

Original Article



Rising Burden of Psychiatric and Behavioral Disorders and Their Adverse Impact on Health Care Expenditure in Hospitalized Pediatric Patients with Inflammatory Bowel Disease

Aravind Thavamani ,¹ Jasmine Khatana ,² Krishna Kishore Umaphathi ,³ and Senthilkumar Sankararaman ¹

¹Division of Pediatric Gastroenterology, Hepatology and Nutrition, UH Rainbow Babies and Children's Hospital, Case Western Reserve University School of Medicine, Cleveland, OH, USA

²Department of Pediatrics, Metro Health Medical Center, Case Western Reserve University School of Medicine, Cleveland, OH, USA

³Division of Pediatric Cardiology, Rush University Medical Center, Chicago, IL, USA

OPEN ACCESS

Received: Sep 10, 2021

1st Revised: Dec 7, 2021

2nd Revised: Jul 9, 2022

Accepted: Oct 7, 2022

Published online: Jan 10, 2023

Correspondence to

Senthilkumar Sankararaman

Division of Pediatric Gastroenterology,
Hepatology and Nutrition, UH Rainbow Babies
and Children's Hospital, Case Western Reserve
University School of Medicine, Cleveland, Ohio
44106, USA.

Email: senthilkumar.sankararaman@uhhospitals.org

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ORCID iDs

Aravind Thavamani

<https://orcid.org/0000-0002-4966-5113>

Jasmine Khatana

<https://orcid.org/0000-0001-5248-5968>

<https://pghn.org>

ABSTRACT

Purpose: The incidence and prevalence of inflammatory bowel disease (IBD) are increasing along with an increasing number of patients with comorbid conditions like psychiatric and behavioral disorders, which are independent predictors of quality of life.

Methods: Non-overlapping years (2003-2016) of National Inpatient Sample and Kids Inpatient Database were analyzed to include all IBD-related hospitalizations of patients less than 21 years of age. Patients were analyzed for a concomitant diagnosis of psychiatric/behavioral disorders and were compared with IBD patients without psychiatric/behavioral disorder diagnoses for outcome variables: IBD severity, length of stay and inflation-adjusted hospitalization charges.

Results: Total of 161,294 IBD-related hospitalizations were analyzed and the overall prevalence rate of any psychiatric and behavioral disorders was 15.7%. Prevalence rate increased from 11.3% (2003) to 20.6% (2016), $p < 0.001$. Depression, substance use, and anxiety were the predominant psychiatric disorders. Regression analysis showed patients with severe IBD (odds ratio [OR], 1.57; confidence interval [CI], 1.47–1.67; $p < 0.001$) and intermediate IBD (OR, 1.14; CI, 1.10–1.28, $p < 0.001$) had increased risk of associated psychiatric and behavioral disorders than patients with a low severity IBD. Multivariate analysis showed that psychiatric and behavioral disorders had 1.17 (CI, 1.07–1.28; $p < 0.001$) mean additional days of hospitalization and incurred additional \$8473 (CI, 7,520–9,425; $p < 0.001$) of mean hospitalization charges, independent of IBD severity.

Conclusion: Prevalence of psychiatric and behavioral disorders in hospitalized pediatric IBD patients has been significantly increasing over the last two decades, and these disorders were independently associated with prolonged hospital stay, and higher total hospitalization charges.

Keywords: Inflammatory bowel disease; Pediatrics; Child; Mental disorders; Epidemiology; Length of stay

Krishna Kishore Umapathi <https://orcid.org/0000-0003-1644-7395>Senthilkumar Sankararaman <https://orcid.org/0000-0003-3094-9703>**Conflict of Interest**

The authors have no financial conflicts of interest.

INTRODUCTION

The incidence and prevalence of inflammatory bowel disease (IBD) are increasing worldwide [1,2]. The increase in prevalence rate among children is projected to be substantially high, from 62 per 100,000 in children in 2008 to an estimated prevalence rate of 159 per 100,000 population by 2030 [2]. With this rising incidence, other comorbid conditions such as psychiatric and behavioral disorders may be increasing. Recent studies in children showed that IBD patients are at increased risk of psychiatric disorders [3,4]. Like other chronic inflammatory diseases, the surge of cytokines and other inflammatory mediators have been hypothesized to affect the emotion and behavior of these patients leading to increased prevalence of mental disorders [5-7]. Further, children with IBD are often malnourished secondary to diminished intake, malabsorption, ongoing inflammation, and protein-losing enteropathy, which might make them prone to body image issues and low self-esteem. Frequent hospitalizations and endoscopic procedures, IBD-related surgeries such as ileostomy or colostomy leading to morphological changes in their body, and effect of medications like corticosteroids may adversely affect their mental well-being and quality of life. Both adult and pediatric studies have shown that psychiatric disorders are associated with poor quality of life in patients with IBD [8,9].

The North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition has recommended active annual screening for depression and anxiety among pediatric IBD patients as they likely have an impact on the quality of life, school attendance, medication compliance, and social functioning [10,11]. Although depression and anxiety are well-known associations of pediatric IBD, data on the prevalence rate of various psychiatric and behavioral disorders and its impact on hospital outcomes are limited among hospitalized pediatric patients. Thus, we decided to evaluate the burden of psychiatric and behavioral disorders among IBD-related hospitalizations using a nationally representative database and analyze their impact on health care resource utilization.

MATERIALS AND METHODS

We analyzed non-overlapping years of two separate databases, National Inpatient Sample (NIS) and Kids Inpatient Database (KID), between 2003 and 2016. Both NIS and KID databases are part of the Health Care Cost and Utilization Project (HCUP) [12]. NIS includes 20% stratified data with sample frame representative of more than 97% of the United States population. NIS database includes patients of all age groups, and data are reported on an annual basis. KID is also a stratified aggregation of pediatric data from more than 4,200 hospitals across the United States and are sampled at a rate of 80%. KID includes data on hospitalizations of patients less than 21 years of age and is released every three years. Both NIS and KID databases contain discharge level data from community hospitals (except long-term acute care and rehabilitation centers) across the United States.

We included all patients less than 21 years of age during the study period with a primary diagnosis of Crohn's Disease (CD) or ulcerative colitis (UC) using the International Classification of Diseases (ICD) 9 and 10 diagnosis codes. We included only encounters with a primary diagnosis of CD or UC to accurately capture the prevalence of psychiatric and behavioral disorders among IBD-related hospitalizations and to evaluate their impact on health care resource utilization. We also analyzed the discharge encounters for a concomitant diagnosis of any of the following psychiatric and behavioral disorders including depression,

anxiety, adjustment disorder, bipolar disorder, post-traumatic stress disorder (PTSD), stress reaction, personality disorders, attention deficit disorder (ADD)/attention deficit hyperactive disorder (ADHD), pervasive developmental disorder, eating disorder, obsessive compulsive disorder (OCD), schizophrenia and substance abuse using ICD codes. Patients with a primary diagnosis of IBD and without a concomitant diagnosis of any of the aforementioned psychiatric and behavioral disorders were categorized as controls for comparison. Various demographic factors were compared between the groups in **Table 1**. Insurance status was grouped into three categories, 1) Public – included Medicaid and Medicare insurances, 2) Private – included all commercial insurances and 3) Others – included patients who were uninsured, self-pay, no charge and others.

We classified the severity of IBD based on validated methods of severity in prior literature which included the presence or absence of parameters such as anemia, parenteral nutrition use, malnutrition, blood transfusion, clostridium difficile infection [13,14]. The severity

Table 1. Comparison of demographics and severity of disease between IBD patients with and without psychiatric and behavioral disorders

Parameters	IBD with psychiatric and behavioral disorders	IBD without psychiatric and behavioral disorders	p-value
Age	16.6±3.2	15.3±3.9	<0.001
Gender			0.35
Male	12,882 (51.0)	69,416 (51.3)	
Female	12,393 (49.0)	65,935 (48.7)	
Race			<0.001
Caucasians	16,071 (63.6)	76,822 (56.5)	
African-American	2,458 (9.7)	16,665 (12.3)	
Hispanics	1,663 (6.6)	12,015 (8.8)	
Others	5,094 (20.1)	30,507 (22.4)	
Insurance			<0.001
Public	8,099 (32.0)	32,263 (23.7)	
Private	14,650 (57.9)	92,102 (67.7)	
Self-pay/uninsured/others	2,537 (10.0)	11,644 (8.6)	
Hospital bed size*			0.23
Small	2,800 (11.1)	15,382 (11.3)	
Medium	6,020 (23.8)	31,796 (23.4)	
Large	16,466 (65.1)	88,831 (65.3)	
Region of hospital			<0.001
Northeast	3,907 (22.3)	19,343 (22.4)	
Midwest	4,690 (26.8)	21,343 (24.7)	
South	5,896 (33.6)	30,829 (35.7)	
West	3,029 (17.3)	14,918 (17.3)	
Admission type			<0.001
Elective	3,955 (15.7)	28,707 (21.2)	
Non-elective	21,273 (84.3)	106,707 (78.8)	
IBD surgeries	3,224 (12.8)	18,313 (13.5)	0.002
IBD severity			<0.001
Low	15,185 (60.1)	87,560 (64.4)	
Intermediate	8,076 (31.9)	40,975 (30.1)	
Severe	2,025 (8.0)	7,473 (5.5)	
Mean length of stay	7.17±0.05	5.83±0.1	<0.001
Total mean hospitalization charges	47,770±482	38,974±149	<0.001
Discharges			<0.001
Routine	22,607 (89.5)	125,626 (92.4)	
Against medical advice	317 (1.3)	543 (0.4)	

Values are presented as mean±standard deviation or number (%).

IBD: inflammatory bowel disease.

*Details of hospital bed size classification is available at https://www.hcup-us.ahrq.gov/db/vars/hosp_bedsize/nisnote.jsp.

score ranges from 0 to 14 for CD and up to 7 for UC. These risk scores predicting the need for surgical intervention among IBD patients and the severity of hospitalization have been used and validated in prior studies evaluating the severity of disease among IBD patients. The risk scores and stratification were described in **Supplementary Table 1**. We also evaluated for common IBD-related surgeries and compared between the groups. For hospital resource utilization, we compared the length of hospital stay and total hospitalization charges between the groups. Total hospitalization charges were adjusted for the year 2016 United States (US) dollars accounting for inflation as per the US Bureau of Labor and Statistics. Multiple regression models were constructed to analyze the relationship between various psychiatric disorders with mean length of stay and mean total hospitalization charges as outcome variables. Appropriate discharge weights provided in the HCUP databases were used to provide nationwide prevalence estimates.

Statistical analysis

Categorical variables were described as proportions and percentages. Continuous variables were described as mean and standard deviations. Categorical variables were compared using χ^2 test and continuous variables using independent student t test. Multivariate logistic regression model was used to calculate the adjusted odds ratio and 95% confidence interval for severity of IBD. Linear regression models were constructed to estimate the effect of psychiatric and behavioral disorders on mean length of hospital stay and mean total charges of IBD-related hospitalizations. Multivariate models were adjusted for all the factors associated with psychiatric and behavioral disorders at a p -value < 0.2 on univariate analysis. Cochran-Armitage test was used for trend analysis of psychiatric disorders over the years.

IBM SPSS Statistics for Windows, Version 24.0 (IBM Co., Armonk, NY, USA) was used for statistical analysis.

RESULTS

We analyzed a total of 161,294 IBD-related hospitalizations between 2003 and 2016. Patients were predominantly admitted with CD (61.9%) compared to UC (30.1%). The mean age of the population was 15.5 ± 3.0 years, and males contributed to 51.3% of the population (**Table 1**). The overall prevalence rate of any psychiatric disorder was 15.7% (25,286). The prevalence rate increased from 11.3 per 100 IBD-related hospitalizations in 2003 to 20.6 per 100 IBD-related hospitalizations in 2016, $p < 0.001$ (**Fig. 1**). The annual percent increase in psychiatric and behavioral disorders was 6% during the study period. The prevalence rate of psychiatric and behavioral disorders increased with age, 3.9% at three years of age to 23.8% at 20 years of age, $p < 0.001$ (**Fig. 2**). Patients with psychiatric and behavioral disorders were slightly older (16.6 vs. 15.3 years) (**Table 1**). There was no gender difference between the groups. When compared to the control population, an increased proportion of IBD patients with psychiatric and behavioral disorders were Caucasians, had public insurance and non-elective hospital admissions. Patients with psychiatric and behavioral disorders had more discharges against medical advice than control population (1.3% vs. 0.4%, $p < 0.001$). There was no mortality in the psychiatric and behavioral disorders group compared to 42 hospital deaths in the control group.

Of the psychiatric and behavioral disorders, substance use and depression were the predominant disorders with a prevalence rate of 4.4% each, followed by anxiety contributing to 4.1%. ADHD/ADD was present in 2.8% and adjustment disorder was present in 1.7%

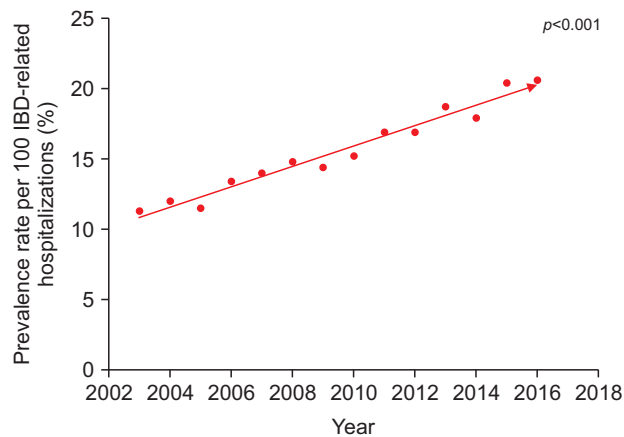


Fig. 1. Prevalence trend of psychiatric and behavioral disorders among pediatric IBD-related hospitalizations between 2003 and 2016.

IBD: inflammatory bowel disease.

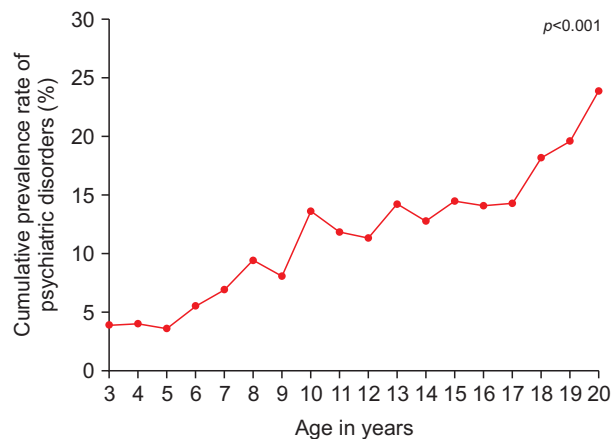


Fig. 2. Cumulative prevalence rate of psychiatric and behavioral disorders by age among pediatric patients hospitalized with IBD between 2003 and 2016.

IBD: inflammatory bowel disease.

of our IBD population. The relative proportion of prevalence of various psychiatric and behavioral disorders were noted in **Fig. 3**. All other psychiatric disorders had a prevalence rate of $\leq 1\%$ individually. Of patients with psychiatric and behavioral disorders, 21.6% (5,513) of the patients had more than one mental health disorder. Multiple logistic regression analysis showed that psychiatric and behavioral disorders were increasingly associated with worsening degree of IBD severity (**Table 2**). In comparison with low severity IBD, intermediate severity was 1.14 times (95% confidence interval [CI], 1.10–1.18; $p < 0.001$), and severe IBD disease was 1.57 times (95% CI, 1.47–1.67; $p < 0.001$) more likely associated with psychiatric and behavioral disorders. After adjusting for various factors and severity of IBD, hospitalized pediatric IBD patients with any psychiatric and behavioral disorders had prolonged mean hospital stay by 1.17 days (CI, 1.07–1.28; $p < 0.001$) and while incurring 8473 \$ (CI, 7,520–9,425; $p < 0.001$) higher mean hospitalization charges (**Table 2**). A full model of multivariate regression was described in **Supplementary Tables 2 and 3**. Similarly, on sub-analysis, both CD and UC patients had increased length of stay and higher hospitalization charges during the study period (**Table 3**). Adjustment disorder and eating disorder had increased odds of association with prolonged hospital stay while incurring higher charges of hospitalization followed by depression and anxiety (**Supplementary Table 4**). ADD/ADHD,

Relative proportion of prevalence of various psychiatric and behavioral disorders in pediatric IBD patients

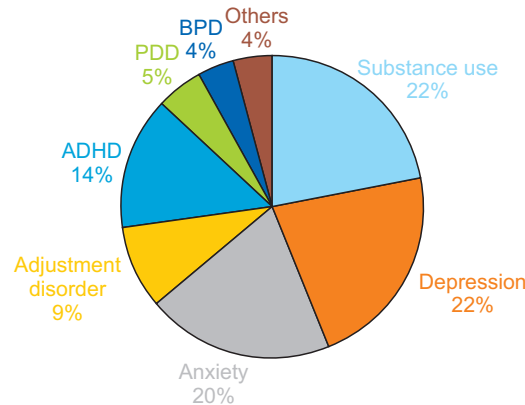


Fig. 3. Pie chart demonstrating relative proportion of prevalence of various psychiatric and behavioral disorders among pediatric patients with IBD.

IBD: inflammatory bowel disease, ADHD: attention deficit hyperactive disorder, PDD: pervasive developmental disorder, BPD: bipolar disorder.

Table 2. Multivariate analysis evaluating the impact of psychiatric and behavioral disorders on the severity of disease in pediatric patients with IBD

Parameters	Odds ratio	95% CI	p-value
IBD severity*			
Low	Reference		
Intermediate	1.14	1.10–1.18	<0.001
Severe	1.57	1.47–1.67	<0.001
Average difference			
Mean length of stay (d)†	1.17	1.07–1.28	<0.001
Total mean Hospitalization costs (USD)†	8,473	7,520–9,425	<0.001

CI: confidence interval, IBD: inflammatory bowel disease, USD: United States dollars.

*Refer to Supplementary Table 2 for a full model of multivariate logistic regression analysis.

†Refer to Supplementary Table 3 for a full model of multivariate linear regression analysis.

Table 3. Multivariate analysis evaluating the impact of psychiatric and behavioral disorders in pediatric patients with ulcerative colitis and Crohn's disease

Parameters	Ulcerative colitis		Crohn's disease	
	OR (95% CI)	p-value	OR (95% CI)	p-value
IBD severity				
Low	Reference		Reference	
Intermediate	1.04 (0.98–1.10)	0.17	1.23 (1.17–1.29)	<0.001
Severe	1.48 (1.34–1.64)	<0.001	1.63 (1.50–1.77)	<0.001
Average difference				
Mean length of stay (d)	1.29 (1.13–1.45)	<0.001	1.09 (0.96–1.22)	<0.001
Total mean hospitalization costs (USD)	9,817 (8,238–11,396)	<0.001	7,429 (6,275–8,583)	<0.001

OR: odds ratio, CI: confidence interval, IBD: inflammatory bowel disease, USD: US dollars.

along with substance use, had shortened hospital stay in comparison with other psychiatric disorders. Acute reaction to stress and personality disorder did not have any significant impact on the hospital stay or total hospitalization charges (**Supplementary Table 4**).

DISCUSSION

Here, we present the largest population-based study evaluating the prevalence of psychiatric and behavioral disorders among pediatric IBD-related hospitalizations and their impact on health care resource utilization. We demonstrated the increasing prevalence of psychiatric

and behavioral disorders among pediatric patients hospitalized with IBD. In 2016, almost 1 in 5 IBD-related hospitalizations had at least one psychiatric and behavioral disorder. Patients with a higher degree of IBD severity had increased association of co-existing psychiatric and behavioral disorder diagnosis. There could be complex interactions between various socio-economic, environmental, and IBD-related factors leading to this increasing prevalence of psychiatric and behavioral disorders in patients with severe IBD. Worsening severity of IBD could be predisposing to psychiatric disorders or untreated active mental health issues may lead to poor compliance to treatment and subsequent worsening of IBD.

After adjusting for various demographic factors, severity of IBD and the need for surgeries, our findings demonstrated that psychiatric and behavioral disorders were independently associated with prolonged mean hospital stay and contributing to higher mean hospitalization charges.

In our study, the overall prevalence rate of psychiatric and behavioral disorders was 15.6% among hospitalized IBD patients less than 21 years of age. In our similar recent population-based study, the prevalence rate of psychiatric disorders was noted to be 21.6% among IBD patients between 5 and 24 years of age [3]. This increased prevalence could be due to the difference in the age group of the population between these two studies, as we demonstrated an increasing prevalence of psychiatric disorders with age. Also, in the current study, we included only patients who were hospitalized, whereas the prior study included all patients with an outpatient or inpatient encounter within the hospital systems of the Explorys database. In a Swedish national study on pediatric-onset IBD between 1973 and 2013, 17.2% (1,117 out of 6,464) had a diagnosis of a psychiatric disorder [4]. In their study, the incidence rate of any psychiatric disorder was reported as 17.1 per 1000 person-years [4].

The prevalence rate increased with age in our study population with a peak prevalence rate of 23.8% at 20 years of age. Caucasians contributed to the majority of IBD patients with psychiatric and behavioral disorders (63.6% vs. 56.5%, $p < 0.001$) and had increased risk of associated psychiatric and behavioral disorders compared to other races, $p < 0.001$. A similar study on adults showed Caucasian predominance among IBD patients with psychiatric disorder [15]. Also, patients with private insurance and other modes of payment had decreased odds of associated psychiatric disorders when compared to patients with public insurance. Similar results were observed in adults as more proportion of IBD patients with mental health disorders had Medicare Advantage plans as opposed to commercial insurances and also belonged to lower income groups [15].

Depression, substance use, and anxiety contributed to the majority of patients with psychiatric disorder, each individually contributing close to 22%. Similar population-based pediatric and adult studies have shown a consistent pattern of psychiatric disorders with depression and anxiety contributing to the majority of mental health issues [3,4,15]. In a cross-sectional study done at a tertiary institution, the reported prevalence for depression was 25%, and they further noted increasing depressive symptoms among patients with moderate to severe disease, which is in line with the findings of our study revealing an increasing rate of psychiatric disorder prevalence in patients with worsening severity of IBD [16]. In a recent study involving adult patients, anxiety disorder was associated with worse IBD outcomes, but a similar association was not noted for depression [17]. Gray et al. [18] conducted a study on adolescents with IBD demonstrated that depression and anxiety symptoms may significantly affect the treatment adherence negatively, and consequently

may contribute to poor disease control. In a study carried out in outpatient settings involving adults with IBD, having comorbid psychiatric diagnoses were noted as risk factors for medical non-compliance and also predisposed to severe disease progression [19].

In our study, IBD patients with psychiatric disorders had prolonged mean hospital stay independent of the disease severity. Depression, anxiety, and eating disorder were associated with an increased mean hospital stay. Patients with co-existing adjustment disorder (additional days – 4.95, $p < 0.001$) and eating disorder (additional days – 4.39, $p < 0.001$) had the highest impact on hospital stay. In a similar study utilizing the KID on pediatric IBD patients, depression was associated with prolonged hospital stay with an odds ratio of 1.5 (1.19–1.90), $p < 0.01$, while no significant association was noted between depression and procedures, imaging or need for surgery during the hospitalizations [20]. Another recent study evaluating depression in adult patients with both CD and UC also demonstrated similar results with higher length of hospital stay in patients with depression [21]. In our study, we found similar results that patients with depression and anxiety had 1.2 and 0.95 additional days of mean hospital stay respectively, after adjusting for other demographic factors and disease severity. Although psychotic disorder prevalence is low among pediatric population, schizophrenia was associated with 1.72 additional days of IBD-related hospitalization. Similarly, pervasive developmental disorders were associated with increased length of hospitalization by 0.8 days whereas ADD/ADHD were associated with a decreased hospital stay by 0.23 days. Substance use and PTSD were associated with decreased length of hospital stay. In our study, having an associated diagnosis of any psychiatric disorder increased the total mean hospitalization charges by an additional \$ 8473 (CI, 7,520–9,425; $p < 0.001$) after adjusting for disease severity and IBD-related surgeries. Szigethy et al. [15] in their article on the cost of mental health disorders, showed that adult IBD patients with mental health issues had higher hospitalization-related charges (\$ 39,205 vs. 29,505, $p < 0.001$).

Our study is the first of its kind to analyze the impact of various psychiatric and behavioral disorders on the health expenditure of hospitalized pediatric patients with IBD. Eating disorder and adjustment disorder contributed to increased hospital expenditure of close to \$35,000. Anxiety and depression were also independently associated with increased hospitalization charges, whereas substance abuse and PTSD were associated with lower charges.

Our study has various limitations. All limitations pertinent to using large administrative databases are applicable here including the retrospective nature of the study. We depend on the ICD codes for diagnosis, and errors related to coding should be considered while interpreting the results. Further, other psychiatric and behavioral issues such as personality disorder, OCD may not be coded during acute disease-related hospitalization, thus potentially underestimating the prevalence rate of psychiatric disorders in hospitalized patients. There is paucity of data on disease activity, which could affect the incidence and prevalence of psychiatric disorders. Further data on crucial factors that could have a profound effect on the prevalence of psychiatric disorders, such as the type of IBD treatment, use of corticosteroids, details of IBD disease course (disease remission period, and duration of disease), and treatment details of the psychiatric disorders are not available for analysis. We do not have data on family history of psychiatric disorders as well. Further, this is analysis of cross-section of data during that particular hospitalization, and the impact on readmission rates and information on longitudinal follow up are lacking. We included only hospitalized patients, and so patients with less severe IBD might have been excluded, and thus underestimation of overall prevalence rate of psychiatric and behavioral disorders is a possibility.

Also, we analyzed hospitalization encounters and not individual patients. Patients with relatively severe disease might have been hospitalized multiple times during the study period resulting in possible overrepresentation of these patients.

Despite these limitations, there are various strengths we intend to depict. We used a nationally representative sample of close to 160,000 discharge encounters, the largest sample size ever analyzed for psychiatric and behavioral disorders in the hospitalized pediatric patients with IBD. This large sample size might limit various study biases related to studies on patients exclusively from tertiary care institutions, who are often complex and might have increased comorbid conditions. Although administrative databases are prone for coding errors, IBD and other psychiatric disorders have distinct codes in both ICD 9 and ICD 10 versions, which were validated and employed in prior studies using administrative databases, thus ensuring reliability and accuracy of the information captured [4,22,23]. Our study sheds light on the individual impact of various psychiatric and behavioral disorders on hospital expenditure. Furthermore, it provides research opportunities focused on preventive interventions aimed to benefit the at-risk population and helps to decrease the adverse impact on health care resource utilization.

In conclusion, the prevalence of psychiatric and behavioral disorders is increasing steadily among pediatric IBD patients at an alarming rate. With the increasing prevalence of IBD, a further increase in the prevalence of psychiatric and behavioral disorders is expected, which may contribute to poor quality of life and an overall increased disease burden in IBD patients. Multidisciplinary care team incorporating psychiatric and behavioral health specialists may play an integral part in addressing this concerning trend and is recommended to provide a holistic care to pediatric IBD patients. Further studies are urgently required to evaluate this need for psychiatric and behavioral health services for IBD patients and their impact on treatment outcomes and a decrease in hospital expenditures.

SUPPLEMENTARY MATERIALS

Supplementary Table 1

Factors used for determining severity and stratification scores

[Click here to view](#)

Supplementary Table 2

Multivariate logistic regression analysis of various factors associated with psychiatric and behavioral disorders in IBD-related hospitalizations

[Click here to view](#)

Supplementary Table 3

Multivariate linear regression analysis for length of stay in IBD patients with psychiatric and behavioral disorders

[Click here to view](#)

Supplementary Table 4

Multivariate analysis evaluating the impact of various psychiatric and behavioral disorders on the, length of stay and total hospitalization charges among patients with IBD

[Click here to view](#)

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