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The prevalence and impact of psychiatric comorbidities on hospitalized inflammatory bowel disease patients in the United States: insights from the National Inpatient Sample from 2009-2018

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Abstract

Background Patients with inflammatory bowel disease (IBD) are at increased risk of anxiety and mood disorders. This study examines the temporal trends and clinical impact of anxiety and mood disorder diagnoses in hospitalized IBD patients in the United States during a 10-year period.

Methods Using the National Inpatient Sample from 2009-2018, all IBD-related discharges in adults were analyzed. Primary outcomes were the prevalence and temporal trends of mood disorder and anxiety diagnoses for IBD-related admissions. The impact of the psychiatric comorbidities on clinical outcomes was also evaluated.

Results A total of 1,718,736 IBD-related discharged were identified. A diagnosis of anxiety or a mood disorder was found to have a prevalence of 16.44% and 18.97%, respectively, amongst IBD-related admissions. The prevalence of anxiety disorders amongst hospitalized IBD patients increased significantly (from 12.13% to 20.26%), whereas the prevalence of mood disorders did not (17.46% and 18.9%). IBD admissions with psychiatric comorbidities had lower rates of IBD-related complications or mortality during hospitalization compared to IBD admissions without comorbid psychiatric diagnoses. This population, however, was more likely to experience certain comorbidities such as *Clostridioides difficile*, pneumonia, and venous thromboembolism, as well as a longer hospitalization.

Conclusions The prevalence of comorbid anxiety among hospitalized IBD patients in the United States matches or exceeds the prevalence of anxiety in the general hospitalized population. Given its association with more in-hospital complications and a longer hospital stay, it is important to further understand how psychological screening and mental health services can improve the management of hospitalized IBD patients.

Keywords Anxiety, mood disorder, inflammatory bowel disease, National Inpatient Sample, psychiatric comorbidities

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Introduction

Inflammatory bowel disease (IBD) is a spectrum of chronic, relapsing and remitting inflammatory conditions of the gastrointestinal tract that includes ulcerative colitis (UC) and Crohn's disease (CD) [1]. IBD is a multifactorial disorder resulting from complex contributors, including a dysregulated immune system, microbial instigators, and genetic predispositions [1]. In addition to bowel symptoms, extra-intestinal manifestations are also reported in up to 47% of IBD patients [2]. The development of new medications, coupled with a better understanding of the disease, has improved the prognosis of IBD patients [3]. The chronic,

waxing and waning course of IBD, the occurrence of extra-intestinal manifestations, and brain–gut interactions impact the psychological wellbeing of the IBD patient [2,4].

Goodhand *et al* demonstrated that patients with IBD, when compared with their age-matched counterparts, are more likely to develop anxiety and mood disorders [5]. Prior systematic reviews and meta-analyses have also reported a significant prevalence of anxiety and mood disorder in IBD patients [6,7]. Female sex, aggressive disease (defined as use of 1 or more biologics at any time during the disease course, prior or current surgery for IBD, perianal involvement, and/or fistulizing disease), and endoscopic or radiological evidence of disease activity have been independently associated with the development of depression in patients with IBD [8]. Anxiety and mood disorder diagnoses also correlate with more active or severe IBD, including more frequent relapses [9], a greater number of hospitalizations, and less likelihood of achieving remission with biologic therapy [10]. There is growing evidence that IBD patients would benefit from mental health screening. Therefore, the American College of Gastroenterology clinical guideline for preventative care in IBD recommends screening for psychiatric comorbidities in the outpatient setting [11].

Hospitalized IBD patients belong to a subset of the IBD population who typically have more severe disease. Understanding the trends in prevalence of psychiatric comorbidities among patients with IBD, as well as the impact of these comorbidities on disease outcomes and healthcare utilization, is important for healthcare teams as well as policymakers.

The Nationwide Inpatient Sample (NIS) is the largest inpatient care database, containing around 7 million inpatient hospital records dating back to 1988, and is representative of all hospitals across the United States. Prior analyses utilizing the NIS has shown that this database has excellent data reliability due to its large sample size, which yields estimates with much smaller standard errors when compared with other available databases [12]. We aimed to examine the prevalence and temporal trends of anxiety and mood disorder diagnoses in hospitalized IBD patients in the United States during a 10-year period, utilizing the NIS. We also examined the impact of these conditions on clinical outcomes and healthcare system utilization associated with IBD hospitalizations.

Materials and methods

Data source

The most contemporary available data were extracted from the NIS between 2009 and 2018. The NIS is maintained by the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality. This database is the largest all-payer inpatient care database in the United States. It is based on a 20% stratified sample of nonfederal hospital admissions. Each admission is weighted to provide statistical national representation. The NIS data concur with the National Hospital Discharge Survey, supporting data reliability [12].

This study was exempt from Institutional Review Board approval, as the data are deidentified and publicly available.

Inclusion and exclusion criteria

All hospital discharges during the time period from 2009-2018 in adults aged 18 years or greater were included. The included discharges had a primary diagnosis of either UC or CD, identified by the International Classification of Diseases, 9th and 10th Revision (ICD-9-CM and ICD-10-CM). Anxiety and mood disorders were also identified using ICD-CM codes. Comorbidities (specifically pneumonia, venous thromboembolism, sepsis, *Clostridioides difficile* [*C. difficile*]), IBD-related complications (fistulae, stricture, perianal disease, obstruction, anemia, hematochezia, malnutrition), and opiate use disorder were also identified using ICD-CM codes.

Statistical analysis

Data were analyzed using the Stata 16.0 SE software package (Stata Corp LP, College Station, TX). These analyses accounted for the stratified 2-stage cluster design using Stata's SVY (survey data) commands incorporating individual discharge-level weights. Weighting functions using these discharge weights were applied to the 20% NIS sample to estimate the total number of hospitalizations over the time period analyzed. Two-way chi-squared analyses were performed to compare categorical variables among different racial groups. Continuous variables were analyzed using Student's *t*-test. Multiple logistic regression analysis was performed for yearly trends, with the year of admission as independent variable and the psychiatric comorbidity of interest as the dependent variable. The yearly prevalence of mood disorder or anxiety disorder diagnoses was obtained using marginal effects following multiple regression analysis. The annual percent change in the odds of the comorbidity of interest was estimated as equal to (odds ratio-1) × 100. This was reported along with the P trend to provide a quantitative estimation. We performed further analysis to evaluate the yearly trends of psychiatric comorbidities, stratified by discharge quarter. This was in order to minimize the impact of the readmissions and to validate the yearly trends amongst IBD patients. The association of psychiatric comorbidities with hospitalization-related outcomes such as in-hospital mortality and length of stay were analyzed using multivariable logistic regression analysis. The regression model was adjusted for demographic features (age, sex, race), social determinants (income, insurance status), hospital-related

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characteristics (teaching status, location), comorbidities (pneumonia, venous thromboembolism, sepsis, *C. difficile*), IBD-related complications (fistulae, stricture, perianal disease, small bowel obstruction, anemia, hematochezia, malnutrition), and opiate use disorder.

Results

Baseline characteristics

A total of 1,718,736 patients who were hospitalized for IBD between 2009 and 2018 were included in the analysis. The study sample had a mean age of 48.63 years and 56.92% were female. Anxiety and mood disorder diagnoses were more frequent in females and younger individuals. CD was more likely than UC to be associated with psychiatric comorbidities (69.06% vs. 30.94% for the anxiety disorder cohort and 69.9% vs. 30.1% for the mood disorder cohort). IBD admissions with psychiatric comorbidities had lower rates of IBD-related complications (i.e., fistula, obstruction, stricture) compared to IBD admissions without comorbid psychiatric diagnoses. This population, however, was more likely to experience certain IBD-related comorbidities such as *C. difficile*, pneumonia, and venous thromboembolism, as well as a longer hospitalization. The baseline demographic information and the clinical and hospital characteristics of the comorbidities of interests are shown in Tables 1 and 2.

Prevalence and temporal trends of anxiety and mood disorders

Over the 10-year study period, the prevalence rates of anxiety disorder and mood disorder were 16.44% and 18.97%, respectively. From 2009-2018, the prevalence of anxiety disorder increased significantly (from 12.13% to 20.26%, P<0.001; Fig. 1). The prevalence of mood disorder did not increase significantly during the same period (17.46% and 18.9%; Fig. 2). The subgroup analysis evaluating trends stratified by discharge quarter substantiated the yearly trends of the psychiatric comorbidities.

In-hospital mortality

The odds ratios (OR) with 95% confidence intervals (CI) for in-hospital mortality during the study period in the hospitalized IBD cohort with comorbid anxiety disorder and mood disorder were 0.81 (95%CI 0.62-1.05), P=0.12, and 0.80 (95%CI 0.63-1.002), P=0.053, respectively (Table 3). After adjustment for confounders, anxiety and mood disorder diagnoses were both found to have no independent association with in-hospital mortality. However, some comorbidities (pneumonia, venous thromboembolism, sepsis) were independent predictors of in-hospital mortality.

Table 1 Characteristics of hospitalized IBD cohort with anxiety disorder

Characteristics	Anxiety disorder in hospitalized IBD cohort	Control group	P-value
Ulcerative colitis	30.94%	36.63%	<0.001
Crohn's disease	69.06%	63.37%	
Females	69.73%	54.46%	<0.001
IBD-related complications			
Fistulae	3.35%	4.6%	<0.001
Stricture	2.33%	3.16%	<0.001
Perianal disease	1.57%	1.8%	<0.001
Obstruction	7.57%	9.55%	<0.001
Anemia	19.75%	21.26%	<0.001
Hematochezia	1.84%	2.17%	<0.001
IBD-related comorbidity			
Pneumonia	1.18%	1.27%	0.091
Sepsis	2.14%	2.31%	0.011
VTE	4.4%	4.18%	0.024
Clostridioides difficile	3.85%	3.2%	<0.001
Opiate use disorder	4.14%	1.22%	<0.001

IBD, inflammatory bowel disease; VTE, venous thromboembolism

Length of hospital stay

The OR and CI for hospital length-of-stay in the anxiety disorder and mood disorder cohorts were 0.05 (95%CI 0.03-0.07), P<0.001, and 0.11 (95%CI 0.09-0.13), P<0.001 during the study period, respectively (Table 4). After adjustment for confounders, both anxiety and mood disorder diagnoses were independently associated with a longer hospital stay. IBD-related comorbidities (pneumonia, venous thromboembolism, sepsis) were also independent predictors of a longer stay.

Discussion

There are multiple factors that could contribute to a higher prevalence of anxiety and mood disorders in patients with IBD. These factors include the long-term nature of the disease, the impact of intermittent periods of disease activity on the quality of life and ability to work, financial hardships due to medical bills, the need for treatment with medications that have a significant risk of adverse effects, and the burden of chronic disease in older patients [2,4]. Given the rising prevalence of IBD worldwide [13], there is a need to better understand the interaction between IBD and psychiatric comorbidities, as well as the impact of these interactions on outcomes in hospitalized IBD patients. This information is vitally important to healthcare providers as they formulate management approaches for these patients, as well as to policy makers and the patients themselves.

Using the NIS cohort for the years 2009-2018, we found that the prevalence of anxiety disorder increased from 12.13% in 2009 to 20.26% in 2018 (P<0.001). The prevalence of mood

Table 2 Characteristics of hospitalized IBD cohort with mood disorder

Characteristic	Mood disorder in hospitalized IBD cohort	Control group	P-value
Ulcerative colitis	30.1%	37%	<0.001
Crohn's disease	69.9%	63%	
Females	68.19%	54.27%	<0.001
IBD-related complications			
Fistulae	2.97%	4.77%	<0.001
Stricture	2.53%	3.14%	<0.001
Perianal disease	1.53%	1.82%	<0.001
Obstruction	7.74%	9.58%	<0.001
Anemia	20.5%	21.13%	<0.001
Hematochezia	1.91%	2.17%	<0.001
IBD-related comorbidity			
Pneumonia	1.4%	1.22%	<0.001
Sepsis	2.05%	2.34%	0.011
VTE	4.87%	4.07%	<0.001
C. difficile	3.47%	3.27%	<0.001
Opiate use disorder	4.13%	1.13%	<0.001

IBD, inflammatory bowel disease; VTE, venous thromboembolism; C. difficile, Clostridioides difficile

Table 3 Predictors of in-hospital mortality

Characteristic	Odds ratio (95% confidence interval)	P-value
Anxiety	0.81 (0.62-1.05)	0.12
Mood disorder	0.80 (0.63-1.002)	0.053
Age	1.07 (1.06-1.07)	<0.001
Clostridioides difficile	1.76 (1.36-2.27)	<0.001
Pneumonia	2.82 (2.17-3.63)	<0.001
VTE	1.54 (1.22-1.94)	<0.001
Sepsis	14.8 (12.48-17.56)	<0.001
Malnutrition	2.29 (1.92-2.74)	<0.001
Obstruction	1.47 (1.15-1.87)	0.002
Fistula	1.60 (1.19-2.13)	0.001
TPN	1.59 (1.21-2.08)	0.001

VTE, venous thromboembolism; TPN, total parenteral nutrition

Table 4 Predictors of length of hospital stay

Characteristic	Coefficient (95% confidence interval)	P-value
Anxiety	0.05 (0.03-0.07)	<0.001
Mood disorder	0.11 (0.09-0.13)	<0.001
Clostridioides difficile	0.34 (0.30-0.37)	<0.001
Pneumonia	0.36 (0.31-0.41)	<0.001
VTE	0.23 (0.20-0.26)	<0.001
Sepsis	0.70 (0.64-0.76)	<0.001
Malnutrition	0.41 (0.38-0.43)	<0.001
TPN	0.63 (0.59-0.66)	<0.001

VTE, venous thromboembolism; TPN, total parenteral nutrition

disorder diagnoses did not increase significantly during the same study period. The mood disorder diagnoses inadvertently acted as a falsification cohort. The falsification cohort validates the annual trend of anxiety disorder, suggesting that the rise in anxiety disorder prevalence was not due to better diagnostic coding strategies. The mood disorder trend noticed in the study is also in accordance with the most recent data from the National Center for Health Statistics [14]. With the population living longer as a result of advances in medicine, there are more older adults with IBD. While advanced age is not an independent risk factor for anxiety or mood disorder, older adults with physical health problems and related disability are more likely to experience psychological effects [15]. Our results may in part reflect the improved identification of anxiety and depression in these patients over time. This may be due to efforts to reduce the stigma associated with mental health disorders, leading to increased patient reporting of symptoms, as well as increased efforts by healthcare providers to screen for these disorders.

Anxiety and mood disorder diagnoses were significantly associated with CD compared to UC in the hospitalized cohort. This may be a consequence of the worse health-related quality of life in CD patients compared to UC patients, as reported in previous studies [7,16]. In a large European study, CD patients were found to have more frequent flare-ups, and were more likely to report that their symptoms affected their ability to enjoy leisure activities or perform job functions, compared to UC patients [17].

Anxiety and mood disorder diagnoses were more frequent in female patients hospitalized with IBD as compared to males. Several factors may have contributed to this finding. Women are more likely to report distress and symptoms related to anxiety and depression. Additionally, women are more likely than men to have a comorbid anxiety disorder with a major depressive disorder [18]. Even though males and females have

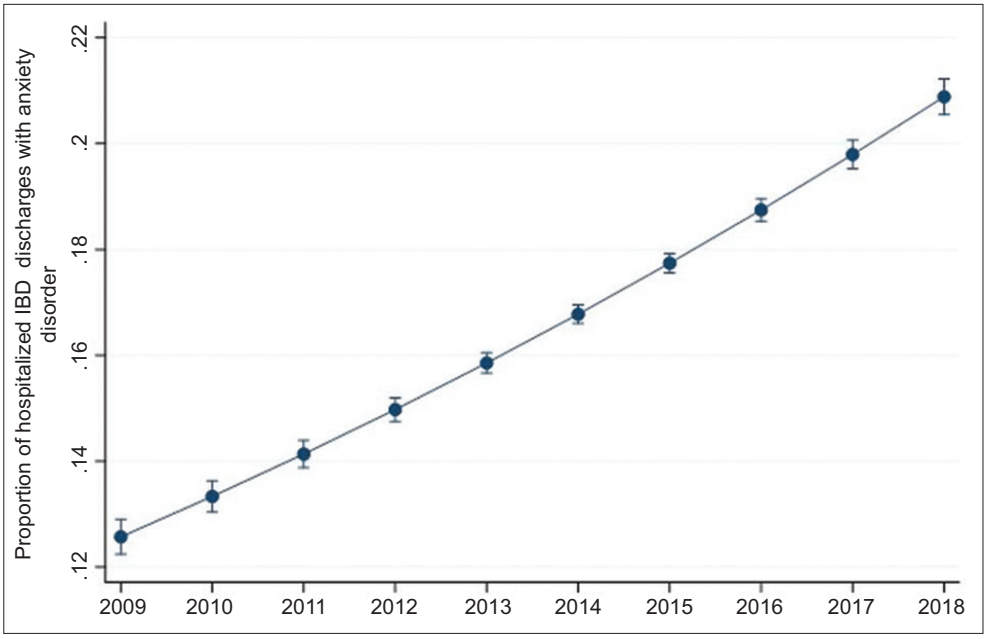

Figure 1 The prevalence of anxiety disorder amongst IBD admissions from 2009-2018
IBD, inflammatory bowel disease

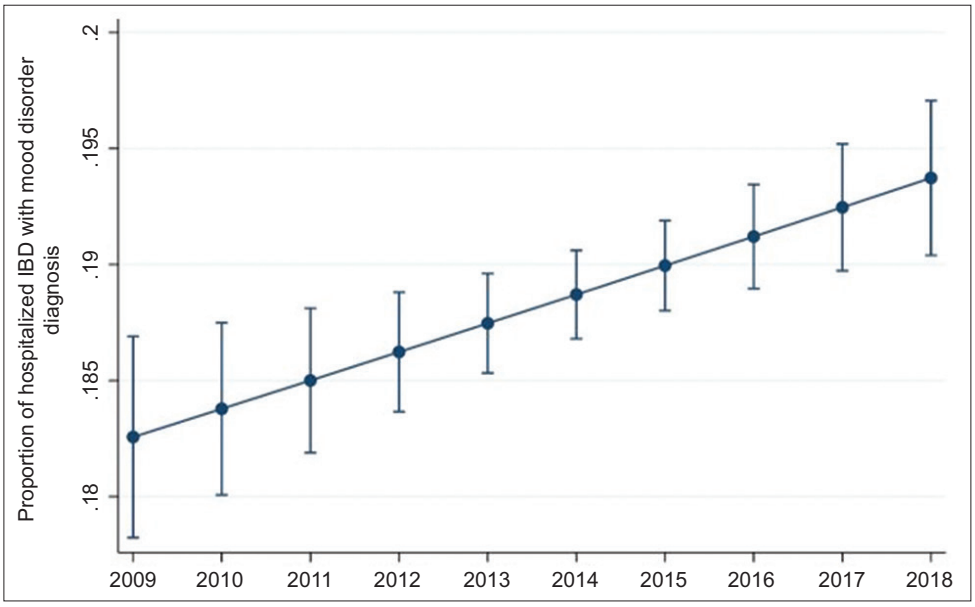

Figure 2 The prevalence of mood disorder amongst IBD admissions from 2009-2018
IBD, inflammatory bowel disease

equivalent physiologic responses to a stressor, women report more irritability and fear, and less happiness compared to males [19]. These findings have also been demonstrated in a systematic review and meta-analysis evaluating psychiatric comorbidities amongst the IBD population [7].

The hospital stay was significantly longer in IBD patients with anxiety or mood disorder, even after adjustment for confounders. It has been demonstrated that stress influences gut activity via several mechanisms, including impaired intestinal barrier function, disturbance of the gut microbiota, intestinal dysmotility, and immune and neuroendocrine dysfunction [20]. A systematic review found that psychosocial factors, including mood disorders and anxiety, are associated with worse IBD-related abdominal pain [21]. Anxiety and mood disorder can therefore contribute to exacerbating symptoms and prolonging the hospital stay. The longer hospital stay may have contributed to the higher rate of hospital-acquired conditions, such as venous thromboembolism and

C. difficile infection, observed in the cohort with anxiety and mood disorders. Although in-hospital mortality was significantly lower in patients with anxiety or mood disorder diagnoses, this difference disappeared after adjustment for confounders.

The increasing burden of psychiatric disorders, particularly anxiety disorder, among hospitalized adults with IBD in the United States emphasizes the importance of a comprehensive assessment of IBD in the hospitalized patient. Psychiatric comorbidities are often not prioritized during the evaluation of the hospitalized IBD patient, because of a lack of sufficient mental health resources. Screening and managing psychiatric comorbidities during the hospitalization of IBD patients could potentially improve overall outcomes by decreasing non-adherence to medications, effectively reducing flare-ups, as well as reducing the number of patients lost to follow up, thus improving quality of life through more consistent management of their disease. It would be worthwhile to adopt a team-based approach to care and involve psychologists, psychotherapists and other behavioral therapists, as indicated by the individual clinical scenario. More research is needed to determine whether the management of anxiety and depression during inpatient stays could lead to shorter hospitalizations, with better medication adherence and outpatient follow up.

National databases such as the NIS are very useful tools for addressing questions such as this on a nationally representative level. However, certain limitations deserve mention. The study findings apply to hospitalized adults with IBD. This could underestimate the true prevalence of anxiety and mood disorder diagnoses in patients with IBD. The increase in the prevalence of anxiety disorder could be because of more frequent coding in recent years. However, we validated the analysis with falsification endpoints and stratification, which reinforces the validity of the findings. It is also possible that increased awareness regarding the impact of psychiatric comorbidities among healthcare providers and patients led to an increase in the diagnosis of these comorbidities and hence a rising prevalence. Nonetheless, the study provides a detailed assessment of the burden of psychiatric comorbidities among hospitalized adults with IBD. The utilization of accurate ICD-9 and ICD-10 codes with appropriate statistical tools, as recommended by HCUP, which allows longitudinal analysis of comorbid diagnoses to obtain national estimates, effectively limits miscoding errors in the administrative database. A prior systematic review has demonstrated that the administrative dataset is fairly accurate in analyzing psychiatric comorbidities, with an average predictive value of 76%. Inherent limitations of the database also include a lack of data regarding the severity of the psychiatric comorbidities and medical therapy of the hospitalized IBD patient. Further studies evaluating the severity of the psychiatric comorbidities and impact of IBD medications are needed to address this important issue.

Summary Box

What is already known:

- Patients with inflammatory bowel disease (IBD) are more likely to develop anxiety and mood disorders
- Anxiety and mood disorder diagnoses correlate with more active IBD, including more frequent relapses and a lower likelihood of achieving remission with biologic therapy
- The American College of Gastroenterology clinical guideline for preventative care in IBD recommends screening for psychiatric comorbidities in the outpatient setting
- The impact of the interaction between IBD and psychiatric comorbidities on outcomes in hospitalized IBD patients has not been well established

What the new findings are:

- The prevalence of anxiety disorder in hospitalized IBD patients increased significantly between 2009-2018
- The prevalence of mood disorders did not significantly change during this time period
- Anxiety and mood disorders were associated with a longer hospital stay and more in-hospital complications
- These findings highlight the importance of incorporating psychological screening and mental health services in the management of the hospitalized IBD patient

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