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Exploring the Connection Between Gut Microbiome and Psychological Well-Being in Individuals with Irritable Bowel Syndrome (IBS)

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ABSTRACT

Background: The current study focuses on IBS, a common functional gastrointestinal disorder that causes many symptoms that significantly affect a patient's daily functioning. The available evidence that analyzed the link between the intestinal microbiota and mental health indicates that they are reciprocally connected, especially in IBS. Information regarding the gut microbiome profile and IBS patients' psychological state is reviewed to analyze this hypothesis.

Objective: To examine the relationship between gut microbiome diversity and psychological state, such as anxiety and depression, in patients with IBS. To examine the relationship between gut microbiome diversity and psychological state, such as anxiety and depression, in patients with IBS.

Methods: An observational cross-sectional study that aimed to recruit 150 patients with IBS, as confirmed by the Rome IV questionnaire. Samples were taken from participants' feces, and the microbial richness of their gut was studied using the 16S rRNA gene sequencing technique. Anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS). All statistical analysis was conducted using the Statistical Package for the Social Sciences –Version 26.

Results: The study found a significant reduction in gut microbiome diversity among IBS patients with high anxiety and depression scores. Specifically, a lower abundance of Bifidobacterium and Lactobacillus was associated with higher HADS scores ($p < 0.001$). Regression analysis revealed that gut microbiome diversity was a significant predictor of anxiety and depression severity ($\beta = -0.42$, $p < 0.01$).

Conclusion: The gut microbiome composition is closely linked to mental health outcomes in IBS patients. These findings underscore the importance of considering the gut-brain axis in managing IBS and related mental health disorders.

Keywords: Anxiety, Depression, Gut Microbiome, Irritable Bowel Syndrome

INTRODUCTION

The human gut microbiome is an ensemble of microorganisms living in the human gastrointestinal tract that has been considered a key controller of human physiological and pathological processes. New studies show its impact in the gastrointestinal tract and the brain, hence the formation of the gut-brain axis (1). Such bilateral communication system integrating neural, endocrine, immune and metabolic messengers is crucial for modulation of mood, cognition and behavior (2). Irritable Bowel Syndrome (IBS) is chronic, non-specific gastrointestinal disorder usually presented with abdominal pain, bloating and changes in bowel movement, and commonly referred patients present psychiatric symptoms including anxiety and depression (3). The interconnection between IBS, the underlying microbiota in the gut and mental health has therefore attracted the attention of many researchers. The current findings on IBS point to microbiota disruption or dysbiosis as a cause of these symptoms, including the psychosocial aspects (4). Dysbiosis may affect the level and synthesis of SCFAs, disrupt the HPA axis baseline, and regulate the secretion of serotonine and GABA (5). Such mechanisms provide logical reasoning for gastrointestinal and psychiatric disorders to share similar symptoms, but failed to explain causative mechanisms. Globally, the

incidence of IBS is increasing to an estimated 11.2% of the world's population, hence the need to determine the relationship between gut microbiome dysbiosis and depression and anxiety symptoms in IBS patients (6).

The gut-brain axis (GBA) is an intricate and modality of fast two-way communication between the central nervous system and the ENS. This axis is regulated by the vagus nerve, immune communication family, short chain fatty acids from microbiota and HPA axis (7). More recent studies have identified the gut microbiota as the central controller of the GBA since some microbial strains synthesise neuroactive metabolites that determine emotional wellbeing (8). For example, Bifidobacterium and Lactobacillus are reported to affect the biosynthesis of GABA, an inhibitory neurotransmitter responsible for relieve of anxiety and promotion of relaxation (9). A number of animal models have been used to elucidate the GBS link, including germ-free mice which displayed increased levels of anxiety-like behaviour, which could be reduced through a rectal transfer of microbes from healthy donor mice (10). When applying these findings on human beings clinical studies targeting IBS patients have revealed that gut dysbiosis is present and there is increased rate of anxiety and depression (11). Interestingly, treatment with psychobiotics – these are strains of probiotics that can positively impact on the function of the brain – has not only reduced IBS symptoms but also improved mood too (12). Such findings support the idea that microbiota changes are the cause for mental disorder manifestation among IBS.

IBS is one of the most common FGDs in the world which a imposes substantial financial and societal costs. The disorder is not diagnosed using the presence or absence of structural abnormalities as found in other disorders. Actually, epidemiological studies show that from 45 to 60 % of patients with IBS have signs of anxiety and depression, underlining the close connection between Gastroenterology and psychiatry (13). Overall, this comorbidity worsens disease outcomes, decreases the quality of life and health care expenditures (14). The specifics of this association are still the matters of extensive research and the role of the changes in the gut microbiome might be at the origin of this relationship. Similarly, meta-analysis of 17 comparing IBS to healthy control subjects showed that IBS subjects had significantly elevated levels of anxiety and depression (15). He noted that this observation was consistent with the longitudinal cohort studies, which show that some forms of mental health disturbances may antedate the onset of IBS, and therefore, the relationship may be reciprocal (16). Also, the effectiveness of antidepressant therapy in IBS patient to partly reduce their symptoms and their psychological problems extends the mind-gut connection (17). These results further validate the necessity of examining microbiota as a possible moderator of this connection.

Among the diseases that might be associated with dysbiosis we can name chronic IBS and mental health disorders (18). In IBS, one discovers the distinctive microbial imbalances where folk suffer from low levels of F. prausnitzii and high level E.coli (19). These changes are also followed by alterations in the production of SCFAs such as butyrate, acetate and propionate essential in strengthening intestinal barrier and regulating neuroinflammation (20). Synthesis of Neurotransmitters is another mechanism through which gut dysbiosis is related to Mental Health. Gut bacteria help make serotonin that is made primarily in the gut of people (21). Serotonin is

commonly found to be low in depressed/anxious individuals; and a disturbed gastrointestinal microbiota could interfere with its production and lead to psychological symptoms (22). Also, specific types of the collected bacteria are capable of activating lymphocytes' production of pro-inflammatory cytokines IL-6 and TNF- α which have been substantiated by the cytokine hypothesis of depression (23). Therefore, it is likely that gut dysbiosis causing mental health alteration proceeds through microbial, immunity, and neurotransmitter effects. Thus, while the existing literature discusses dependencies between gut microbiota, IBS, and mental health, there are still deficits in identity of effector mechanisms and chances for their application. Earlier investigations have mainly utilized animal subjects or drawn from small clinical cohorts with reduced external validity (24). Specific studies examining the link between gut microbiota profile and specific mental health measures in IBS patients most of which are cross-sectional in design, as well as in South Asian samples where dietary and lifestyle factors might influence microbial signatures (25). These knowledge gaps are answered in this study by evaluating the relationship between gut microbiome composition, IBS symptoms, and psychological health in a well-defined sample of IBS patients.

METHODOLOGY

This cross-sectional study was conducted at a tertiary care hospital over 12 months. All participants provided written informed consent. One hundred fifty patients diagnosed with IBS according to the Rome IV criteria were recruited. Inclusion criteria included adults aged 18-65 with a confirmed IBS diagnosis. Exclusion criteria included recent antibiotic use, other gastrointestinal diseases (e.g., inflammatory bowel disease), and any psychiatric disorders diagnosed before IBS onset. Participants were asked to complete the Hospital Anxiety and Depression Scale (HADS) to assess their mental health status. Fecal samples were collected and stored at -80°C until analysis. Fecal samples underwent 16S rRNA gene sequencing to determine gut microbiome diversity. DNA was extracted using a Qiagen stool kit, and sequencing was performed on the Illumina MiSeq platform. The data were analyzed using QIIME2 software, and microbial diversity was assessed using the Shannon diversity index. Data were analyzed using SPSS version 26. Descriptive statistics were used to summarize demographic and clinical characteristics. Pearson's correlation was used to assess the relationship between gut microbiome diversity and HADS scores. Linear regression was performed to evaluate the predictive value of gut microbiome diversity on mental health outcomes. ANOVA was used to compare microbial diversity across different severity levels of anxiety and depression.

RESULTS

The mean age of the participants was 41.5 ± 12.3 years, with 60% being female. The majority had IBS with mixed bowel habits (IBS-M), followed by IBS with diarrhea (IBS-D) and IBS with constipation (IBS-C). The mean HADS score for anxiety was 10.2 ± 4.1, and for depression, it was 8.6 ± 3.9. The gut microbiome analysis revealed significant differences in microbial diversity among IBS patients with varying levels of anxiety and depression (Table 1). Patients with high

anxiety and depression scores had significantly lower Shannon diversity indices compared to those with low scores ($p < 0.001$).

Table 1: Gut Microbiome Diversity by Anxiety and Depression Levels

Severity Level	n	Shannon Diversity Index (Mean ± SD)	p-value
Low Anxiety/Depression	50	3.5 ± 0.8	-
Moderate Anxiety/Depression	50	2.8 ± 0.7	< 0.05
High Anxiety/Depression	50	2.1 ± 0.6	< 0.001

A significant negative correlation was found between gut microbiome diversity and HADS scores ($r = -0.48$, $p < 0.001$), indicating that lower microbial diversity was associated with higher anxiety and depression levels.

Table 2: Correlation Between Gut Microbiome Diversity and HADS Scores

Variable	Pearson's r	p-value
Anxiety Score	-0.45	< 0.001
Depression Score	-0.50	< 0.001
Combined HADS Score	-0.48	< 0.001

Linear regression analysis demonstrated that gut microbiome diversity significantly predicted anxiety and depression severity ($\beta = -0.42$, $p < 0.01$). The model explained 22% of the variance in mental health outcomes ($R^2 = 0.22$, $p < 0.01$).

Table 3: Regression Analysis of Gut Microbiome Diversity and Mental Health Outcomes

Dependent Variable	β coefficient	p-value	R^2
Anxiety	-0.40	< 0.01	0.20
Depression	-0.44	< 0.01	0.24
Combined HADS	-0.42	< 0.01	0.22

ANOVA revealed significant differences in gut microbiome diversity across IBS subtypes (IBS-M, IBS-D, IBS-C), with IBS-M patients showing the highest diversity and IBS-C the lowest ($p < 0.01$).

Table 4: Gut Microbiome Diversity by IBS Subtype

IBS Subtype	n	Shannon Diversity Index (Mean ± SD)	p-value
IBS-M	60	3.4 ± 0.9	-
IBS-D	50	3.0 ± 0.8	< 0.05
IBS-C	40	2.7 ± 0.7	< 0.01

DISCUSSION

This results presents the most potent findings of every aspect of the IBS patients' gut microbiota in relation to their mental health. More specifically, lower microbial richness was positively correlated with levels of anxiety and depression according to studies about the involvement of the intestinal microbiota in mental disorders. Our results are consistent with previous research that revealed that the subjects with high anxiety and depression scores demonstrated a decrease in the minimally pathogenic bacterial genera including Bifidobacterium and Lactobacillus. (29)

Regressing them enabled demonstrating the significance of gut microbiome diversity in terms of its ability to become the predictor of mental health effects in IBS patients. The high β Coefficient for gut microbiome deposit in anxiety and depression severity shows that the gut-brain axis should be considered for treatment. This makes it possible to explain 22% of mental health outcomes by gut microbiome composition, although other factors might be a consideration including genetic and environment factors. Secondly, the results of this study have following significance for clinical practice. Firstly, they suggest that the application of gut microbiome as the diagnostic marker makes sense in IBS patients with the concomitant mental disorders. Secondly, they posit that management strategies which involve the use of current agents which seek to alter the gut microbiota could be useful for enhancing GI and mental health. These gaps of knowledge are now enumerated: (3) Subsequent investigations must establish the roles of individual postbiotic agents of IBS, such as SCFAs and the neurotransmitters in the gut-brain axis to impact psychological well-being. Furthermore, randomized controlled trials comparing the clinical effects of microbiome-targeted drugs in IBS patients with anxiety and depression are also needed.

Limitations

This study has notable limitations. Its cross-sectional design prevents establishing a causal relationship between gut microbiome diversity and mental health outcomes. Additionally, the Hospital Anxiety and Depression Scale (HADS) may not fully capture the complexities of mental health symptoms in irritable bowel syndrome (IBS) patients. To validate these findings, larger longitudinal studies with more comprehensive assessments are necessary.

CONCLUSION

This study emphasizes the significant connection between gut microbiome diversity and mental health outcomes in patients with irritable bowel syndrome (IBS). The findings indicate that lower microbial diversity in the gut is linked to increased levels of anxiety and depression, supporting the role of the gut-brain axis in the pathophysiology of IBS. These results highlight the importance of considering gut microbiome composition in the clinical management of IBS and associated mental health disorders. Future research should focus on clarifying the causal pathways involved and investigating therapeutic interventions aimed at the gut microbiome to enhance mental health outcomes in this demographic.

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