

# Clinical Predictors of Depression among Patients with Inflammatory Bowel Diseases: A Cross-sectional Analytical Study from Oman

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## ARTICLE INFO

### Article history:

Received: 17 April 2021

Accepted: 1 September 2021

### Online:

DOI 10.5001/omj.2022.48

### Keywords:

Depression; Cross-Sectional Studies; Patient Health Questionnaire; Colitis, Ulcerative; Crohn Disease; Prevalence; Oman.

## ABSTRACT

**Objectives:** Many studies suggest that depression is prevalent among patients suffering from inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC). Both depression and IBD have a significant disease burden. However, these studies have mostly been conducted among European and American populations and there is a paucity of studies from Arab countries. This study aimed to examine the prevalence and predictors of depressive symptoms among adult IBD patients attending a tertiary care hospital in Muscat, Oman. **Methods:** We conducted a cross-sectional study among a random sample of patients aged  $\geq 18$  years who attended the gastroenterology clinic at Sultan Qaboos University Hospital, Muscat, Oman, between June 2018 and January 2019. Participants were asked to complete the Patient Health Questionnaire-9, which is used to assess depression, and a sociodemographic survey. Logistic regression analysis was used to identify the independent predictors of depressive symptoms among the study sample. Adjusted odds ratios (aORs) were also reported. **Results:** This study included 201 participants, with an average age of 36 years. Just over half (51.2%) of participants were female. The mean duration of the patients' IBD diagnosis was  $1.9 \pm 0.3$  years, the majority ( $n = 174$ , 86.6%) of the participants had UC, 80.1% ( $n = 161$ ) of the participants had received steroids, and 5.5% of the sample had a history of a surgical stoma. The medical comorbidities among the participants were cerebrovascular accidents (24.9%), hypertension (24.5%), and diabetes mellitus (23.9%). The prevalence of depressive symptoms was 23.4%. The logistic regression analysis resulted in four independent predictors of depression: being female (OR = 2.090,  $p = 0.047$ ), history of surgical stoma (OR = 5.737,  $p < 0.001$ ), comorbid diagnosis of hypertension (OR = 2.846,  $p = 0.007$ ), and history of a cerebrovascular accident (OR = 2.651,  $p = 0.011$ ). **Conclusions:** Depressive symptoms are prevalent among Omani patients with IBD. Certain clinical factors appeared to increase the risk of depression among this population. The findings of this study fill a gap in the existing literature and call for further work aiming at screening and managing depression among IBD patients.

Depression is a serious mental health condition characterized by the loss of interest in activities that an individual usually enjoys, persistent feelings of sadness, and effects on their daily functioning.<sup>1</sup>

Depression is one of the most common psychiatric disorders, with a high burden on an individual's health and wellbeing, with an overall decreased overall quality of life, high treatment costs, impact on family life, and reduced productivity at work.<sup>2</sup>

Inflammatory bowel disease (IBD) is a broad term used to describe a group of inflammatory conditions of the gastrointestinal (GI) tract, including Crohn's disease (CD) and ulcerative colitis (UC).<sup>3</sup> IBD is incurable and has a relapsing and remitting course, negatively impacting the quality of life. The prevalence of IBD in North Africa and the Middle East is expected to increase by 2.3-fold between 2020 to 2035.<sup>4</sup> The prevalence of depression is higher among patients with chronic diseases than in the

general population. Therefore, having a long-term medical illness is a risk factor for depression.<sup>2</sup> There is evidence that IBD is associated with higher rates of depression compared to the general population. One study showed that the prevalence of depression among an IBD population ranged from 15%–30%.<sup>5,6</sup> According to the current literature, symptoms of depression are commonly associated with increased disease activity and reduced quality of life among patients with IBD. Therefore, it can be surmised that IBD and depression might share a common environmental, behavioral, or genetic etiology. There are several possible explanations for the concurrence of depression and IBD.<sup>7</sup> Some evidence suggests that psychological stress may impact neuro-enteric pathways, mediating, and enhancing gastrointestinal inflammation. Conversely, psychological distress may be secondary to disease activity and/or potential side effects of treatment (e.g., corticosteroids).<sup>8,9</sup> The neurobiological risk factors associated with depression among IBD patients include IBD-related inflammation, abdominal pain, and sleep disturbance.<sup>2</sup> With regards to prognosis, two national Canadian surveys showed that 17% of patients with IBD, also suffering from depression, and had suicidal ideation in the past 12 months.<sup>10</sup>

Evidence also suggests that depression is associated with more aggressive forms of IBD.<sup>8</sup> Other psychological factors are also important to consider in patients with IBD, such as illness perceptions and coping with the disease. These factors are related to psychosocial outcomes and could impact the course of IBD.<sup>11,12</sup> Several factors seem to increase the risk of depression and IBD comorbidities. One study has suggested an increased risk of depression among IBD patients who are older, have more severe and active disease, have had surgery, have a stoma, and among those with a poor socioeconomic status.<sup>13</sup> It is vital to identify those at higher risk of developing psychological ailments, such as depression so that they can be offered the appropriate treatment and support, which could lead to improved overall outcomes and quality of life.<sup>12</sup>

Notably, there is a dearth of studies exploring the comorbidity of IBD and depression worldwide. This gap in the literature calls for efforts to quantify the magnitude and determinants of depression among IBD patients in this region. Therefore, we sought to determine the prevalence of depression among adult patients with IBD attending a tertiary care

gastroenterology clinic in Muscat, Oman, and to explore the clinical and sociodemographic factors associated with depression.

## METHODS

This cross-sectional study was conducted at a gastroenterology clinic at Sultan Qaboos University Hospital (SQUH), Muscat, Oman, from June 2018 to January 2019. The gastroenterology clinic at SQUH accepts referrals from secondary healthcare facilities across Oman, where healthcare services are universally free for all citizens. Healthcare services in Oman are divided into primary, secondary, and tertiary care. There are several primary healthcare centers spread throughout the country, and patients that cannot be seen at a primary care center are referred to secondary or tertiary care centers.

In this study, all patients aged  $\geq 18$  years that met the standard criteria for CD and/or UC based on a combination of investigations (including clinical, biochemical, stool, endoscopic, imaging, and histopathology reports) and attended their regular appointment at the gastroenterology clinic during the study period were eligible for inclusion in the study. The diagnosis of CD and UC was based on the third European Evidence-based Consensus on Diagnosis and Management of Crohn's disease and Ulcerative Colitis.<sup>14</sup> Patients with pre-existing psychiatric disorders (mood disorders, psychosis, dementia, and intellectual disability) diagnosed before their IBD,  $< 18$  years of age, and those who did not consent were excluded from the study.

The required sample size was calculated using MedCal software. Based on the prevalence of depression among patients with IBD in a previous study,<sup>15</sup> allowing for a 5% type I error and 80% power, the minimum sample size was calculated as 177. Taking into consideration a 20% attrition rate, including non-completed questionnaires and unsigned consent forms, we recruited 213 participants. A simple random sampling method was used to recruit the study participants from the list of patients expected to attend the gastroenterology clinic during the study period. Randomizer software generated a list of participants. Those who were selected randomly and did not meet the inclusion criteria or opted not to participate were substituted with the next randomly selected participant until the required sample size was met.

Data collection took place while the patients attended their gastroenterology clinic appointments. All the questionnaires were available in both English and Arabic. The instructions were given clearly, aided by a single investigator who assisted the participants, especially those who were illiterate, to ensure that the study participants understood the questionnaires' content and were asked to sign a consent form. All patients were assured in writing that their participation would remain anonymous and voluntary, that the data gathered would be aggregated, and that they could withdraw from the study at any time. All of the questionnaires were given a study number to ensure the anonymity of the recruited participants; all measures were taken to ensure confidentiality.

A sociodemographic questionnaire comprising questions regarding the participant's full social and medical history was designed. We collected data relating to age, sex, marital status, highest educational level attained, occupation, smoking status, type of IBD (UC or CD), duration of diagnosis, exposure to IBD medical therapies, including treatment with steroids, medical comorbidities, history of a surgical stoma, and need for surgery.

Patient Health Questionnaire-9 (PHQ-9) is a multipurpose, self-reported questionnaire that has been validated and found reliable for use in screening, diagnosing, monitoring, and measuring the severity of depressive symptoms. It contains items derived from the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition.<sup>16</sup> The frequency of symptoms is rated, which is included in the scoring severity index. PHQ-9 is brief and a useful tool in clinical practice.<sup>17</sup> A PHQ-9 score  $\geq 10$  has a sensitivity and specificity of 88% for major depression,<sup>18-20</sup> for which the calculated Cronbach's alpha (0.76), showed an acceptable reliability level. In 2014, Al-Ghafri et al,<sup>21</sup> conducted a study to examine the diagnostic validity of the Arabic version of PHQ-9 using an Omani medical resident population to establish a cut-off point. The cut-off score of 12, rather than 10, on the PHQ-9 resulted in best trade-off with a sensitivity of 80.6% and a specificity of 94.0% for detecting the presence of depressive symptoms.<sup>21</sup> Therefore, we used the Arabic version of the PHQ-9 with score of 12 and above to define case-ness.<sup>22</sup>

Descriptive statistics, including frequency, percentage, mean, standard deviation, median,

and range, were used to report the patients' profiles according to their sociodemographic and clinical factors. Participants who scored  $\geq 12$  on the PHQ-9 were considered depressed. Next, univariate comparison between the depressed and non-depressed group was evaluated using odds ratios (ORs), chi-square, Fisher's exact test, and the independent *t*-test to determine associations differences between the demographic and clinical variables. Following this, multivariate logistic regression (backward Wald) was used on univariate analysis variables with  $p < 0.050$ , to identify the independent predictors associated with depression. Data were analyzed using IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, N.Y., USA), set at a 5% significance level.

This work was granted ethics approval by the College of Medicine and Health Sciences at Sultan Qaboos University, Muscat, Oman (MREC#1836). Written informed consent was collected from all participants. The study was conducted following the Declaration of Helsinki and the American Psychological Association, regarding ethical human research, concerning confidentiality, privacy, and data management.

## RESULTS

A total of 201 participants returned completed questionnaires and signed consent forms, giving a response rate of 94.4% (201/213), which was achieved by explaining the study clearly to the participants, highlighting the relevance of conducting the research, and supporting the respondents during the process of data collection while ensuring privacy and confidentiality.

The average age of the participants was  $36.2 \pm 9.1$  years, ranging from 20.0 to 60.0 years [Table 1]. Using the PHQ-9, the prevalence rate of depressive symptoms in this cohort was 23.4% ( $n = 47$ ). Of the total sample, 51.2% were females. Regarding education level, 58.7% ( $n = 118$ ) of the participants had a diploma or below, and  $> 67.7\%$  ( $n = 136$ ) were working. The average time they had lived with their diagnosis was  $1.9 \pm 0.3$  years, and the majority (86.6%,  $n = 174$ ) had UC, took steroids (80.1%,  $n = 161$ ), and some had a history of surgical stoma (5.5%,  $n = 11$ ). The participants had multiple comorbidities, including cerebrovascular accidents (24.9%), hypertension (24.5%), and diabetes mellitus (23.9%).

**Table 1:** Sociodemographic and clinical factor of the study subjects.

Variables	n (%)
<b>Sociodemographic factors</b>	
Gender	
Female	103 (51.2)
Male (ref)	98 (48.8)
Marital status	
Married	131 (65.2)
Divorced/widowed/single (ref)	70 (34.8)
Age, years	
Mean $\pm$ SD	36.2 $\pm$ 9.1
Median (range)	35.0 (20.0–60.0)
Educational level	
High school or below	56 (27.9)
Diploma	62 (30.8)
Under/post-graduate (ref)	83 (41.3)
Job	
Unemployed	65 (32.3)
Employed (ref)	136 (67.7)
Smoking	
Yes	58 (28.9)
No (ref)	143 (71.1)
<b>Clinical factors</b>	
Disease diagnosis	
Crohn's disease	27 (13.4)
Ulcerative colitis (ref)	174 (86.6)
Years since diagnosis	
Mean $\pm$ SD	1.9 $\pm$ 0.3
Median (range)	2.0 (1.0–2.0)
Steroids use	
Yes	161 (80.1)
No (ref)	40 (19.9)
History of a surgical stoma	
Yes	11 (5.5)
No (ref)	189 (94.5)
Hypertension	
Yes	49 (24.5)
No (ref)	151 (75.5)
Diabetes mellitus	
Yes	48 (23.9)
No (ref)	153 (76.1)
Cerebrovascular accident	
Yes	50 (24.9)
No (ref)	151 (75.1)
Hypothyroidism	
Yes	46 (22.9)
No (ref)	155 (77.1)

SD: standard deviation.

Table 2 highlights the univariate and multivariate (logistic regression) analysis of the sociodemographic and clinical factors predicting depressive symptoms in the participants who had chronic IBD. From a sociodemographic standpoint, the univariate analysis showed that sex ( $p = 0.021$ ) and smoking status ( $p = 0.046$ ) were significantly associated with the presence of depressive symptoms. In clinical terms, having a history of surgical stoma ( $p = 0.022$ ), hypertension ( $p < 0.001$ ), diabetes mellitus ( $p = 0.001$ ), cerebrovascular injury ( $p = 0.005$ ), and hypothyroidism ( $p = 0.013$ ) showed significant association with the presence of depressive symptoms.

Logistic regression analysis showed that sex, history of surgical stoma, hypertension, and cerebrovascular injury were significant risk factors for depression. The model had a good fit according to the Hosmer-Lemeshow goodness-of-fit test ( $\chi^2 = 1.804$ ,  $p = 0.772$ ), with a predicting power  $R^2$  of 73.4%. Female patients are twice (OR = 2.090,  $p = 0.047$ ) as likely to be depressed compared to males. In terms of the clinical variables, participants who had a surgical stoma, hypertension, and cerebrovascular injury were 5.7-times (OR = 5.737,  $p < 0.001$ ), 2.8-times (OR = 2.846,  $p = 0.007$ ), and 2.6-times (OR = 2.651,  $p = 0.011$ ) more likely to be depressed than patients who did not have these factors, respectively.

## DISCUSSION

To the best of our knowledge, this is the first study conducted in an Arab country to explore the prevalence and predictive factors of depressive symptoms among patients with IBD. In the current study, the prevalence of depressive symptoms (defined by a PHQ-9 score  $\geq 12$ ) was 23.4%. This is higher than the prevalence reported in a large systematic review.<sup>13</sup> Also, the rate of depressive symptoms in the current sample seemed higher than that previously described in several survey-based reports. Two large Canadian health surveys reported a prevalence of depression among patients with IBD ranging from 14.7%–16.3%.<sup>23</sup> Lower depression rates have been reported in some European studies. A French study reported a prevalence of depression among IBD patients of 10%,<sup>10</sup> and another study from Germany found a prevalence of 10.2%.<sup>13,24–26</sup> Conversely, the rate in this study was noted to be lower than what

**Table 2:** Univariate and multivariate (logistic regression) analysis of the sociodemographic and clinical factors predicting depression in participants with chronic inflammatory bowel diseases.

Variables	Depression (PHQ-9)		Univariate analysis		Multivariate analysis	
	Yes (n = 47, 23.4%)	No (n = 154, 76.6%)	OR	p-value	OR	p-value
	n (%)	n (%)				
<b>Sociodemographic factors</b>						
Sex						
Female	31 (66.0)	72 (46.8)	2.207	0.021	2.090	0.047
Male (ref)	16 (34.0)	82 (53.2)				
Marital status						
Married	26 (55.3)	105 (68.2)	0.578	0.105		
Divorced/widowed/single (ref)	21 (44.7)	49 (31.8)				
Age, years						
Mean ± SD	36.5 ± 9.8	36.1 ± 8.9	0.244	0.808		
Median (range)	38.0 (20.0–60.0)	35.0 (20.0–60.0)				
Educational level						
High school or below	15 (31.9)	41 (26.6)	1.232	0.600		
Diploma	13 (27.7)	49 (31.8)	0.894	0.782		
Under/Post-graduate (ref)	19 (40.4)	64 (41.6)				
Job						
Unemployed	18 (38.3)	47 (30.5)	1.413	0.318		
Employed (ref)	29 (61.7)	107 (69.5)				
Smoking						
Yes	19 (40.4)	39 (25.3)	2.001	0.046		
No (ref)	28 (59.6)	115 (74.7)				
<b>Clinical measurements</b>						
Disease diagnosis						
Crohn's disease	5 (10.6)	22 (14.3)	0.714	0.521		
Ulcerative colitis (ref)	42 (89.4)	132 (85.7)				
Years since diagnosis						
Mean ± SD	1.9 ± 0.3	1.9 ± 0.4	0.639	0.523		
Median (range)	2.0 (1.0–2.0)	2.0 (1.0–2.0)				
Steroid use						
Yes	41 (87.2)	120 (77.9)	1.936	0.162		
No (ref)	6 (12.8)	34 (22.1)				
History of a surgical stoma						
Yes	6 (12.8)	5 (3.3)	4.332	0.022	5.737	< 0.001
No (ref)	41 (87.2)	148 (96.7)				
Hypertension						
Yes	22 (46.8)	27 (17.6)	4.107	< 0.001	2.846	0.007
No (ref)	25 (53.2)	126 (82.4)				
Diabetes mellitus						
Yes	20 (42.6)	28 (18.2)	3.333	0.001		
No (ref)	27 (57.4)	126 (81.8)				
Cerebrovascular accident						
Yes	19 (40.4)	31 (20.1)	2.692	0.005	2.651	0.011
No (ref)	28 (59.6)	123 (79.9)				
Hypothyroidism						
Yes	17 (36.2)	29 (18.8)	2.443	0.013		
No (ref)	30 (63.8)	125 (81.2)				

PHQ-9: patient health questionnaire-9; SD: standard deviation; OR: odds ratio.

has been reported in a recent meta-analysis which shows the prevalence of depressive symptoms is 25.2%.<sup>27</sup> Another study conducted recently among an American sample of IBD patients using PHQ-8, reported that 38% of CD and 32% of UC patients had significant depressive symptoms.<sup>28</sup> Regionally, a study conducted among patients with IBD in Saudi Arabia found that 30.1% had borderline depression, and this was higher than what was reported in our study.<sup>29</sup>

This notable difference between the rates of depression from the current study compared with other studies in the existing literature could be due to the heterogeneous samples across those studies. Furthermore, differing methods/tools and cut-offs can contribute to this variability.<sup>23,30</sup> The PHQ-9 questionnaire also shares symptoms that may overlap with IBD symptoms, such as changes in appetite and fatigue. As such, the PHQ-9 may overestimate depression in IBD patients. There are several possible explanations for the development of depression among patients with IBD. It is known that a bidirectional relationship exists between IBD and depression.<sup>26</sup> IBD may be a risk factor for poor mental health, with abdominal pain perception, sleep dysfunction, non-adherence to medication and negative illness perceptions being likely manifestations of psychological morbidity in people with IBD.<sup>31</sup> Stress has been shown to impact intestinal permeability and immune factors, both important contributors to IBD.<sup>31</sup> Another factor that may contribute to depression is the presence of pro-inflammatory mediators in IBD.<sup>32-34</sup> The use of corticosteroids and antibiotics for the treatment of IBD has side effects of depression and may play a role in its increased prevalence.<sup>30,34</sup>

The second aim of this study was to investigate the independent predictors of depressive symptoms among patients with IBD. The results from this study mirrored the current literature in terms of sex and depression in the general population,<sup>35,36</sup> with female participants with IBD being twice (OR = 2.090,  $p = 0.047$ ) as likely to report depression as males. In a recent systematic review and meta-analysis among patients with IBD confirmed this sex disparity.<sup>27</sup>

Being female was also a risk factor for depression in a recent study examining the risk factors for depression in patients following IBD-related surgery.<sup>36</sup> Conversely, in French<sup>37</sup> and

German<sup>24</sup> cohorts, this difference was not noted. The noted differences among these studies may be due to variable definitions of depression, cultural differences, regional decisions in disease management, and socioeconomic or cultural factors among the populations. It has been proposed that a lower health-related quality of life among women<sup>38</sup> may explain the higher incidence of depression. Studies have shown that women with IBD tend to have a high rate of depression, anxiety, and poor quality of life compared to men.<sup>3,23,38-40</sup> Genetics and environmental factors play a role in the pathogenesis of IBD and mental illness. There is a high probability that genetics and environmental factors influence the change of mental health burden among women with IBD. Recent research has explored the role of sex-specific factors, including the influence of symptoms on body image and self-confidence, as potential mechanisms for the increase in psychological distress among women,<sup>39</sup> the perceived and societal burden of gastrointestinal symptoms may be more impairing for women.<sup>41</sup> Additionally, major depressive disorder is known to be more prevalent among females.<sup>41</sup>

This study indicated that participants who have a surgical stoma were six times more likely to have depression than those without a stoma. Having to live with a stoma could pose an additional risk of maladjustment along with reactive depressive symptoms. This can occur in the presence or absence of active disease.<sup>42</sup> This finding is consistent with previously reported research, that IBD patients with stoma showed an elevated risk of depression and anxiety.<sup>43</sup> A study showed that the presence of depressive symptoms in patients with CD or UC increases the risk for surgery by 1.3-times.<sup>28</sup>

The results from this study indicated that IBD participants with either hypertension or a history of cerebrovascular injury have a three-fold increase in the risk of developing depressive symptoms compared to participants who do not have these factors. This is in line with the existing literature, which indicates that IBD patients with comorbid chronic medical conditions, including metabolic syndrome, hypertension, cardiovascular diseases, and stroke, are at an increased risk of depression.<sup>44-47</sup> These chronic comorbidities seem to moderate an additional physical and psychosocial burden among IBD patients. Owing to its impact on brain vascularization, hypertension, and cerebrovascular injury have been linked to mood disorders in many studies.<sup>48-50</sup>

This study has several limitations. The cross-sectional design is not optimal to ascertain causality, whereas cohort designs are more robust. Also, the population assessed was drawn from a tertiary IBD clinic, which may have resulted in a patient population with more severe or active IBD, or more comorbidities than community samples. Further, the disadvantages in setting type one error at 0.05 significance level, as opposed to 0.01, is false-positive results and wide confidence intervals. Moreover, this study did not include any patients that were currently hospitalized. Notable, the diagnosis of depression was not performed using a gold standard clinical interview. However, the cut-off score used in this study has reasonable sensitivity and specificity for a depression diagnosis. This study also did not look at associations between the severity of the disease using a validated scale and depression.

## CONCLUSION

Almost one in four patients with IBD struggles with depressive symptoms. Being female, having a history of surgical stoma, comorbid diagnosis of hypertension, and cerebrovascular injury is associated with an increased risk of depressive symptoms. The findings from this study will add to the current literature regarding the magnitude and risk of depression among IBD patients in Arab countries. Patients with IBD who are at risk should undergo screening and referral for psychological assessment and treatment, given the significant disease burden of this comorbidity. Further studies are necessary to explore the possible pharmacological and non-pharmacological interventions, aiming at lowering the risk and treating depression among this population.

### Disclosure

The authors declared no conflicts of interest. No funding was received for this study.

### Acknowledgements

We would like to thank all who participated in this study.

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