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ORIGINAL ARTICLE

Decoding the gut-brain axis in irritable bowel syndrome: a cross-sectional analysis of anxiety and depression symptoms in constipation and diarrhoea predominant subtypes

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ABSTRACT

Aim The gut–brain axis is pivotal in the pathophysiology of irritable bowel syndrome (IBS), with anxiety, depression and quality of life. IBS-C (constipation-predominant) and IBS-D (diarrhoea-predominant) are frequently linked with psychological comorbidities. Neither in Indonesia nor globally has research been conducted regarding the relationship between subtypes of IBS and depression and anxiety. This study aimed to identify the relationship between depression and anxiety and subtypes of IBS.

Methods From January to December 2023, a cross-sectional study was conducted on 49 IBS patients at Dr Saiful Anwar General Hospital, Indonesia. Demographic data and colonoscopy reports were gathered. Psychological status was measured using the Hospital Anxiety and Depression Scale (HADS). The χ^2 test and Spearman's correlation analysis were performed to examine associations between demographic characteristics, IBS subtype, and psychological scores.

Results There were no significant associations between sex, age, or IBS subtype and the presence of anxiety or depression symptoms. Anxiety and depression scores were modestly correlated overall ($r = 0.503$; $p = 0.000$). Subgroup analysis revealed a strong correlation in IBS-C ($r = 0.613$; $p = 0.009$) and a moderate correlation in IBS-D ($r = 0.461$; $p = 0.008$), indicating a notable interrelationship within these subtypes.

Conclusion Moderate relationship between anxiety and depression was found in IBS patients, strongest in IBS-C and moderate in IBS-D. Neither demographics nor IBS subtype was significantly related to psychological symptoms independently. The findings warrant routine screening for mental health and multidisciplinary management in IBS patient.

Keywords: anxiety disorder, constipation, depressive disorder, diarrhea, irritable bowel syndrome

INTRODUCTION

Irritable bowel syndrome (IBS) is a chronic disorder of gut-brain interaction, characterized primarily by recurrent abdominal pain associated with changes in stool frequency or form, without identifiable structural or biochemical abnormalities (1,2). Recent meta-analysis covering studies from 2006 to 2024 found a global prevalence of 14.1% for IBS (3,4).

The global burden IBS is colossal, affecting millions of people worldwide and imposing enormous personal, social, as well as economic burdens. It is a colossal burden due to its chronic nature and challenges in a control (5,6). In China, the yearly cost per IBS patient is approximately CNY 18,263 (approximately USD 2,933), with inpatient and outpatient treatment accounting for over two-thirds of the costs and productivity loss accounting for approximately a quarter (7,8). These findings emphasize that IBS, even though not harmful, incurs significant direct medical expenses and significant indirect expenses due to absenteeism from work and reduced productivity, and thereby is defined as a significant socioeconomic impact worldwide (9,10).

A large meta-analysis showed IBS-D was the most common subtype globally (40%), followed by IBS-C (35%) (10). A large meta-analysis of 2006-2024 found globally, IBS-D is the most common subtype (31.5%), followed by IBS-M (3,11).

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The prevalence of irritable bowel syndrome subtypes varies according to the diagnostic criteria and population (11,12).

The majority of recent international research, including substantial meta-analysis, is not available for Indonesia-specific subtype distributions. A recent Indonesian study gave overall IBS prevalence in COVID-19 survivors but did not report subtype distribution (13). Asian literature shows considerable variation in percentages of subtypes, with IBS-D being variable (0.8% to 74%) and IBS-C (12% to 77%) but no recognizable pattern for Indonesia (14,15). There is extremely limited published information specifically detailing the prevalence of IBS subtypes within Indonesia, highlighting the need for population-specific epidemiology (13). Pathophysiology of IBS is strongly rooted in brain-gut axis disorders with a close relationship to anxiety and depression (16). Recent large-scale genetic research has identified several susceptibility genes for IBS that map to mood and anxiety disorders, suggesting common biological pathways, particularly those involving neural signalling and brain development, are responsible for causing gastrointestinal and psychological symptoms (17). This further adds validity to the fact that IBS is not a gastrointestinal illness, but a complex syndrome with bidirectional brain-gut-microbiome interaction in which central and enteric nervous system alterations aggravate symptoms (18). Irritable bowel syndrome with constipation (IBS-C) and diarrhoea (IBS-D) have been particularly interesting subtypes to study given their distinct and strongest correlation with depression and anxiety among all IBS subtypes. Recent meta-analyses and network analyses suggest that both IBS-C and IBS-D patients report significantly higher prevalence and frequency of depression and anxiety compared to non-affected controls, with IBS-C showing the highest prevalence rates of psychological comorbidity among all subtypes (19).

The biological interplay between gastrointestinal hormones and emotional states appears especially relevant in these subtypes, as altered levels of somatostatin and vasoactive intestinal peptide have been observed in IBS-C and IBS-D patients with anxiety and depression, suggesting a mechanistic link between gut motility disturbances and psychological distress (20,21).

The bidirectional relationship between psychological symptoms and IBS severity underscores the importance of systematic screening for and addressing mental health in these populations, as anxiety and depression not only exacerbate gastrointestinal symptoms but also influence treatment outcomes and healthcare-seeking behaviour (22).

This research is the first international study from Indonesia regarding the association between anxiety, depression, and IBS subtypes, i.e., constipation-predominant (IBS-C) and diarrhoea-predominant (IBS-D), which are the most prevalent forms globally.

The aim of the study was to evaluate the association between psychological distress (anxiety and depression), and irritable bowel syndrome (IBS) subtypes, with particular emphasis on constipation-predominant (IBS-C) and diarrhoea-predominant IBS (IBS-D). In view of the central role of the gut–brain axis in IBS and the scarcity of evidence on subtype-specific psychological comorbidities, particularly in Indonesia, this study sought to delineate the relationship between anxiety and depression across IBS subtypes and to examine their interrelationship within each subtype.

PATIENTS AND METHODS

Patients and study design

This observational cross-sectional study with total sampling data from January to December 2023 was carried out in the Endoscopy and Colonoscopy Clinic, Gastroenterology and Hepatology Department, Dr Saiful Anwar General Hospital (Indonesia). All subjects who fulfilled the selection criteria and were willing to participate were included. The inclusion criteria were adult patients aged ≥ 18 years, patients who met IBS-C and IBS-D diagnostic criteria based on the Rome IV (23) and underwent a colonoscopy, and patients who were not currently undergoing inpatient care. The exclusion criteria were history of tumours or malignancies outside the digestive tract, patients with limited physical mobility or sequelae of stroke, previous history of depression and anxiety, and history of comorbid diabetes or autoimmune disorder.

Patient data were collected upon arrival at the Clinic. The Hospital Anxiety and Depression Scale (HADS) questionnaire (24) was used for evaluation of patients' mental health.

All participants provided written informed consent before enrolment.

This study received ethical approval from the Health Research Ethics Commission of Dr. Saiful Anwar General Hospital, with the approval number 400/229/K.3/302/2023.

The diagnosis of IBS-C and IBS-D was based on the Rome IV criteria (23) and colonoscopy findings (23). To calculate the scores for depression and anxiety symptoms, the HADS questionnaire (24) was used, with scores > 7 indicating the presence of anxiety and depression symptoms (24) (Figure 1).

Data were collected using a total sampling method involving all 223 patients who underwent colonoscopy from January to December 2023. Among those, 17 patients were diagnosed with constipation-predominant irritable bowel syndrome (IBS-C) and 32 with diarrhea-predominant irritable bowel syndrome (IBS-D).

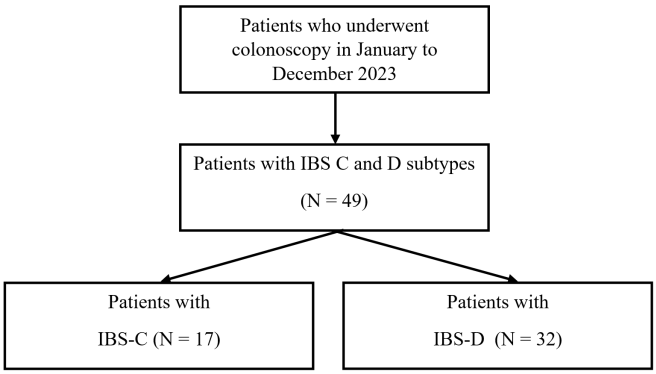

Figure 1. Flowchart for patient selection process

A correlation analysis between the occurrence of IBS with anxiety and depression in general was conducted. We obtained 53 patients with all types of IBS, of which four patients were excluded (three patients with IBS-M, and one patient with IBS-U), leaving 49 patients diagnosed with IBS-C and IBS-D to observe the correlation between the two most common subtypes of IBS and analyse the correlation with the prevalence of anxiety and depression.

Table 1. Baseline characteristics of 49 patients with irritable bowel syndrome (IBS) by psychological outcome

Characteristics	No.(%) of patients	Anxiety p	Anxiety OR (CI-95%)	Depression p	Depression OR (CI-95%)
Sex					
Male	25 (51.0)	0.524	1.579 (0.385–6.483)	0.830	1.142 (0.338–3.859)
Female	24 (49.0)				
Age (Mean±SD):	45.87±13.62				
<60 years	41 (83.7)	0.544	1.969 (0.213–8.163)	0.224	2.732 (0.416–17.938)
≥60 years	8 (16.3)				
Types of IBS					
IBS-C	17 (34.7)	0.727	1.306 (0.290–5.870)	0.849	1.091 (0.302–3.937)
IBS-D	32 (66.3)				
Types of psychological disorders¶					
Anxiety Score (Mean±SD): 10.87±3.59¶					
Depression Score (Mean±SD): 6.42±2.48					
Anxiety	39 (79.6)				
Normal (without anxiety)	10 (20.4)			0.962	1.037 (0.228–4.712)
Depression	15 (30.6)	0.962	1.037 (0.228–4.712)		
Normal (without depression)	34 (69.4)				

IBS, irritable bowel syndrome; IBS-C, constipation-predominant IBS; IBS-D, diarrhoea-predominant IBS; IBS-M, mixed IBS; IBS-U, unclassified IBS; SD, standard deviation.

Statistical analysis

A χ^2 test was conducted to compare anxiety and depression levels with different IBS subtypes, using a significance level of $p < 0.05$. For abnormally distributed data, Spearman's correlation (rho) with t-transformation (if there was > 10 patient data) was applied to evaluate the relationship between anxiety and depression with IBS-C and IBS-D.

RESULTS

A total of 49 IBS patients was enrolled, of which 17 patients with IBS-C and 32 patients with IBS-D; 25 (51.0%) were males and 24 (49.0%) were females, with a mean age of 45.87 ± 13.62 years. Majority of patients, 41 (83.7%), were < 60 years, and eight (16.3%) were ≥ 60 years (Table 1).

The distribution of IBS subtypes revealed that the most frequently identified subtype was IBS-D (66.3%) followed by IBS-C (34.7%). The mean anxiety score was 10.87 ± 3.59, and the mean depression score was 6.42 ± 2.48. Anxiety emerged as the predominant psychological disorder observed in 39 (out of 49; 79.6%), whereas depression was identified in 15 (out of 49; 30.6%) patients.

No statistically significant associations between sex, age group, or IBS subtype and the presence of anxiety or depression was found (all $p > 0.05$). Specifically, sex was not significantly related to anxiety ($p = 0.524$) or depression ($p = 0.830$), age group showed no association with anxiety ($p = 0.544$) or depression ($p = 0.224$), and IBS subtype was not associated with anxiety ($p = 0.727$) or depression ($p = 0.849$).

A significant positive relationship between anxiety and depression scores in the overall IBS group (Spearman $r = 0.503$, $p < 0.001$) was found, indicating a moderate association. The direction of this correlation was positive, meaning that higher anxiety scores were associated with higher depression scores. The clustering of data points along the regression line further supports the presence of a meaningful linear association (Figure 2).

Subgroup analysis demonstrated a strong positive correlation in IBS-C patients (Spearman $r = 0.613$, $p = 0.009$). The upward pattern of the data points highlighted the strength of this relationship. In IBS-D patients, the correlation remained statistically significant, with a moderate positive correlation (Spearman $r = 0.461$, $p = 0.008$). These results indicate that while anxiety and depression were correlated across all IBS patients, the association was stronger in IBS-C than in IBS-D.

DISCUSSION

The present study demonstrated a significant moderate positive correlation between depression and anxiety in IBS patients, aligning with recent evidence (25) and meta-analyses indicating higher rates of both depression and anxiety in IBS compared to

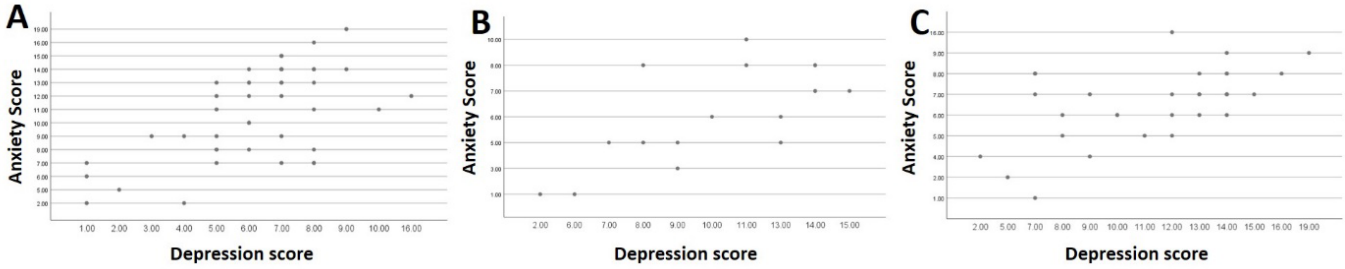

Figure 2. A) Correlation between anxiety and depression in IBS; B) Correlation between anxiety and depression in IBS-C; C) Correlation between anxiety and depression in IBS-D

Table 2. Correlation of anxiety and depression in patients with irritable bowel syndrome (IBS)

IBS types	Correlation of anxiety and depression in IBS patients	p	Rho
IBS (N = 53)	Significant moderate positive correlation	< 0.001*	0.503
IBS-C (N = 17)	Significant strong positive correlation	0.009*	0.613
IBS-D (N = 32)	Significant moderate positive correlation	0.008*	0.461

* statistically significant ($p < 0.05$).
Rho, Spearman correlation.

healthy controls (26,27). Subgroup analysis revealed a stronger correlation in IBS-C compared to IBS-D. Literature data confirm that both subtypes exhibit higher psychopathology than controls (28), IBS-C frequently presents with the highest prevalence of anxiety and depression (19,29), whereas IBS-D is often associated with greater quality-of-life impairment due to symptom unpredictability (22).

Although not directly measured in this study, these associations are likely underpinned by gut-brain axis dysregulation, creating a "vicious cycle" where emotional disturbance exacerbates gut symptoms (30). Potential mechanisms include microbiome-driven neurotransmitter modulation and immune activation (18,31–33), alongside causal genetic links and structural brain changes such as in the anterior cingulate cortex (34,35). Furthermore, neuroendocrine alterations, specifically elevated somatostatin and Vasoactive Intestinal Peptide (VIP) levels (20), as well as cortisol, serotonin, and dopamine dysregulation (36,37), may mediate the subtype-specific variations in psychological burden observed here (20,36).

Consequently, these findings fill a critical gap in Indonesian national data and underscore the necessity of a biopsychosocial approach (32,38). Given the established correlations, routine psychological screening is imperative for both IBS-C and IBS-D patients to optimize clinical outcomes and guide future longitudinal interventions.

Our study has several limitations, including the single centre study and the small number of patients with unequal subtype distribution. Conducting multi-centre research with a larger sample size will yield more accurate and comprehensive analyses of IBS subtypes.

This research illustrates a clinically relevant moderate relationship between depression and anxiety in IBS patients, with the strongest correlation in IBS-C and moderate correlation in IBS-D subtypes. The absence of a direct relationship between demographic factors or IBS subtype alone and psychological symptoms highlights the intricacy of the gut-brain axis in IBS pathophysiology. These results have important clinical implications: anxiety and depression screening should always be included in the diagnostic and management plans of IBS-C and IBS-D patients to enable early detection of psychological comorbidities.

FUNDING

No specific funding was received for this study.

CONFLICTS OF INTEREST

None to declare.

ETHICS STATEMENT

This study received ethical approval from the Health Research Ethics Commission of Dr. Saiful Anwar General Hospital, with the approval number 400/229/K.3/302/2023.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are not publicly available due to ethical and privacy restrictions, as they contain sensitive patient health information. Data may be available from the corresponding author upon reasonable request, subject to institutional and ethics committee approval.

AUTHOR CONTRIBUTIONS (CRediT)

Conceptualization: S.M., H.S.; **Data curation:** S.M.; **Formal analysis:** S.M.; **Investigation:** S.M., A.F.F., A.B.S., A.N.H.; **Methodology:** S.M., A.F.F., A.B.S., A.N.H.; **Project administration:** H.S.; **Supervision:** H.S.; **Validation:** A.F.F., A.B.S., A.N.H., H.S.; **Visualization:** S.M.; **Writing – original draft:** S.M.; **Writing – review & editing:** S.M., A.F.F., A.B.S., A.N.H., H.S. All authors have read and agreed to the published version of the manuscript.

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