS-U was not taken for analysis as only one patient belonged to that group.

**Table 1: Distribution of socio-demographic and clinical variables**

Variables	Number	Percentage (%)
Mean Age	$37.5 \pm 12.9$	
<b>Gender</b>		
Male	40	80
Female	10	20
<b>Comorbid conditions</b>		
No comorbidity	27	54
Diabetes mellitus	19	38
Hypertension	3	6
Dyslipidaemia	1	2
<b>Chronic stressor</b>		
Present	32	64
Absent	18	36

**Table 2: Correlation between IBS severity score and HAM-A, HAM-D score at baseline and at various time frames of follow up Correlation between IBS severity score and HAM-A score at various time frames**

Time	r value	P value
Baseline	0.21	0.1
Week 4	0.54	0.03*
Week 10	0.3	0.09
Week 18	0.32	0.07
Week 30	0.40	0.001*
Week 42	0.37	0.02*
Week 54	0.35	0.04*

**Table 3: Correlation between IBS severity score and ham-d score at various time frames**

Time	r value	P value
Baseline	0.33	0.02*
Week 4	0.61	0.002*
Week 10	0.49	0.001*
Week 18	0.48	0.05*
Week 30	0.48	0.003*
Week 42	0.50	0.001*
Week 54	0.46	0.002*

\* Indicate statistically significance at  $p \leq 0.05$

## Discussion

In our study, 50 patients were followed up over 1 year. Standardized guideline for diagnosis of IBS was used with classification according to the Rome IV criteria. The depression and anxiety symptoms were assessed by HAM-D and HAM-A, respectively, which are objective, clinician-rated scales and thus have an advantage over other commonly used self-rated scales. IBS being a functional disorder, there is a chance of over-reporting of symptoms in self-rated scales, which has been clearly avoided using the above-mentioned clinician-rated scales.

The mean age of our study population was 37.5 ± 12.9 years. A large community-based multicentric study from India has reported a mean age of 39.4 years. [11] It has been reported that 50% of the first symptoms of IBS happen before the age of 35 years, but it can occur in any age group from children to the elderly. [12] Our study reported a preponderance of males. The multicentric study by Ghoshal et al. showed that 68% of the IBS patients were males. Male preponderance has been observed in other Indian studies where it ranges from 66% to 87%. [13,14] This male predominance may be due to differing patterns of health-care-seeking behaviour between males and females in our country.

The presence of stressful life event was prominent and also the presence of chronic stressor. The presence of adverse life events in IBS plays an important role. Prospective studies have shown that chronic life stress is the most significant predictor of IBS symptom severity for 16 months. Long-term effects on exposure to stress in early life have shown epigenetic changes. [15] The most common physical comorbidity was diabetes mellitus. A study comparing the prevalence of diabetes mellitus in patients with IBS and healthy controls showed that the incidence of DM is significantly higher in IBS patients. Kabra and Nadkarni found the prevalence of anxiety disorder to be 37.1% in the patients with IBS. [16] Similarly, Modabbernia et al [17] in a study of patients with IBS in Iran found the prevalence of anxiety symptoms in 35.5% of patients.

The majority of our patients had IBS-D (84%). Various studies show a mixed pattern of IBS. The diagnostic criteria used for subtyping varied, and it was seen that the Rome IV criteria when applied to the Asian population showed more of an unclassified type, whereas the Asian criteria were better in assessing subtypes of IBS. This was because of the difference in dietary patterns in the Indian and Western populations with a high fiber content in the Indian population and thus a decreased intestinal transit time. [18] The severity of the anxiety symptoms was assessed by HAM-A.

The mean score at baseline was 27.5, which indicates moderate-to-severe anxiety. The existence of anxiety symptoms has been well described in studies all over the world. The connection between stress, anxiety, and IBS has been researched well. The biopsychosocial approach is linked to the sensation of stress and GI function. In the health-seeking population of IBS, the anxiety symptoms are even more prominent as they represent the more severe spectrum of the disorder. This finding is in agreement with several Indian as well as Western studies. Makharia et al. [19] in a study comparing 184 patients with IBS with 198 normal controls found significantly higher levels of panic and other anxiety syndrome in patients with IBS. Similar findings have also been reported from India by Kabra and Nadkarni. [16] Koloski et al. [14] and Locke et al. [20] have reported similar findings from Western population. Our study also followed these patients over 1 year at time frames of 4, 10, 18, 30, 42, and 54 weeks. It was seen that comprehensive treatment of IBS and associated anxiety symptoms not only caused a decrease in IBS severity but also an associated decrease in anxiety symptoms, which was statistically significant at all time frames.

The depressive symptoms as assessed by HAM-D showed a mean baseline score of 20.5, which indicates moderate-to-severe depressive symptoms. Various biological pathways (kynurenine pathway) can explain this association. [21] Previous Indian studies have also shown that depressive disorders are common in patients with IBS. [10,11,22]

The association between the anxiety and depressive severity and IBS severity scores was performed by correlation. We found a significant positive correlation between IBS severity score and depressive symptom severity from baseline, which implies that as the severity of IBS increased depressive symptoms also increased. With anxiety symptoms, a positive correlation was obtained from baseline, but it did not reach a significant level. However, in subsequent follow-up, it was seen that there is a significant correlation between IBS severity score and HAM-A score. This indicates that as the symptom severity of IBS was higher, anxiety symptoms were also higher. On the other way, as IBS symptom severity decreased there was a significant decrease in anxiety, which was evident in the first follow-up at 4 weeks. This, along with a drop in HAM-A score at week 4 to mild-to-moderate anxiety, points to the fact that treatment in the initial period is helpful to allay the anxiety much. The improvement in anxiety symptoms was pretty faster and more evident than the improvement in depressive symptoms, which took longer time to drop. Van der Veek et al. [23] and Sugaya et al [24] have also reported higher levels of anxiety and depression in patients with IBS in

comparison to healthy controls. Among the etiological models of IBS, there is support for the hypothesis that dysfunction in brain-gut axis plays an important role in the presentation of the condition. [25,26] This hypothesis of IBS has two models. According to the bottom-up model, abdominal symptoms secondarily influence anxiety and depression. As per the top-down model, the psychological factors such as stress, anxiety, and depression themselves influence physiological factors such as motor functions, sensory threshold, and stress reactivity of the gut through vagal and sympathetic afferents. Our findings of elevated levels of anxiety and depression in patients with IBS lend further support to the inseparable role of psychological factors in this disorder. Thus, looking for comorbid anxiety and depression in patients with IBS will not only help in understanding this disease better but also contributes in terms of better treatment outcome.

The link between these symptoms points to the fact that depressive and anxiety symptoms should be assessed thoroughly in patients with IBS. Treating the concomitant symptoms helps in improving the symptoms of IBS also. In a recent study of genome-wide analysis of 53400 people, six genetic susceptibility loci were identified. Of them, four had been associated with anxiety and mood disorders. Thus, shared pathogenic pathways can be the underpinning for the high prevalence of anxiety and depression in IBS patients. [8]

The study is a hospital-based study and is conducted on a clinical sample, and the sample size was low to generalize the findings. Community-based studies on a larger population can be helpful in establishing causality and the association stronger. There is a need for consensus about the evaluation methods of depression and anxiety in IBS patients.

### Conclusion

The presence of anxiety and depressive symptoms in patients of IBS shows the importance of their screening in both psychiatry and GI clinics. The association of the severity of IBS symptoms and HAM-D and HAM-A scores points to a common ground and thus the need for adequate treatment of all domains for a better recovery and improved quality of life. The high prevalence of psychiatric comorbidities such as anxiety and depression in IBS samples in our study provides evidence in favor of proper screening for these disorders in GI clinics. Recognition and treatment for these comorbidities can improve the quality of life as well as overall outcomes.

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