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ORIGINAL ARTICLE

Burden of anxiety and depression among hospitalized patients with irritable bowel syndrome: a nationwide analysis

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Abstract

Background and aim Irritable bowel syndrome (IBS) is the most common functional gastrointestinal disorder that affects patients both physically and mentally. Our study aimed to investigate the burden of psychiatric disorders in IBS patients.

Methods We conducted a retrospective analysis of the National inpatient sample (NIS) from 2016 to 2019. We recruited patients admitted with a diagnosis of IBS and determined the prevalence of anxiety, depression, and suicide attempt/ideation.

Results We found a total of 1,256,325 hospitalizations with a diagnosis of IBS. Among them, 478,515 (38.1%) had anxiety and 344,165 (27.4%) had depression. The prevalence of psychiatric disorders including anxiety (38.1% vs. 15.1%), depression (38.1% vs. 15.1%), bipolar disorder (5.22% vs. 2.38%), suicidal attempt/Ideation (3.22% vs. 2.38%), and eating disorder (0.32% vs. 0.08%) was significantly higher in IBS patient population when compared to general adult population ($p < 0.001$). Patients with IBS had greater odds of anxiety (AOR 2.88, 95% CI 2.85–2.91, $P < 0.001$), depression (AOR 2.16, 95% CI 2.14–2.19, $P < 0.001$) and suicidal attempt/ideation (AOR 1.94, 95% CI 1.88–2.00, $P < 0.001$) in comparison to general population. IBS subtypes including diarrhea-predominant, constipation-predominant and mixed type were independently associated with increased odds of anxiety, depression, and suicide attempt/ideation. Patients with IBS and a co-diagnosis of anxiety or depression had increased mean length of hospital stay by 0.48 (95% CI 0.43–0.52, $P < 0.001$) and 0.52 (95% CI 0.06–0.97, $P < 0.03$) days, respectively.

Conclusion The presence of IBS is associated with an increased associated prevalence of psychiatric disorders such as anxiety, depression, and suicide attempt/ideation.

Keywords Anxiety · Constipation · Depression · Diarrhea · Irritable bowel syndrome · Suicide

Introduction

Irritable bowel syndrome (IBS) is a prevalent and potentially disabling functional bowel disorder characterized by recurrent abdominal pain or changes in bowel habits [1]. It has an estimated global prevalence of 11.2%, varying between 1.1 and 45% among the general population [2], and can impose a significant cost burden on healthcare services and society [3, 4]. The annual cost estimate per patient in the USA varies between $742 and $7547. The annual direct medical cost is estimated at $1.7 billion to $10 billion [3–5]. Anxiety and depression are the most prevalent psychiatric disorders in the US population. National institute of mental health (NIMH) data shows that 31.1% of the US adult population suffer from anxiety at some point in their lifetime, and 17.3 million US adults had at least one depressive episode in 2017 [6, 7].

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Studies have shown that a diagnosis of IBS is associated with poor quality of life, loss of employment, poor work management, medication non-compliance, and increased hospital readmission rates. Some studies have suggested its association with mental health–related conditions, such as anxiety and depression. Major psychosocial problems have been observed in 50–60% of IBS patients [8, 9]. A meta-analysis of 24 studies reported that 20–40% of IBS patients presented with depressive symptoms [10].

In our study, we analyzed the data obtained from the US National Inpatient Sample (NIS) to determine the burden of psychiatric disorders in the IBS population. We queried the prevalence of common psychiatric disorders, including anxiety, depression, and suicidal ideation/attempt in IBS patients. We compared it with the general adult population and individuals with other chronic medical conditions. We performed a detailed analysis of the impact of anxiety and depression among patients with IBS since these two conditions contribute to most of the burden of psychiatric illnesses.

Methods

Study design and data source

This is a retrospective cohort study of hospitalization data using the NIS database for four consecutive years between 2016 and 2019. The data were extracted using a principal diagnosis of IBS with a secondary diagnosis of the psychiatric condition (anxiety, depression, bipolar disorder, schizophrenia, suicidal attempt/ideation, and eating disorder). The NIS consists of data from 48 states plus the District of Columbia and represents more than 97% of the US population. It is the largest publicly available database maintained by the Healthcare Cost and Utilization Project (HCUP) agency. The NIS contains a 20% stratified sample of discharges from more than 4000 non-federal acute care hospitals in the USA. It has both patient and hospital level discharge data. Patient-level data includes age, gender, zip code, race, annual household income, principal diagnosis, secondary diagnosis, list of procedures performed, length of stay (LOS) at the hospital, and resource utilization. Hospital level data includes hospital location, teaching status, and bed size. The NIS database from 2016 to 2019 contains a record of about 28 million hospital discharges.

Study population

The inclusion criteria were (i) age > 18 years; (ii) patients with a principal diagnosis of IBS; and (iii) patients with a secondary diagnosis of anxiety, depression, and suicidal ideation/attempt. The International Classification of Diseases (ICD) 10^{th} revision codes were used to select these populations. A total of 1,256,325 (1.04%) patients with a principal diagnosis of IBS were included in the analysis. We further differentiated the patients into IBS-Diarrhea (IBS-D), IBS-Constipation (IBS-C), and IBS-mixed type (IBS-M).

Study outcomes and variables

The primary outcomes of interest were prevalence, odds of occurrence, and predictors of anxiety and depression in IBS patients. The secondary outcomes we investigated were prevalence and predictors of suicidal attempt/ideation and resource utilization (LOS and total hospital charges). We also investigated the prevalence rate of other common psychiatric disorders like schizophrenia, bipolar disorder, and eating disorders (anorexia nervosa, bulimia nervosa, and other eating disorders). The variables of interest were patient demographics which included age, sex, race/ethnicity, household income, insurance status, and pre-existing co-morbidities such as diabetes mellitus (DM), hypertension, obesity, history of smoking, alcohol use disorder, coronary artery disease (CAD), congestive heart failure (CHF), hyperlipidemia, obesity, chronic kidney disease (CKD), cerebrovascular accident (CVA), malignancy, and malnutrition. The other variables were hospital characteristics, including teaching status, location, and bed size.

Statistical analysis

We utilized STATA, version 17 (College Station, TX, USA), to conduct the statistical analysis. Fischer's exact test was used to compare proportions. We used a univariate regression model to calculate the unadjusted odds of outcome variables. Multivariable regression analysis was performed to obtain adjusted odds ratios (AORs). Variables included in the multivariate regression model were age, race/ethnicity, hospital teaching status, hospital bed size, hospital location, median household income, insurance status, Charlson's co-morbidity index (CCI), and history of CKD, CVA, CAD, CHF, hyperlipidemia, obesity, alcohol use, cigarette smoking, and malnutrition. These variables were selected as confounders in multivariable regression analysis based on significant association seen in univariate analysis with a cut-off p-value of 0.2. Logistic regression was used for binary outcomes (anxiety, depression, suicidal attempt/ideation, eating disorder), and linear regression was used for continuous variables (LOS, hospital charges).

Results

Patients characteristics

A total of 1,256,325 hospital discharges with a primary diagnosis of IBS were included in the analysis, out of

which 478,515 (38.1%) had anxiety and 344,165 (27.4%) had depression. Table 1 delineates the characteristics of the study population. The IBS patients with anxiety were younger (58.8 vs. 63.4 years) than those without it. The mean age of IBS patients with and without depression was 61. 4 vs. 61.7 years, respectively. Most patients in both anxiety and depression groups were female, 84.9% and 85.3%, respectively. The rate of anxiety and depression was higher among those who were white (87.8% vs. 87.5%) compared to other races. The prevalence of anxiety varied in different income groups, highest in patients with a 26th–50th percentile of median household income. The prevalence rate was 27.1% vs. 25%, 26.6%, 21.4% for groups 1st–25th, 51st–75$^{th.}$, and 76th–100thpercentiles respectively ($P < 0.001$). A similar distribution of median household income was seen in IBS patients with depression.

The majority of IBS patients with anxiety and depression were admitted to hospitals in the Southern region (36.3%, 36.2%), followed by Midwestern (30.1%, 30.2%), Northeastern (19.4%, 18.1%), and Western (14.3%, 15.5%) regions, respectively. Most of the patients with anxiety and depression were insured by Medicare (54.1%, 58.6%), followed by private/self-insurance (27.5%, 25.6%) and Medicaid (13.9%, 18.1%), respectively. A vast majority of these were admitted to urban teaching hospitals. Presence of co-morbidities showed similar trends in both anxiety and depression populations; smoking (25.1% vs. 25.7%), alcohol use (4.8% vs. 4%), obesity (20.1% vs. 22%), hypertension (43% vs. 44.6%), dyslipidemia (36.3% vs 0.40.4%), DM (21.1% vs. 25%), CHF (9.99% vs. 11.7%), CAD (14.6% vs. 16.6%), CVA (0.26% vs. 0.33%), CKD (11.8% vs. 14.7%), malnutrition (5.6% vs. 6%), and malignancy (4% vs. 4.5%), respectively.

Prevalence of psychiatric disorders in IBS

Patients with IBS had a significantly higher prevalence of psychiatric disorders compared to the general adult population. These include anxiety (38.09% vs. 15.15%, $P < 0.001$), depression (27.39% vs. 12.33%, $P < 0.001$), bipolar disorder (5.22% vs. 2.38%, $P < 0.001$), suicidal attempt/Ideation (3.22% vs. 2.38%, $P < 0.001$), and eating disorders (0.32% vs. 0.08%, $P < 0.001$). On the contrary, prevalence of schizophrenia was higher in patients without IBS (0.89% vs. 0.06%, $P < 0.001$) (Fig. 1).

Adjusted odds of anxiety, depression, and suicide

We used multivariate regression models to calculate the odds of anxiety, depression, and suicidal attempts/ideation among IBS patients. Patients with IBS have higher odds of anxiety (AOR 2.88, 95% CI 2.85–2.91, $P < 0.001$). Patients with IBS also had higher odds of depression (AOR 2.16, 95% CI 2.14–2.19, $P < 0.001$) and suicidal attempt/ideation (AOR 1.94, 95% CI 1.88–2.00, $P < 0.001$). Diagnosis of IBS was independently associated with increased odds of having depression, anxiety, and suicidal attempt/ideation after adjusting for patient and hospital level variables and confounders like smoking, alcohol use, dyslipidemia, CAD, MI, CHF, DM, malnutrition, malignancy, obesity, and CVA (Table 2).

Subgroup analysis

We investigated the odds of anxiety, depression, and suicide attempt/ideation in IBS-C, IBS-D, and IBS-M subtypes. We found that IBS-D was associated with higher odds of anxiety (AOR 2.76, 95% CI 2.69–2.83, $P < 0.001$) and depression (AOR 2.12, 95% CI 2.07–2.18, $P < 0.001$). Similarly, IBS-C and IBS-M was associated with higher odds of anxiety (AOR 3.41, 95% CI 3.28–3.55, $P < 0.001$ and AOR 3.37, 95% CI 3.13–3.63, $P < 0.001$) and depression (AOR 2.31, 95% CI 2.22–2.42, $P < 0.001$ and AOR 2.19, 95% CI 2.02–2.38, $P < 0.001$), respectively. All three subtypes IBS-D, IBS-C, and IBS-M were independently associated with higher odds of suicide attempt/ideation, AOR 1.74, 95% CI 1.60–1.88, $P < 0.001$; AOR 2.43, 95% CI 2.19–2.71, $P < 0.001$; and AOR 2.86, 95% CI 2.33–3.51, $P < 0.001$, respectively (Table 3).

Predictors of anxiety, depression, and suicide in IBS

The odds of having anxiety were greater in young patients, whereas the odds of depression were higher in older IBS patients. Females had higher odds of having anxiety and depression but lower odds of suicide attempts/ideation. White IBS patients had increased odds of anxiety, depression, and suicide attempt/ideation compared to other races. Low socioeconomic status was associated with increased anxiety, depression, and suicide attempts/ideation odds. Smoking, alcohol use, obesity, malnutrition, dyslipidemia, and CHF were independently associated with higher odds of depression, but only alcohol use showed increased odds of suicide attempt/ideation (Fig. 2A-C).

Resource utilization

Patients with IBS and a diagnosis of anxiety or depression had increased mean length of hospital stay by 0.48 (95% CI 0.43–0.52, $P < 0.001$) and 0.52 (95% CI 0.06–0.97, $P = 0.03$) days, respectively compared to those without these psychiatric illnesses. The mean hospital charges were higher by $691 (95% CI $92–$1292, $P = 0.02$) in patients with depression. Those with anxiety had less mean total charges by $1355 (95% CI, $1883 to $826, $P < 0.001$) (Table 4).

Table 1 Baseline characteristics of patients with irritable bowel syndrome and co-existing diagnosis of anxiety and depression

Baseline characteristics	Total number of IBS patients 1,256,325 (1.04%)		*P*-value [anxiety]	*P*-value [depression]
	Anxiety, *n* = 478,515 (38.09%)	Depression, *n* = 344,165 (27.39%)		
Mean age [years]	58.8 (58.6–58.9)	61.5 (61.3–61.6)	< 0.001	0.003
Female gender [*n* (%)]	406,355 (84.92%)	293,710 (85.34%)	< 0.001	< 0.001
Race [*n* (%)]			< 0.001	< 0.001
White	420,375 (87.85%)	301,144 (87.50%)		
Black	4,785 (5.70%)	21,476 (6.24%)		
Hispanic	19,763 (4.13%)	13,904 (4.04%)		
Asians	239 (0.05%)	1755 (0.51%)		
Native Americans	1579 (0.33%)	1101 (0.32%)		
Others	7130 (1.49%)	4784 (1.39%)		
Charlson's co-morbidity index [*n* (%)]			< 0.001	< 0.001
0	147,478 (30.82%)	91,100 (26.47%)		
1	128,003 (26.75%)	87,452 (25.41%)		
2	80,630 (16.85%)	61,399 (17.84%)		
3 or more	122,404 (25.58%)	104,179 (30.27%)		
Median household income (quartile)*			< 0.001	< 0.001
1st (0–25th)	119,294 (24.93%)	85,732 (24.91%)		
2nd (26th–50th)	129,438 (27.05%)	93,372 (27.13%)		
3rd (51st–75th)	127,189 (26.58%)	91,445 (26.57%)		
4th (76th–100th)	102,594 (21.44%)	73,583 (21.38%)		
Hospital region [*n* (%)]			< 0.001	< 0.001
Northeast	92,928 (19.42%)	62,397 (18.13%)		
Midwest	143,842 (30.06%)	103,938 (30.20%)		
South	173,462 (36.25%)	124,485 (36.17%)		
West	68,332 (14.28%)	53,346 (15.50%)		
Insurance status [*n* (%)]			< 0.001	< 0.001
Medicare	258,733 (54.07%)	201,818 (58.64%)		
Medicaid	66,322 (13.86%)	40,061 (11.64%)		
Private/self pay	131,544 (27.49%)	88,210 (25.63%)		
Uninsured	1005 (0.21%)	6333 (1.84%)		
Hospital bed size [*n* (%)]			0.21	0.0001
Small	100,727 (21.05%)	70,554 (20.50%)		
Medium	135,563 (28.33%)	97,261 (28.26%)		
Large	242,272 (50.63%)	176,350 (51.24%)		
Hospital teaching status [*n* (%)]			0.007	0.009
Rural	42,875 (8.96%)	30,252 (8.79%)		
Urban non-teaching	103,264 (21.58%)	72,722 (21.13%)		
Urban teaching	332,377 (69.46%)	241,191 (70.08%)		
Co-morbidities [%]				
Smoking	25.14	25.73	0.002	< 0.001
Alcohol abuse	4.83	4.04	< 0.001	< 0.001
Obesity	20.06	21.95	< 0.001	< 0.001
Hypertension	42.99	44.59	0.001	< 0.001
Dyslipidemia	36.29	40.56	< 0.001	< 0.001
Diabetes mellitus	21.14	25.01	< 0.001	< 0.001
Congestive heart failure	9.99	11.74	< 0.001	< 0.001
Coronary artery disease	14.65	16.62	< 0.001	0.14
Cerebrovascular accident	0.26	0.33	< 0.001	0.89

Table 1 (continued)

Baseline characteristics	Total number of IBS patients 1,256,325 (1.04%)		*P*-value [anxiety]	*P*-value [depression]
Chronic kidney disease	11.84	14.74	< 0.001	0.002
Malnutrition	5.64	6.03	0.16	< 0.001
Malignancy	4.3	4.51	< 0.001	< 0.001

*Median household income for the patient's Zip Code: 1st Quartile: $1-$42,999, $1-43,999, $1-45999, 1-47,999 for NIS 2016,2017,2018 and 2019, respectively. 2nd quartile: $43,000-$53,999, $44,000-$55,999, $46,000-$58,999, and 48,000-60,999 for NIS 2016,2017,2018 and 2019, respectively. 3rd quartile: $54,000-$70,999, $56,000-$73,999, $59,000-$78,999, 61,000-81,999 for NIS 2016,2017,2018 and 2019, respectively. 4th quartile: >$71,000,>74,000,> 79,000, >82,000 for NIS 2016, 2017, 2018, and 2019, respectively

Discussion

Using the US NIS database, our study identified the prevalence of common psychiatric disorders in hospitalized patients with IBS. We studied IBS as a predictor of developing common psychiatric disorders in the US adult population. To our knowledge, this has previously not been reported utilizing a national registry like the NIS. Our findings showed that patients with a history of IBS have higher odds of having concurrent depression, anxiety, and bipolar disorder when compared to the general adult population. Our findings showed a statistically significant association of anxiety and depression with IBS even after adjusting for chronic medical illnesses like DM, cancer, and vascular comorbidities like CAD, MI, and CVA. We recommend that healthcare providers who manage IBS patients with chronic medical conditions screen them with questionnaire-based tests to assess for psychiatric illnesses.

Age is an essential non-modifiable risk factor for diseases. Studies have shown that mood disorders are prevalent in younger patients [11], which is in accordance with our research in which we documented increased odds of anxiety and suicide attempt/ideation in younger patients. Still, in contrast, we found higher odds of depression in older patients. This could be because of increasing age and years spent with a diagnosis of IBS, a cumulative effect of prolonged stress of disease process, subsequently increasing the risk of depression. Our study also demonstrated that the female gender is associated with higher odds of anxiety and depression, which is consistent with other studies showing similar results [12]. More prospective studies are needed to understand this effect in the general population, specifically in IBS patients.

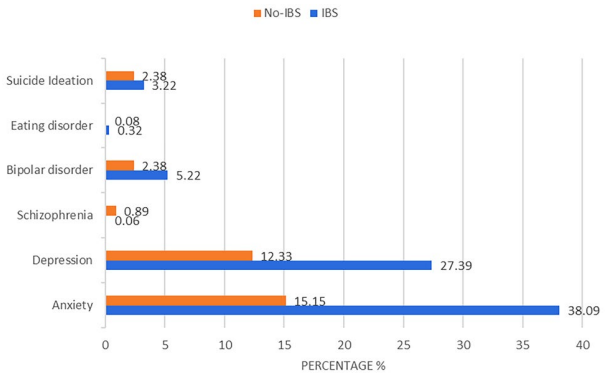

Fig. 1 Prevalence of Psychiatric diseases in IBS

The nature of IBS and its disease course has a risk of poor quality of life among many of these patients. A Polish study suggested that QOL (quality of life) was lower in patients with IBS than in the control group [13]. Few studies revealed that QOL in IBS patients was significantly lower than in patients with other chronic diseases, like gastroesophageal reflux disease, end-stage kidney disease, inflammatory bowel disease, liver disease, CHF, DM, and chronic pancreatitis [14–16]. This can lead to psychological stress and financial hardships, which generates a vicious cycle of perpetuating further mental stress leading to anxiety and depression. Our analysis shows that patients in a lower income group had higher odds of having anxiety and depression. A similar study by Nilsson et al. reported an increased prevalence of these conditions in the unemployed population [17]. Hence, it is imperative to adequately treat IBS and the associated mental illnesses promptly to prevent the worsening of economic and healthcare burden.

People with psychiatric disorders are prone to bad lifestyle choices such as smoking [18]. Our analysis showed higher odds of smoking in IBS patients with anxiety and depression. Interestingly, a Swedish study showed that there might be an association between smoking and IBS-D but not IBS-C [17]. Smoking is known to slow gastric emptying and oro-cecal transit times but is less likely to alter colonic transit [19–22]. At the same time, an association with IBS-C might then be

Table 2 Adjusted odds of having a co-diagnosis of a psychiatric disorder in patients with irritable bowel syndrome

Outcomes	Adjusted odds ratio	95% CI	*P*-value
Anxiety	2.88	2.85–2.91	< 0.001
Depression	2.16	2.14–2.19	< 0.001
Suicide attempt/ ideation	1.94	1.88–2.00	< 0.001

Table 3 Adjusted odds of having a co-diagnosis of a psychiatric disorder in patients with different subtypes of irritable bowel syndrome

Outcomes	IBS-Diarrhea		IBS-Constipation		IBS-Mixed	
	Adjusted odds ratio	*P*-value	Adjusted odds ratio	*P*-value	Adjusted odds ratio	*P*-value
Anxiety	2.76 (2.69–2.83)	<0.001	3.41(3.28–3.55)	<0.001	3.37 (3.13–3.63)	<0.001
Depression	2.12 (2.07–2.18)	<0.001	2.31 (2.22–2.42)	<0.001	2.19 (2.02–2.38)	<0.001
Suicide attempt/ ideation	1.74 (1.60–1.88)	<0.001	2.43 (2.19–2.71)	<0.001	2.86 (2.33–3.51)	<0.001

expected if smoking is a risk factor, it is also possible that delayed small intestinal transit could predispose to small intestinal bacterial overgrowth, which has been identified in a subset with IBS, and this by itself can cause chronic diarrhea [23].

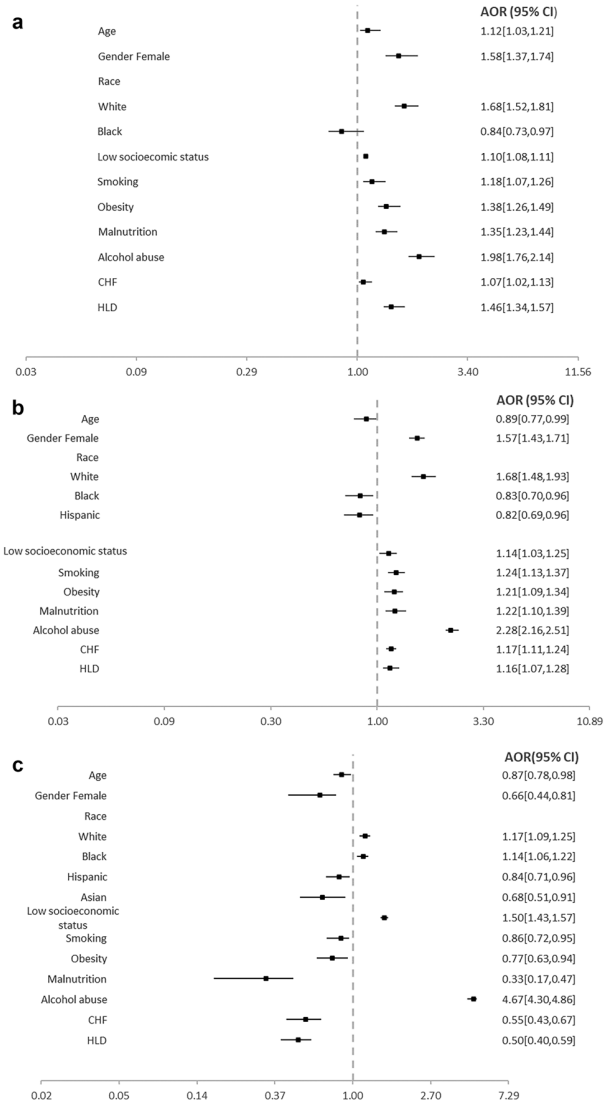

Fig. 2 **A** Predictors of depression in patients with irritable bowel syndrome. **B** Predictors of anxiety in patients with irritable bowel syndrome. **C** Predictors of suicide attempt or ideation in patients with irritable bowel syndrome

Furthermore, nicotine reduces pancreatic juice secretions, which may also potentially induce diarrhea due to malabsorption [24]. Previous studies have reported conflicting results regarding the association between smoking status and IBS [25]. An earlier systematic review identified 26 articles where smoking was not a risk factor for IBS [26]. Prospective studies could identify this relationship further, but it would be unethical to advise patients to start smoking to assess those effects. Regardless of the pathophysiological benefits, the psychosocial harm is enough to pursue smoking cessation instead of its promotion.

In our study, we found that Caucasians have a significantly higher risk of developing anxiety and depression when compared to other races. People admitted to urban teaching hospitals were more frequently diagnosed with anxiety and depression than those in rural hospitals. This is in line with what is generally observed, with people living in cities experiencing more stressful lives than those living in small towns and rural areas. We also analyzed inpatient mortality and hospital LOS; however, no significant differences were observed in mortality or higher mean LOS.

One possible explanation for the relationship between IBS and psychiatric co-morbidities could be the "brain-gut" axis. Changes in the immune system, colonic motility, autonomic nervous system, and microbiota composition have been reported in IBS patients with anxiety and depression [27]. Previous psychophysiological and neuroimaging studies suggested that dysfunction of the brain-gut axis, a bidirectional neurological pathway between the brain and digestive system, could likely lead to symptoms of IBS. Based on this explanation, IBS symptoms influence anxiety and depression, and on the other hand, psychiatric conditions or psychological factors may increase the tendency to cause IBS symptoms [28, 29]. Chronic diseases like IBS can have a destabilizing effect on the quality of life and are known to be associated with stress, work impairment, and cost burden. Therefore, treating IBS symptoms and recognizing mood disorders is integral to improving quality of life. It is recommended that physicians treating patients with anxiety and depression assess them for underlying IBS. If symptoms suggestive of IBS are recognized and treated, it would significantly improve psychiatric co-morbidities. Like in the case of a psychiatric condition, studies have shown

Table 4 Resource utilization for hospitalized patients with irritable bowel syndrome

Outcomes	Anxiety		Depression	
	AOR (95% CI)	*P*-value	AOR (95% CI)	*P*-value
Adjusted mean LOS	0.48 (0.43–0.52)	< 0.001	0.52(0.06–0.97)	0.03
Adjusted mean total hospital charges	− $1355 (− $1883 to − $826)	< 0.001	$691 ($92 to $1292)	0.02

CI Confidence Interval, *LOS* Length of Stay

the efficacy of antidepressants and psychological therapies in treating patients with IBS [30, 31].

While the NIS allows analysis of a large population, increasing our study's power, several limitations exist. Our study has a retrospective design and, as such, can help determine disease associations but not causality. Since the various treatment options do not have ICD coding, we could not analyze the effects of antidepressant medications, anxiolytic medications, or non-pharmacologic therapies. Similarly, the impact of IBS treatment could not be analyzed. The data gathered is based on ICD-10 codes, and misclassification can cause a bias in data collection. Although we addressed an exhaustive list of confounding factors, residual confounding is still possible.

Conclusions

In our study, we found that IBS patients had a greater prevalence of anxiety, depression, and suicide attempts/ideation compared to the general population. IBS subtypes are independently associated with increased odds of psychiatric disorders. Based on these findings, we recommend that physicians treating patients with IBS pay attention to the presence of concurrent depression and anxiety and consider psychiatric evaluation. Early evaluation and treatment of psychiatric co-morbidities in IBS patients can help to improve their overall health and quality of life.

Author contribution ZT, UF, FK, MG, YG: concept and design of the study, data collection, data analysis, interpretation of results, writing of the manuscript, and final revision. MT, SR, YZ, RS: interpretation of results and manuscript writing. All authors approved the final version of the manuscript.

Data availability The analysis is based on the National Inpatient sample, which is a publicly available database maintained by the Agency of Healthcare cost and utilization project. Data can be shared on request.

Declarations

Conflict of interest The authors declare no competing of interests.
Ethical declaration.
All included authors declare no outside interests directly or significantly related to this paper.

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