Depression and anxiety associated with functional bowel disorders and its impact on quality of life: A cross-sectional study

ABSTRACT

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Background: Functional bowel disorder (FBD) is conceptualized as a “biopsychosocial disorder.” Psychological factors are important moderators of symptom severity and persistence, treatment seeking and response to treatment. We investigated psychological factors and quality of life (QOL) in patients with FBD. Methods: Seventy patients visiting the department of medical gastroenterology diagnosed as FBD were included in the study. Severity of FBD was rated with FBD Severity Index. The Depression, Anxiety, and Stress Scale was applied and patients were divided into two groups, i.e., with moderate stress (Group A) and with severe stress (Group B). QOL in both the groups was assessed by WHOQOL-BREF Scale. Chi-square, t-test was done to compare the groups. Regression analysis was done to find predictors of poor QOL. Results: Patients of Group B had a longer duration of illness and had higher prevalence of depressive disorder (P = 0.03) in comparison to patients in Group A, who had higher prevalence of anxiety disorders (P = 0.06). Severity of FBD was positively correlated with depression (r = 0.8; P = 0.02). Physical and psychological QOL was significantly impaired in Group B patients having depression (P = 0.02; P = 0.03). Regression analysis showed a positive trend for presence of depressive disorder (P = 0.05), anxiety disorder (P = 0.08) and severity of FBD (P = 0.09) as predictors of poor QOL. Conclusion: In our study, the high prevalence of stress, anxiety and depression in patients with FBD indicates the need for routine screening of such symptoms along with a collaborative and holistic treatment approach. Several etiological perspectives explaining the complex gut–brain interaction are also provided.

Keywords: Anxiety, depression, functional bowel disorder, quality of life, stress

Functional gastrointestinal disorders are common in the general population and one of the most prevalent disorders in patients attending gastroenterology clinic. Based on the Rome III criteria for classification, the rubric of functional bowel disorders (FBDs) includes several groups, namely irritable bowel disorder (IBS), functional bloating disorder, functional diarrhea, and functional constipation.[1] Although considered to be mutually exclusive disorders, there is a high rate of overlap between the groups. FBDs are chronic in nature with a waxing–waning course, and recent studies show a substantial transition among the disorders over time.[2] IBS is a prototype of FBD with symptoms of abdominal pain associated with alteration of bowel habits in the absence of identifiable organic disease to explain the symptoms.[3]

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One in twenty five Indians suffer from FBD. However, studies on patients with FBD are limited. Most studies have focused on patients with IBS, which is the largest diagnostic group among functional gastrointestinal (GI) disorders. The prevalence rate of IBS ranges from 3% to 20% in the US and Europe. It is also common in Japan, China, and India, accounting for 20%–50% of all referrals to gastroenterology clinics. IBS is estimated to affect approximately 11% of the global population. In Western countries, it is reported more frequently by women than men (2:1) in the age group between 20 and 40.

The biopsychosocial model was first applied to IBS by Drossman, emphasizing interactions between biology (e.g., genetic predisposition, disordered gut motility, altered gut microbiota, and low-grade inflammation), behavior (e.g., illness behavior and symptom avoidance), cognitive processes (e.g., brain–gut dysregulation, visceral anxiety, and coping skills), and environment (e.g., trauma and stressful life events). FBDs can be conceptualized as a “biopsychosocial disorder” since psychological factors play an important role as moderators of symptom severity, symptom persistence, decisions to seek treatment, and response to treatment. Gastrointestinal symptoms are well known to occur in relation to fear, anxiety, and stress. The gut motility is reactive to changes in the emotional state, and stress affects both motility and visceral hypersensitivity.

Psychiatric disorders are common in FBD with a prevalence of 42%–61%, particularly in severe or refractory cases. The most prevalent diagnoses include anxiety disorders, mood disorders (including major depression), and somatoform disorders, such as pain and somatization disorders. The onset of psychiatric illness often predates or coincides with the onset of bowel disorder. Conversely, symptoms of FBD have been reported in 30%–70% of patients with psychiatric disorders. Community studies comparing psychological profiles of consultants, nonconsultants, and controls demonstrated higher anxiety and depression scores in IBS consulters than either counterpart. The health-related quality of life (QOL) of IBS patients is similar to that of patients with diabetes mellitus, cancer, and end-stage renal disease and is poorer compared to general population.

The present study sought to investigate psychological factors (stress) and psychiatric comorbidities (viz. depression and anxiety) and their impact on QOL in patients with FBD. In addition to FBD, the impact of psychological variables on QOL was also explored. The findings from our study can have important clinical implications in terms of the following. Screening of FBD patients attending medical gastroenterology clinic can be useful to rule out cases of depression and anxiety. The information gathered may contribute to more integrative, holistic, and efficient management of patients with FBD. Furthermore, in spite of the presence of psychosocial disturbances in this group of patients, clinicians are often poorly trained or poorly motivated to deal effectively with such issues. Further, in contrast to majority of previous studies which focused on patients with IBS alone, we chose to include a broad group of patients with FBD for greater generalizability of findings. Moreover, there is dearth of studies on Indian population in this area.

METHODS

The study was a cross-sectional one conducted in the department of psychiatry and the department of gastroenterology of a tertiary care hospital. Institute ethical committee clearance was taken before the onset of the study. All adult patients of the age group of 18–50 years, belonging to both sexes, diagnosed as FBDs which included IBS (diarrheal type, constipation type, mixed type), functional bloating, functional dyspepsia, functional belching, and unspecified FBD were included in the study. Patients recruited for the study were first diagnosed clinically by an expert medical gastroenterologist in the outpatient department of medical gastroenterology and later referred for psychiatric consultation. The diagnosis of FBD was based on Rome III criteria, and all organic causes were ruled out by investigations such as endoscopy, colonoscopy, and ultrasonography by the consultant medical gastroenterologist. All patients who gave consent for the study underwent psychiatric evaluation. Patients who did not give consent for psychiatric evaluation or diagnosed to have a past history of psychiatric disorder were excluded from the study.

Sample size calculation was done using the formula, 

\[ n = Z^2 \times (1 - P) / \alpha^2 \times (1 - \beta) \]

where \( Z = 1.96 \) (for a 95% confidence level), \( \alpha = 0.01 \), and \( \beta = 0.01 \), and a sample size around 60 was considered to be adequate. A total of 75 patients who fulfilled the criteria of FBD during the period of January 2016 to June 2017 were included in the study. However, final sample and analysis included seventy patients who consented for the study, as three patients dropped out of the study and two of them had a past psychiatric history. None of the patients had a positive family history of psychiatric disorders. A study-specific sociodemographic and clinical profile was prepared, which also included the dietary habits of the patients. Patients were assessed with the FBD Severity Index (FBDSI), a brief self-rating scale. The 21-item Depression, Anxiety, and Stress Scale (DASS-21) was administered to screen those patients for depression, anxiety, and their current stress level. DASS-21 has a definite

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scoring pattern with three subscales for anxiety, depression, and stress which are categorized as mild, moderate, severe, and extremely severe. A validated Tamil version of DASS 21 was used as patients predominantly spoke Tamil.[33,34] Patients were subsequently divided into two groups: moderate stress group (Group A) and severe stress group (Group B) based on their stress score on DASS-21. Patients having higher levels of anxiety and depression on DASS-21 were further evaluated by the consultant psychiatrist for the presence or absence of anxiety and depressive disorders using ICD-10 criteria. Furthermore, patients diagnosed with depressive and anxiety disorders were treated with pharmacotherapy and /psychotherapy, as required, and followed up in the psychiatric OPD as per protocol. Finally QOL was assessed in both patient groups using the WHOQOL-BREF Scale.[35]

Statistical analysis was done using SPSS version 21.0. (SPSS Inc., Chicago, IL, USA). Descriptive statistics was used to describe both the groups. Chi-square test was used to compare the two groups of patients on anxiety, depression and QOL. Spearman's rank-order correlation was used to find the association between severity of FBD symptoms and psychiatric diagnosis. Regression analysis was done to find the predictors of poor QOL. P < 0.05 was considered as statistically significant.

RESULTS

The mean age of the cohort was around 39 years. Most of the patients were married (88%) and belonging to middle and lower socioeconomic status (86%) and hailing from rural background (68%). Most of them were nonvegetarian (63%) and on high protein and carbohydrate diet. The mean duration of symptoms was 3.75 years (range 3 months to 6.2 years). The cohort of patients suffering from FBD was divided into two groups based on the level of stress experiences as measured by DASS-21. Group A, consisting of 42 patients, had moderate level of stress on DASS-21, whereas Group B consisting of 28 patients had severe level of stress on DASS-21. Both the groups were fairly matched in terms of sociodemographic profile, i.e., age of patient, gender ratio, marital status, area of domicile, and meal preference.

In relation to clinical profile, patients in Group B had a longer average duration of illness in comparison to Group A. Irritable bowel syndrome was the most frequent diagnosis in both the groups, followed by functional dyspepsia [Table 1]. The patients in both the groups were screened for anxiety and depressive symptoms using DASS-21, and patients screened positive were referred to a consultant for further detailed clinical assessment.

| Table 1: Comparison of sociodemographic and clinical characteristics of the sample |
|-----------------------------------|---------------------------------|---------------------------------|---------------------------------|
| Variables                          | Total sample (patients with FBD) | Patients with mild-to-moderate stress on DASS-21 (Group A) | Patients with severe stress on DASS-21 (Group B) |
| Age of patient, mean±SD            | 38.95±10.60                      | 38.50±10.92                      | 39.45±10.27                      |
| Sex (male:female)                  | 2:1                             | 2:1                             | 1.5:1                           |
| Marital status (percentage of patients married) | 88                              | 86                              | 92                              |
| Area of domicile (percentage of patients in rural areas) | 69                              | 66                              | 72                              |
| Meal preference (percentage of patients taking nonvegetarian diet) | 63                              | 65                              | 60                              |
| Duration of symptoms in years (range) | 3.8 years                      | 3.2 years (3 months-3 years)    | 4.3 years (6 months-6.2 years)  |
| Severity of FBD (n)                |                                 |                                 |                                 |
| Mild                               | 12                              | 10                              | 2                               |
| Moderate                           | 18                              | 12                              | 6                               |
| Severe                             | 40                              | 20                              | 20                              |
| Diagnosis of functional bowel disorder, n (%) | 50 (71.4)                      | 30 (15D, 10C, 5M)               | 20 (10D, 8C, 2M)                |
| Irritable bowel syndrome           | Functional bloating             | 4 (5.71)                        | 2                               |
| 4 (4.28)                           | Functional belching             | 12 (17.14)                      | 4                               |
| Functional dyspepsia               | Unspecified FBD                 | 1 (1.43)                        | 0                               |
| Psychiatric symptoms, n (%)        | Anxiety symptoms                | 37 (52.8)                       | 25 (59.5)                       | 12 (42.8)                       |
| Depression symptoms                | 29 (41.4)                       | 15 (35.7)                       | 14 (50.0)                       |
| Psychiatric diagnosis, n (%)       | Anxiety disorder                | 28 (40)                         | 20 (47.6)                       | 8 (18.6)                        |
| Depression disorder                | 20 (28.6)                       | 10 (23.8)                       | 10* (25.7)                      |

*3 patients had moderate depression; No patient had severe depression. D – IBS-diarrheal subtype; C: IBS-constipation subtype; M: IBS-mixed subtype; IBS – Irritable bowel disorder; SD – Standard deviation; FBD – Functional bowel disorder; DASS – Depression, Anxiety, and Stress Scale
for the presence of anxiety and depressive disorder based on ICD-10 criteria. Group A had higher anxiety disorder (47.6%) in comparison to Group B (28.6%), whereas Group B had higher depressive disorder (35.7%) in contrast to Group A (23.8%) [Table 1]. While comparing both the groups in terms of anxiety and depressive disorders, depression was higher in Group B, which was statistically significant ($P = 0.03$), whereas anxiety disorder was higher in Group A, but not statistically significant ($P = 0.06$) [Table 2]. The severity of FBD as measured by FBDSI was directly correlated with depression in these groups of patients ($r = 0.8; P = 0.02$). The physical and psychological domain of the WHOQOL-BREF Scale was significantly affected in Group B in patients having syndromal depression ($P = 0.02; P = 0.03$) [Table 3].

Odds ratio and confidence interval for prediction of poor QOL in patients with FBD were calculated as using variables such as duration of illness, severity of functional bowel disease, presence of anxiety, and depressive disorder. There were no statically significant predictors of poor QOL; however, the presence of depressive disorder ($P = 0.05$), presence of anxiety disorder ($P = 0.08$), and severity of FBD ($P = 0.09$) showed a positive trend [Table 4].

DISCUSSION

In contrast to some similar previous Western studies, our findings showed a male preponderance and older age group of patients which may be a specific sociocultural phenomenon of this part of the subcontinent. A heterogeneous sample of patient representation may also contribute to this as our study included all subtypes of FBD, whereas previous studies mainly focused on IBS. Most of our patients were married considering their age group and the fact that they hailed from a rural community and a traditional society like ours. This distinct socioeconomic and cultural background could also be responsible for lower representation of female patients in our sample. Most women belonging to such communities may be homebound with limited opportunity to access health-care services.

Our results found all FBD patients to be experiencing stress symptoms, which in agreement with most previous researches emphasizes the strong association of psychological stress with overall symptoms of FBD irrespective of subtype. Stress is known to play an important role in precipitation, predisposition, maintenance, and worsening of IBS symptoms as well as its clinical outcome. IBS patients report more lifetime stressful events and early life exposure to stressors and show greater reactivity to stress. The gastrointestinal tract and gut functioning are very susceptible to stress, which can disrupt the gut–brain pathway to produce FBD symptoms. It is widely reported that adverse psychological factors impact intestinal sensitivity, motility, secretion, and permeability. This is because the central stress response system regulates behavioral, neuroendocrine, and autonomic responses to stress through the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic nervous system (SNS). Hyperactivation of this pathway is involved in the pathophysiology of FBD [Figure 1]. Psychological interventions are known to improve IBS and other GI symptoms by thereby altering this circuitry. Following such interventions, psychological distress and QOL are also said to improve possibly due to improved bowel functioning.

Our findings on impaired physical and psychological QOL in patients with severe grade of FBD and severe levels of stress are similar to several previous studies. Symptoms of bowel disorder have a significant psychosocial impact.

Table 2: Comparison of anxiety and depressive disorder across the groups

| Variables          | Group A (n=42), n (%) | Group B (n=28), n (%) | $\chi^2$ | df | P  |
|--------------------|-----------------------|-----------------------|----------|----|----|
| Anxiety disorder   |                       |                       |          |    |    |
| Present            | 20 (47.62)            | 8 (28.57)             | 5.69     | 2  | 0.06|
| Absent             | 22 (52.38)            | 20 (71.42)            |          |    |    |
| Depressive disorder|                       |                       |          |    |    |
| Present            | 10 (23.81)            | 10 (35.71)            | 11.60    | 2  | 0.03*|
| Absent             | 32 (76.19)            | 18 (64.28)            |          |    |    |

*P<0.05
on person’s general well-being and daily functioning. IBS patients are reported to have an impaired health-related QOL that is comparable to other patients with chronic medical and psychiatric disorders. The QOL of patients with IBS is said to be closely related to disability, health-care resource utilization, and clinical response to treatment. Other factors known to affect QOL include extra-intestinal symptoms, psychiatric symptoms, and disease severity, as observed in our study.

Our study showed a 28–40% prevalence of psychiatric morbidity related to depression and anxiety in the FBD group which supports earlier findings. However, the prevalence or rate of psychiatric morbidity in our study is lower than some previous Western studies. Higher prevalence could be due to the inclusion of patients with functional GI disorders in some earlier studies, whereas our study population (FBD) included a subgroup of it. Few other studies, however, mentioned that in 30–90% of IBS patients, psychological symptoms were severe enough to warrant a comorbid psychiatric diagnosis, and our results fall within this range. Our study also showed that greater level of stress was associated with more severe depressive symptoms and poorer QOL as reported by previous studies.

The relationship between psychological distress and FBD can be conceptualized in light of the following. First, the “gut” and “brain” communicate in an integrated bidirectional fashion, mainly through autonomic nervous system (ANS) and HPA axis. Within central nervous system (CNS), gut is controlled by the limbic system, which also plays a key role in emotionality and associated physiological changes. Known as the region of “mind/body interaction,” limbic system is also involved in the “top–down” modulation of visceral pain and visceral perception. Altered limbic functioning or impaired ANS regulation may contribute to brain-gut dysregulation resulting in psychiatric symptom evolution and exacerbation along with FBD. The neuroimmune pathways via interleukins and C-reactive proteins are said to play a vital role in interacting with the ANS and the HPA axis. Second, serotonin (5-HT), an important neurotransmitter in the enteric nervous system as well as CNS, activates and inhibits pain pathways and initiates peristaltic reflex. Altered autonomic regulation and extraintestinal symptoms, reported in FBD patients, indicate a generalized CNS dysfunction. Therapies targeting CNS serotonergic transmission (antidepressants and anxiolytic) have shown efficacy in treating symptoms associated with IBS. Third, FBDs involve a disruption in the microbial flora of the gastrointestinal tract. The gut microbiome contributes to CNS activity via pro- and anti-inflammatory cytokines. Disruption of this flora plays a significant role in the etiology of FBD. Hence, the current model of FBD is renamed “microbiome–gut–brain axis” dysregulation [Figure 1].

In our study, the “severe stress” group of patients (Group B) was characterized by higher prevalence of depressive disorder, greater symptom (FBD) severity, and significantly impaired QOL. Previous research has shown that stress is associated not merely with onset of IBS but also with more severe symptoms. Psychological distress experienced as symptoms of anxiety and depression is said to be more frequent and intense in IBS patients, which is our predominant population, and to be associated with more gastrointestinal symptoms, disability, and QOL impairment. Moreover, symptoms of anxiety and depression can precede the onset of symptoms of bowel disorder and further worsen due to difficulties of coping with a chronic fluctuating condition. This fact is also supported by neuroimaging studies in IBS patients, showing that such patients have alterations in circuits related to emotion, pain modulation, and interpretive information processing. Studies with positron emission tomography and functional magnetic resonance imaging showed that IBS patients had greater activation of the anterior cingulate gyrus and thalamus in response to painful distension than nonpainful stimulation. Increased activation of amygdala and decreased activation in several prefrontal areas of IBS patients were reported in quantitative meta-analysis studies.

Our study has direct implications for clinical practice. It calls for collaboration between medical gastroenterologists and psychiatrists to diagnose FBD patients with comorbid psychiatric disorders. This collaboration will lead to the timely treatment for the psychological symptoms and will improve patient’s QOL.
and behavioral medicine specialists in outpatient clinics to facilitate effective evaluation, referrals, and treatment, reduce disease stigma, and promote the use of simple standardized screening tools and emphasizes the importance of biopsychosocial model in FBD. One of our methodological strengths was the careful inclusion of true cases through endoscopic and other investigative procedures by a consultant gastroenterologist. Furthermore, there is greater generalizability of findings as we included a more heterogeneous group of patients with FBD instead of patients with IBS alone.

**Limitations**

The study did not use a comprehensive psychiatry rating scale like MINI[7] to assess other psychiatric comorbidities associated with FBD. However, it would not have been feasible to administer a lengthy scale in an outpatient set up. Also, we sought to detect most common conditions like anxiety and depression using a simple screening tool with high precision. Such screening tools can be easily applied and interpreted by a gastroenterologist or any other nonpsychiatric professional treating such disorders. Another limitation of our study was that we did not conduct a follow-up study in these patients further to explore the relationship between improvement in psychiatric symptoms and corresponding changes in QOL in them.

**CONCLUSION**

All FBD patients in our study reported experiencing stress, ranging from mild to severe. Severe stress levels were found to be associated with severe grade of FBD and longer duration of illness as well as significant impairment in physical and psychological QOL. Nearly half of the FBD patients with mild-to-moderate stress were found to have anxiety disorder, whereas approximately one-third of those with severe levels of stress were found to suffer from depressive disorder. The prevalence of anxiety and depressive disorders in our study population was 40% and 28%, respectively. Our study findings have important future implications for planning necessary assessment and intervention in this group of patients. This will enable an integrated and collaborative approach to manage a chronic and relapsing condition like FBD, which remains a treatment challenge for health professionals. Future research may conduct longitudinal studies to understand the long-term course of FBD symptoms, their interaction with psychiatric comorbidities, focus on neurobiological aspects and investigate relevant biomarkers.

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**Conflicts of interest**

There are no conflicts of interest.

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