

Inflammatory bowel disease (IBD) activity and depression

Abstract

Background: The interaction between IBD and psychosocial health is poorly understood. The prevalence of depression in IBD is three times higher than in the general population.

Objective: We assessed the prevalence of and risk factors for developing depression in a tertiary care outpatient setting. A secondary objective was to assess adherence to recommended depression screening.

Methods: We collected data from patients seen in the outpatient IBD clinic at the MedStar Georgetown University Hospital (MGUH) from August 2017 to March 2018. All patients were supposed to be screened for depression with the patient health questionnaire (PHQ-2). A score of score ≥ 3 was consistent with depression and prompted the provided to complete a PHQ-9 questionnaire. Patients who were under the age of 18 years were excluded.

Results: We included 201 (CD) patients and 169 (UC) patients who had PHQ-2 data available. Only 55% (370 of 676) of patients had a documented PHQ-2 score. The prevalence of depression in this study was 3% (11 of 370). There were no significant differences observed between CD and UC patients in regards to gender, age, disease duration, race, or presence of depression. Depression did not vary based on disease severity ($p=0.13$ for CD, $p=0.62$ for UC).

Conclusions: The prevalence of depression in this cohort is less than in the general population (6.7%). The majority of patients had CD, smoke, have an ostomy, had IBD-related surgery, and were in remission. Patients with depression should be identified early and referred for therapy, because left untreated, depression can lead to aggressive disease.

Keywords: inflammatory bowel disease, depression, provider adherence

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Introduction

Inflammatory bowel disease (IBD) is a chronic inflammatory condition of the gastrointestinal tract that comprises Crohn's disease (CD) and ulcerative colitis (UC). Over one million individuals in the United States are living with IBD.¹ The impact of IBD on physical well-being is established, but less is known about the psychosocial impact. Concomitant depression and anxiety have been shown to have a worse quality of life and a subsequent worse course of disease than those with IBD and no psychiatric co-morbidities.¹⁻⁶ The incidence of co-existing mood disorders is high in this patient population, yet many of these patients may not be adequately treated.⁷⁻¹² It has been reported in the literature that depression is three times more prevalent in people with IBD than in the general population.¹

A review by Neuendorf et al.,¹³ found that of 171 relevant studies using the Hospital Anxiety and Depression Scale (HADS) or the Beck Depression Inventory (BDI) the pooled estimate of depression in patients with IBD was 20.5%.¹³ Patients with active IBD had higher rates of depression than those in remission, 40.7%, and 16.5%, respectively. Furthermore, they reported a higher prevalence of depression in Crohn's disease (25.3%) as compared to ulcerative colitis (16.7%). The rate of anxiety was 35.1% in all IBD patients, and similarly, those with active disease had a higher prevalence of anxiety when compared to those in remission, 75.6% and 31.4%, respectively.

A seminal study by Kochar et al.,¹⁴ of seven academic medical centers found that using a single item questionnaire, 18% of their study participants with IBD were depressed at baseline and 36% scored positive on the PHQ-8 questionnaire.¹⁴ They found that patients

with Crohn's disease who were depressed were at increased risk for disease relapse, hospitalization, and IBD-related surgery at follow-up visits.¹⁵ For ulcerative colitis patients with depression, there was an increased relative risk for hospitalization, having IBD-related surgery, as well as starting a new biologic prescription at follow-up visits.¹⁵ Similarly, van Langenberg et al.,¹⁵ found that an increase in symptom severity, frequency of flares, and rates of hospitalization is associated with depression and anxiety.¹⁵

The relationship between depression and IBD is multifactorial but several authors suggested that a deregulated immune system and an elevation in inflammatory markers might play a role.¹⁶ Hannestad et al.,¹⁷ reported that IBD patients with higher inflammatory markers have a higher prevalence of depression than those IBD patients with normal inflammatory markers.¹⁷ Similarly, depressed patients are reported to have higher levels of CRP and IL-6, both markers of inflammation, when compared to the general population.¹⁸ Thus, there may be a bi-directional relationship. IBD may affect sensory pathways that influence central pain perception that, in turn, modifies processing of emotions.

Much of what we know about depression and IBD is based on cross-sectional data^{10,19} and only two prospective studies have assessed changes in disease activity in IBD patients with depression.^{11,20} We aimed to assess the compliance of practitioners with depression screening of all patients seen in an outpatient, tertiary care, IBD clinic. Of the cohort that was screened, we aimed to assess the prevalence of depression and risk factors that contributed to the development of depression.

Methods

This is a retrospective, single center (MedStar Georgetown University Hospital (MGUH)) study of patients who visited the outpatient IBD clinic between August 2017 and March 2018. There were 201 patients with CD and 169 patients with UC who had PHQ-2 data available. Depression was assessed using two methods. Depression was assessed at each outpatient clinic visit first by the medical assistant using the PHQ-2 questionnaire, and if positive (a score greater than or equal to 3), then a provider was prompted to complete a PHQ-9 questionnaire.^{21,22} A score of 5 to 9, 10 to 14, 15 to 19 and 20 to 27 was considered mild, moderate, moderately severe, and severe depression, respectively. Data regarding gender, age, disease duration, race, smoking status, presence of an ostomy, history of any IBD-related surgery, and biologic use, were obtained from chart review.

Disease severity was reported using the Harvey-Bradshaw Index for CD and the Partial Mayo Scoring Index for UC. Patients who were under the age of 18 years or those who did not have a confirmed diagnosis of IBD in their records were excluded.

Continuous variables were described by means and standard deviations and t-test was used to examine if there is a statistically significant difference in the average values between two groups.

Categorical variables were described by frequencies and percentages and Chi-square and Fisher exact (when cells have counts less than 5) tests as appropriate were used to compare proportions of categorical variables. P-value of <.05 was indicative of a statistically significant difference.

Results

Using two, distinct ICD-10 codes for CD and UC, we identified a total of 680 patients who had attended the outpatient IBD clinic at MGUH from August 2017 to March 2018; however, 4 patients did not have a biopsy proven IBD and thus incidentally had an ICD code associated with their name without a true diagnosis of IBD. Since August 2017, our clinic began to implement mandatory screening for depression by medical assistants using a simple two-item questionnaire, the PHQ-2. A positive questionnaire then alerts the provider to complete the PHQ-9, which is a nine-item questionnaire that includes a question about suicidal ideation.

Only 370 patients had a documented PHQ2 score (55%) (Figure 1). Of those, 54% were women, with a median age of 41 years and disease duration of 13 years (Table 1). Of all IBD patients in this cohort, 3% currently smoke, 4% have an ostomy, 30% had undergone any IBD-related surgery, and 73% were in clinical remission.

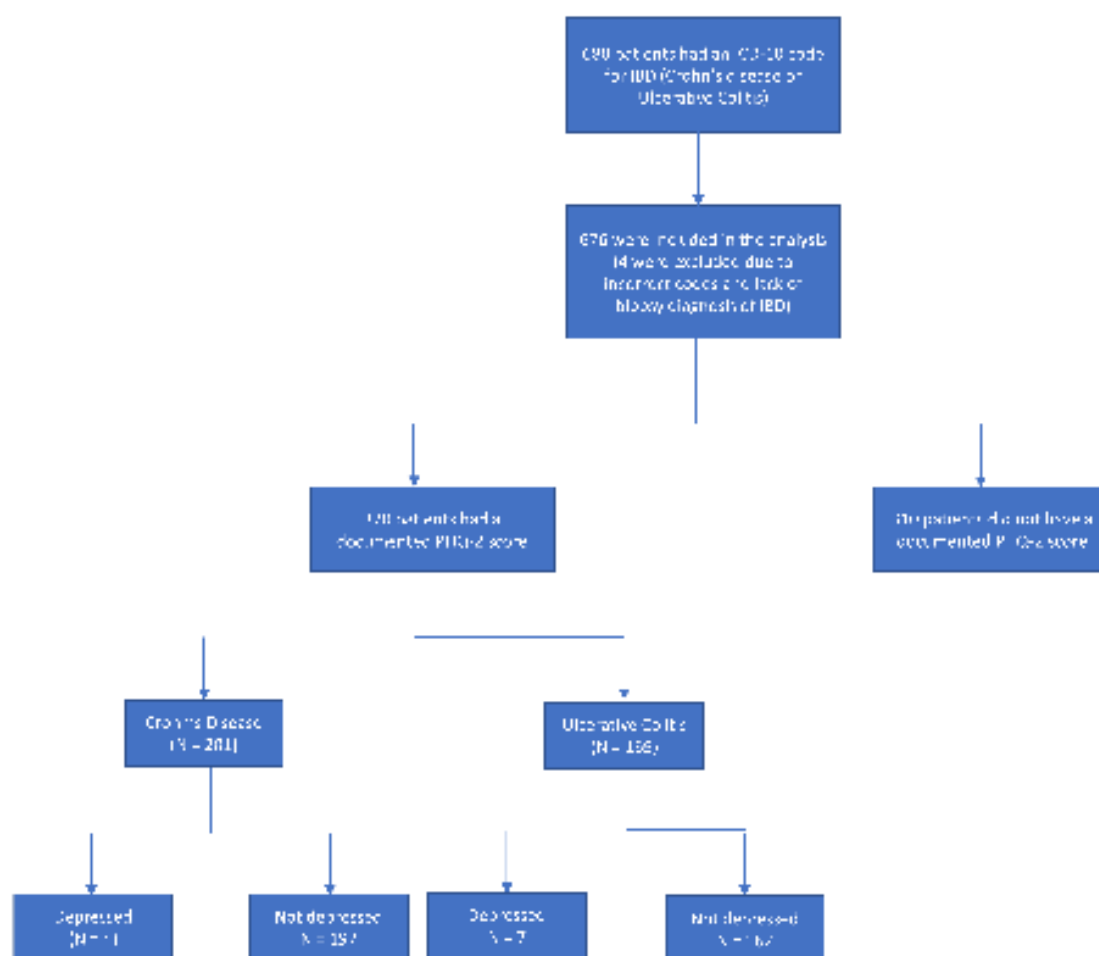


Figure 1 Flowchart of potential selection.

Table 1 Characteristics of study population

Characteristics	N=370
Female	201(54.3)
Mean Age(S.D.)	41.4(±15.2)
Mean Disease duration(years)(S.D.)	12.9(±11.3), N=354
Race	
White	230(62.3)
Black	73(19.8)
Other	32(8.7)
Unknown	29(7.9)
Asian	1(0.3)
Declined to answer	2(0.5)
multiple	1(0.3)
American Indian or Alaska Native	1(0.3)
Current Smoker	10(2.7)
Current Ostomy	16(4.3)
History of IBD-related surgery	112(30.3)
Disease severity	
Remission	269(72.7)
Mild Disease	86(23.2)
Moderate Disease	13(3.5)
Severe Disease	2(0.5)
Depressed by PHQ-2	11(2.97)

PHQ-2: Patient Health Questionnaire, depression is defined as PHQ-2 score ≥ 3 .

All values are presented as mean values or raw numbers with percentages in parentheses, unless otherwise specified.

The prevalence of depression in this study was 3%(11 of 370) based on the PHQ2 score of 3 or higher. Of these 11patients, only 1(9%) was appropriately screened with the PHQ9 questionnaire; however, 10 were not (91%).

Among the 201 CD patients in this cohort, 53% were women. The mean age was 42years and the mean disease duration was 14years (Table 2). According to the Harvey-Bradshaw Index (HBI), 79%had achieved clinical remission, 18%, 3%, and 1% met criteria for mild, moderate, and severe disease, respectively.

Of the 169 UC patients in this cohort, 56% were women. The mean age was 41years and the mean disease duration was 12years (Table 2). According to the Partial Mayo Scoring Index, 66% were in remission, 29%, 5%, and 1% met criteria for mild, moderate, and severe disease, respectively.

In this cohort of IBD patients, 3% reported being depressed at their clinic visit that occurred between the months of August 2017 and March 2018.Of all patients with UC, 7% were depressed, and 4% of CD patients were depressed. The majority of patients in both CD and UC in this cohort were white, 63% and 62%, respectively.

Smoking status did not vary significantly between CD and UC, (4% and 2%, respectively, $p=.36$). Seven percent of CD patients had an ostomy at the time of the clinical visit, whereas only 2% of UC patients had an ostomy ($p=.04$). 50% of CD patients had a history of at least one IBD-related surgery, while only 7% of UC patients reported a history of surgery ($p<.0001$). There were no significant differences observed between CD and UC patients in regards to gender, age, disease duration, race, or presence of depression. Depression did not vary based on disease severity (Table 3), (Table 4) ($p = .13$ for CD, $p = .62$ for UC).

Discussion

Treatment of patients with IBD involves a multidisciplinary approach that requires attention to the physical, social and psychosocial well-being of the individual. Several studies have reported that people with IBD report a lower quality of life when compared to age and gender matched populations.²³⁻²⁶ Magalhaes et al.,²⁴ studied patients in Portugal with IBD and found that the most strongly correlated factor in regards to a lower quality of life was female gender, which is consistent with prior findings as well. Some reports suggest that up to two-thirds of patients with CD, and one-third of patients with UC, will require surgery at least once in their lifetime.²⁷⁻³⁰ Patients with severe UC that is not amenable to pharmacological management should be considered for surgery, with the preferred intervention being a proctocolectomy with an ileal-pouch anal-anastomosis.²⁹ Ananthakrishnan et al.,³⁰ reported similar rates of depression and anxiety after surgery.³⁰ They found that female gender, younger age, surgery within 3years of diagnosis, and presence of a stoma were risk factors for depression, consistent with other studies as well.^{2,30}

We present data from an observational cohort study of IBD patients recording the prevalence of depression. As of August 2017, our outpatient IBD clinic began to screen all patients for depression. We found that only 370 (55%) of patients had a documented PHQ-2 score and thus were included in our analysis. Of this group, only 3% had depression. Only 9% of the patients with a positive screen for depression based on their PHQ-2 score, had PHQ-9 scores documented. Our results demonstrate that patients are not being screened for depression and that healthcare practitioners in the IBD clinic (physicians and physician assistants) are not using the PHQ-9 questionnaires to assess more thoroughly for depression despite a positive PHQ-2 screen.

In contrast to a prospective trial by Kochar et al.,¹⁴ who found that despite 64% of CD and 45% of UC patients being in remission, 20% of CD and 14% of UC patients were reportedly depressed, by self-report.¹⁴ Patients with baseline depression were at increased risk for disease relapse, surgery, or hospitalization for both CD and UC. Thus, they concluded that baseline depression was an important marker of more aggressive IBD. Our patients had higher rates of IBD patients in remission, however our patients had a markedly lower rate of depression, and depression was more prevalent in UC than in CD although not statistically significant. Our study highlights the importance of screening for depression. Perhaps depression is under-reported by patients, or perhaps the higher rates of patients in remission in our study accounted for the lower rates of depression. Our patients had similar baseline patient characteristics as the landmark trial by Kochar et al.¹⁴ Their mean age was 41 and 42 years for CD and UC. Our mean age was 42 and 41years for CD and UC, respectively. Their mean duration of disease was 13 and 10years, and ours was 14 and 12years, for CD and UC, respectively. Strength of their study was the ability to follow patients over time. Future studies

should consider assessing patient's medications, and the use of antidepressants should be taken into consideration. Perhaps our low rate of depression is representative of adequate control of active disease or

success of medications in treating depression. However, our study is currently limited by the small sample size and low number of positive depression screens.

Table 2 Characteristics of study population by IBD type

Characteristics	Crohn's disease N=201	Ulcerative colitis N=169	P value
Female	106(52.7)	95(56.2)	0.5037
Age(S.D)	41.7(±16.0)	41.0(±14.2)	0.6664
Disease duration(S.D)	13.9(±12.0), N=191	11.7(±10.4), N=163	0.0688
Race			0.4287
White	126(63.0)	104(61.5)	
Black	43(21.5)	30(17.8)	
Other	16(8.0)	16(9.5)	
Unknown	13(6.5)	16(9.5)	
Asian	0(0.0)	1(0.6)	
Declined to answer	0(0.0)	2(1.2)	
multiple	1(0.5)	0(0.0)	
American Indian or Alaska Native	1(0.5)	0(0.0)	
Current Smoker	7(3.5)	3(1.8)	0.3557
Current Ostomy	13(6.5)	3(1.8)	0.0377*
Surgery	100(49.8)	12(7.1)	<.0001*
Disease severity			0.0291*
Remission	158(78.6)	111(65.7)	
Mild Disease	37(18.4)	49(29.0)	
Moderate Disease	5(2.5)	8(4.7)	
Severe Disease	1(0.5)	1(0.6)	
Depressed by PHQ-2	4(1.99)	7(4.1)	0.3575

PHQ-2: Patient Health Questionnaire, depression is defined as PHQ-2 score ≥3.

All values are presented as raw numbers with percentages in parentheses, unless otherwise specified.

*Statistical significance ($p < .05$)

Patients with IBD have higher prevalence rates of depression and anxiety when compared to the general population. Furthermore, those with active disease have even higher rates than those in remission. This study underscores the importance of early identification of and screening for co-morbid mood/psychological conditions in patients with IBD. Clinically significant depression or anxiety have been linked to a shorter time to a clinical recurrence events, such as flares, fistula formation, or stenosis, in patients with IBD.²⁴ Although the literature has established that there is a significant relationship between depression and fistulizing Crohn's, surgery, biologic and steroid use, we did not find this in our study.¹⁹ They also found that anxiety was associated with ulcerative colitis flares, biologic use in Crohn's disease, and steroid use in both Crohn's disease and ulcerative colitis.

These results are similar to other assessments of health-related quality of life in patients receiving an ileo-anal pull-through. A study

by Provenzale et al.,³¹ found that surgery for UC was associated with a better quality of life than those patients with IBD who did not undergo surgery.³¹ Another study by Fazio et al.,³² found that in patients receiving a restorative procto-colectomy with ileal pouch-anal anastomosis for UC, there was an excellent quality of life and satisfactory level of continence using the SF-36 (short form 36) questionnaire.³² This study however did have an 83% attrition rate. Both of these studies however were performed in the 1990s. In contrast to the study by Fazio, Martin et al.,³³ had a 22% attrition rate and found that in an Italian cohort using a validated disease specific self-administered questionnaire examining intestinal, systemic, emotional, and social function, UC patients had lower quality of life compared to controls irrespective of remission status.³³ Those who had undergone surgery had scores comparable to, even four year post-operatively, those who were in remission or who had mild disease.³³ Quality of life may differ amongst cultures, which presents a challenge when

attempting to analyze populations in cohorts. For years, the success of operations was determined by mortality. However, given the advances in technology seen today, the focus has now turned to evaluating quality of life as a measure of the success of a surgery. Quality of life extends beyond measures of physical health. It encompasses the whole individual taking into account the social and emotional responses as well. Future studies should also consider evaluating patient-decision making in order to provide further insight into the process behind which choices of medical versus surgical therapies are pursued.

Table 3 Depression in Crohn's disease based on disease severity

Frequency of depression(Column Percentage)			
Disease severity	Not depressed	Depressed	Total
Remission	155(79%)	3(75%)	158
Mild Disease	37(19%)	0(0%)	37
Moderate Disease	4(2%)	1(25%)	5
Severe Disease	1(0.5%)	0(0%)	1
Total	197	4	201

Fisher's exact test

P-value 0.1346

Table 4 Depression in Ulcerative colitis based on disease severity

Frequency of depression(Column Percentage)			
Disease severity	Not depressed	Depressed	Total
Remission	107(66%)	4(57%)	111
Mild Disease	46(28%)	3(43%)	49
Moderate Disease	8(5%)	0(0%)	8
Severe Disease	1(1%)	0(0%)	1
Total	162	7	169

Fisher's exact test

P-value 0.6201

More recently, Thirlby et al.³⁴ found that CD patients undergoing resections and UC patients undergoing ileal pouch-anal anastomoses had significant improvement in health-related quality of life measures post-operatively. In fact, at 6-year follow-up, these patients had scores that were higher than or equal to those seen in the general population.³⁴ The hypothesis that intestinal resection in CD would improve quality of life was further supported by the work of Wright et al.³⁵ Their group found a statistically significant improvement of QOL scores 6months post-operatively. Interestingly, a lower QOL was noted in females and smokers. Drug therapy or inflammatory markers did not affect QOL, however, a higher disease severity was associated with a worse QOL.³⁵ However, we did not find a statistically significant difference in disease severity and depression. More patients with CD had a history of IBD-related surgery than patients with UC. However, there were more depressed UC patients than there were CD patients. Thus, although there may be a relationship between surgery and less depression, causality in this case cannot be implied. Future studies should continue to use validated screening tools and should consider inclusion of control patients. Depression and anxiety screening should become routine practice for patients with IBD. There is a need for more objective measurements of depression and anxiety in future research, as much of our understanding is currently based on self-reported questionnaires. Patients who screen positive for depression should be appropriately referred to a specialist. Treatment of comorbid

psychiatric illnesses could potentially improve IBD severity, as suggested by Yanartas et al.,³⁶ using objective scoring measures such as the Crohn's disease activity index and the modified Mayo score.³⁶ Although studies have suggested that patients with IBD and depression are at higher risk for more aggressive disease, hospitalizations, surgeries, and new biologic prescriptions, the mechanism are less clear.¹⁹ Perhaps people with depression are less compliant with their medications, thus increasing the risk of developing complications associated with IBD. Future studies should also consider evaluating the concomitant use of anti-depressants. Patients with IBD may experience issues with body image, social isolation, fatigue, and sexual inadequacy. Improved outcomes may be established if there is more focus on the physician-patient relationship as well as improving access to resource-rich environments.

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Conflicts of interest

The author declares no conflict of interest.

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