The Role of Probiotics in Depression and Quality of Life in Patients with Irritable Bowel Syndrome

Diana Erlita[1], Hamzah Shatri[2], Achmad Fauzi[3], Murdani Abdullah[3], Rudi Putranto[2], Eka Ginanjar[4], Irsan Hasan[3] Andhika Rachman[5]

[1]Psychosomatic and Palliative Subspecialty Study Program, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia - Cipto Mangunkusumo General Hospital, Jakarta, Indonesia.
[2]Psychosomatic and Palliative Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia - Cipto Mangunkusumo General Hospital, Jakarta, Indonesia.
[3]Gastroenterology and hepatology Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia - Cipto Mangunkusumo General Hospital, Jakarta, Indonesia.
[4]Cardiovascular Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia - Cipto Mangunkusumo General Hospital, Jakarta, Indonesia.
[5]Hematology Medical Oncology Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia - Cipto Mangunkusumo General Hospital, Jakarta, Indonesia.

**Corresponding Author:*
Hamzah Shatri, MD., PhD. Psychosomatic and Palliative Division, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia - Cipto Mangunkusumo. Jl. Diponegoro 71, Jakarta 10430, Indonesia.
Email: hshatri@yahoo.com

ABSTRACT

Background: *Irritable Bowel Syndrome (IBS) is a functional gastrointestinal disorder frequently accompanied by psychological disturbances such as depression and reduced quality of life. Probiotic intervention has been studied as a potential adjunct therapy to address psychological symptoms and improve the quality of life in IBS patients. This study aims to evaluate the effect of probiotic supplementation on depressive symptoms and quality of life in IBS patients at Dr. Cipto Mangunkusumo National General Hospital using the Beck Depression Inventory-II (BDI-II) and SF-36 instruments.* ***Methods:*** *This study was a double-blind randomized controlled trial with a pre-post intervention design. A total of 70 participants were randomly assigned into two groups: the intervention group (n=35), which received probiotics, and the control group (n=35), which received a placebo. Depressive symptoms were assessed using the BDI-II, while quality of life was measured using the SF-36 questionnaire, both before and after the intervention. Statistical analysis was performed using the Mann-Whitney test and independent t-test, with a significance level of $p<0.05$.* ***Results:*** *After the intervention, the probiotic group showed a significant reduction in BDI-II scores compared to the placebo group ($p<0.0001$). In addition, the probiotic group demonstrated significant improvements in almost all domains of the SF-36 compared to the placebo group, including physical functioning, role physical, bodily pain, general health, vitality, social functioning, emotional well-being, and mental health ($p<0.0001$).* ***Conclusion:*** *Probiotic supplementation significantly reduces depressive symptoms and improves quality of life in IBS patients. These findings support the potential of probiotics as an adjunct therapy in the comprehensive management of IBS.*

Keywords**:** *Probiotics, Irritable Bowel Syndrome, Depression, Quality of Life, BDI-II, SF-36*

INTRODUCTION

Irritable Bowel Syndrome (IBS) is a common functional gastrointestinal disorder characterized by changes in stool form and frequency, often accompanied by abdominal pain and/or constipation. This functional disorder is classified as a non-life-threatening condition that reduces quality of life and contributes to economic losses in society.[1,2]

Depression is a commonly encountered mood disorder. Depressive episodes may occur independently or as part of bipolar disorder. In the United States, depression is estimated to affect 6.7% of the adult population. Several studies have demonstrated a causal effect of psychological stress, such as depression and anxiety, in triggering gastrointestinal symptoms associated with IBS. A higher prevalence of depression and anxiety has been reported in IBS patients, with about 30% seeking medical consultation. Many studies have shown that IBS patients have a lower quality of life compared to the general population, similar to patients with chronic conditions such as gastroesophageal reflux disease, diabetes, depression, and end-stage renal disease.[3]

The human gastrointestinal tract is inhabited by approximately 100 trillion microorganisms, most of which reside in the distal small intestine and colon. In a healthy population, the gut is colonized by approximately 20% Bacteroidetes, 80% Firmicutes, 1–3% Proteobacteria, and 3% Actinobacteria. Previous studies comparing the gut bacterial composition of IBS subjects to healthy controls have reported increases in Proteobacteria, Veillonella, and Firmicutes, including Lactobacillus and Ruminococcus. These changes are commonly accompanied by reduced quantities of *Bifidobacterium, Faecalibacterium, Erysipelotrichaceae, and methanogens*. A meta-analysis of 13 studies found significant differences in the expression of Lactobacillus, Bifidobacterium, and Faecalibacterium prausnitzii in IBS patients compared to healthy controls, but no significant dysbiosis was found for Bacteroides-Prevotella, Enterococcus, Escherichia coli, Clostridium coccoides, and other species. Further analysis revealed that IBS-D (diarrhea-predominant IBS) patients experienced a significant decrease in Lactobacillus and Bifidobacterium compared to healthy controls and constipation-predominant IBS patients.[4,5]

Gut microbiota dysbiosis can enhance pro-inflammatory communication, leading to increased intestinal permeability and pro-inflammatory signaling to the brain's stress system (either directly or via the vagus nerve/visceral afferents). Pro-inflammatory communication has been shown to negatively affect feedback mechanisms in the hypothalamic-pituitary-adrenal (HPA) axis and induce hypercortisolemia. Elevated cortisol levels and inflammatory markers have been implicated in anxiety and depressive disorders. This communication is bidirectional, where increased stress can raise cortisol levels, which in turn signal the gut—affecting immune function, gut permeability, and microbiota composition.[3,6]

Patients with depression have been found to have lower levels of Lactobacillus and Bifidobacterium among IBS subjects. Additionally, the immunomodulatory effects of probiotics have been linked to anxiolytic and antidepressant outcomes in IBS patients.[5] Therefore, this study aims to investigate the role of probiotics in depression among IBS patients and to evaluate their impact on quality of life in these individuals.

METHODS

Study Design and Setting

This study is a randomized double-blind clinical trial using a comparative test between the intervention group and the control group to evaluate the role of probiotics in depression and quality of life among patients with Irritable Bowel Syndrome (IBS). The study was conducted at Cipto Mangunkusumo National General Hospital (RSUPN dr. Cipto Mangunkusumo) from January 2025 to April 2025.

Study Population

The inclusion criteria were patients aged 18–59 years, IBS patients with depression as diagnosed in medical records, no history of colorectal cancer, and willingness to complete and sign informed consent. The exclusion criteria included: patients with psychotic disorders, pregnant or breastfeeding women, patients

currently taking probiotics, and patients currently on antibiotic treatment. Subjects were divided into two groups: the intervention group receiving probiotics and the control group. Each group consisted of 35 subjects.

Data Collection

Sample collected using consecutive random sampling. Subjects will be divided into two groups: the intervention group, which will receive group probiotics, and the control group. Each group will consist of 35 subjects. In this study, depression was assessed using the Beck Depression Inventory-II (BDI-II) questionnaire, and quality of life was measured using the Short Form-36 (SF-36) questionnaire. Assessments were conducted before and after the intervention. Additionally, demographic characteristics were collected.

Data Analysis

Subject characteristics will be presented in tabular form. Categorical data will be presented as percentages. Numerical data will be presented as the median with the interquartile range. Data distribution will be tested using the Shapiro-Wilk normality test since the number of subjects in each group is ≤ 50. If the data distribution is normal, an independent t-test will be used; if not, the Mann-Whitney test will be applied. All statistical analyses will be performed using SPSS 25.0.

Ethical Approval

This study has received Ethical Clearance from the Ethics Committee of FKUI-RSCM with approval number KET-1608/UN2.F1/ETIK/PPM.00.02/2024.

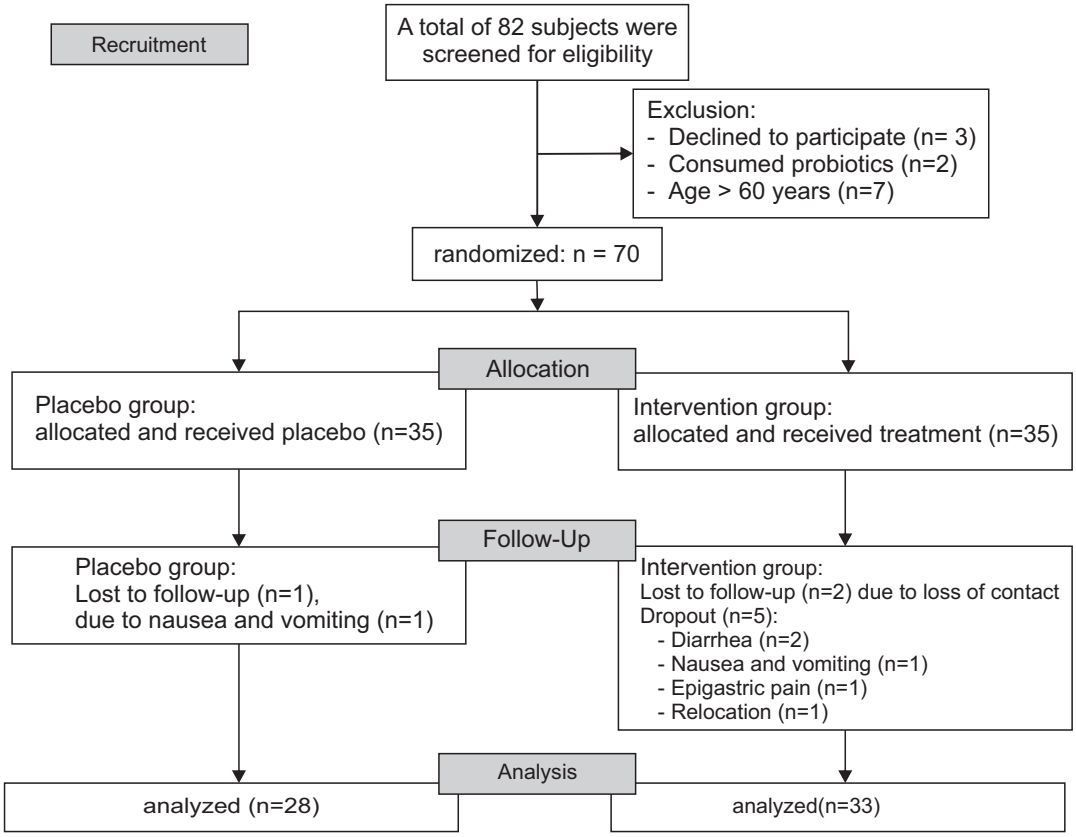

Figure 1. Subject Recruitment Flowchart

RESULTS

The study sample consisted of 70 subjects, with 35 subjects allocated to the probiotics group and the remaining 35 subjects to the control group. The characteristics of the patient are shown in **Table 1**. The majority of study participants were female, with 26 subjects (74.3%) in the intervention group and 25 subjects (71.4%) in the control group. The mean age of participants in the intervention group was 43 years, while the control group had a younger average age of 35 years. The participants had varying levels of education. In the intervention group, most subjects had completed senior high school (62.9%), followed by higher education (31.4%). Similarly, in the control group, the most common education level was also senior high school (42.9%), followed by higher education (48.6%).

The most common body mass index (BMI) category in both groups was normal weight. The most prevalent IBS subtype was IBS-C, with 17 subjects (48.6%) in the intervention group and 17 subjects (48.6%) in the control group. Meanwhile, the majority of participants in both groups received psychotherapy and psychopharmacological treatment, with 14 subjects (40.0%) in the intervention group and 14 subjects (40.0%) in the control group. Assessment of depressive symptoms using the BDI-II score was conducted at baseline, before probiotic administration, and again at 8 weeks after probiotic administration. The effect of probiotics on depression is presented in **Table 2**. The post-test score in the intervention group decreased to 10 (SD 6–14), whereas the control group score remained nearly unchanged at 17 (SD 15.5–23.5). Statistical analysis showed a significant difference between the two groups ($p < 0.0001$).

Table 1. Baseline Characteristics of Study Subjects

Characteristic	Probiotic (n=35)	Placebo (n=35)
Age (years), median (IQR)	43 (33 – 51)	35 (30 – 43)
Sex, n (%)		
Male	9 (25,7)	10 (28,6)
Female	26 (74,3)	25 (71,4)
Highest Education, n (%)		
Primary School	0 (0,0)	1 (2,9)
Junior High School	2 (5,7)	2 (5,7)
Senior High School	22 (62,9)	15 (14,9)
College/University (Diploma/Bachelor/Master)	11 (31,4)	17 (48,6)
Occupation, n (%)		
Private employee	10 (28,6)	11 (31,4)
Civil servant	2 (5,7)	0 (0,0)
Entrepreneur	3 (8,6)	4 (11,4)
Unemployed/Student/Housewife	19 (54,3)	13 (37,1)
Others	1 (2,9)	7 (20,0)
Marital Status, n (%)		
Single	12 (34,3)	17 (48,6)
Married	22 (62,9)	16 (45,7)
Widowed	1 (2,9)	2 (5,7)
IMT, mean (SB)	23,12 (4,44)	25,47 (6,39)
IMT, n (%)		
Underweight	4 (11,4)	5 (14,3)
Normoweight	22 (62,9)	12 (34,3)
Overweight	7 (20,0)	10 (28,6)
Obesity	2 (5,7)	8 (22,9)
Number of comorbidities, median (IQR)	0 (0 – 1)	0 (0 – 1)
Comorbidities, n (%)		
Hypertension	6 (17,1)	8 (22,9)
Diabetes mellitus	2 (5,7)	4 (11,4)
Heart disease	2 (5,7)	1 (2,9)
Lung disease	4 (11,4)	1 (2,9)
Others	6 (17,1)	8 (22,9)

Smoking status, n (%)		
Yes	1 (2,9)	2 (5,7)
No	34 (97,1)	33 (94,3)
Alcohol consumption, n (%)		
Yes	1 (2,9)	0 (0,0)
No	34 (97,1)	35 (100,0)
IBS subtype, n (%)		
IBS-C	17 (48,6)	17 (48,6)
IBS-D	6 (17,1)	5 (14,3)
IBS-M	12 (34,3)	13 (37,1)
Terapi, n (%)		
Psychotherapy	6 (17,1)	4 (11,4)
Psychopharmacology	0 (0,0)	2 (5,7)
Psychotherapy and psychopharmacology	14 (40,0)	14 (40,0)
No psychotherapy or psychopharmacology	15 (42,9)	15 (42,9)

Table 2. The Effect of Probiotic Supplementation on Depression Symptoms in Patients with Irritable Bowel Syndrome

Variable	Group		P-value
	Probiotic	Placebo	
BDI			
Pre, median (IQR)	19 (14 – 27)	17 (15 – 23)	0,934
Post, median (IQR), n=61	10 (6 – 14)	17 (15,5 – 23,5)	<0,0001
Delta, median (IQR), n=61	-8 (-10 – (-6))	0 (-2,5 – 1,5)	<0,0001

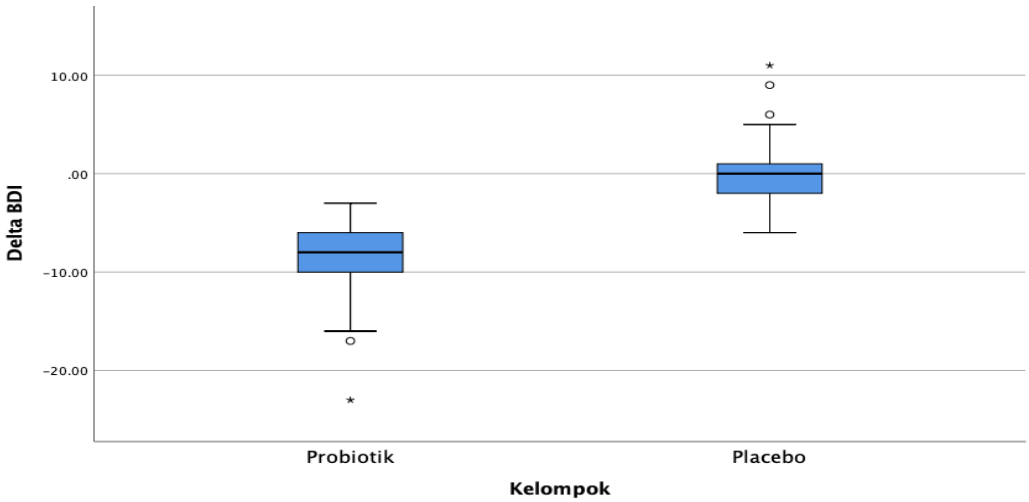

Figure 2. Delta BDI after probiotic/placebo administration for 8 weeks

Quality of life was assessed using the SF-36 score before the intervention and again at 8 weeks after the intervention. The effect of probiotics on SF-36 quality of life is presented in **Table 3**. Statistical analysis showed a significant difference between the two groups ($p < 0.0001$). The SF-36 quality of life consists of eight domains: physical functioning, role limitations due to physical problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health. The SF-36 scores for the domains of role limitations due to emotional problems and mental health in the intervention group increased to 67 (range: 67–100) and 71.14 (SD 15.18), respectively. In contrast, scores in the control group remained the same or showed minimal change, at 67 (range: 33–67) and 53.55 (SD 15.78), respectively.

Table 3. The Effect of Probiotics on SF-36 Quality of Life in Patients with Irritable Bowel Syndrome

Variable	Group		P-value
	Probiotic	Placebo	
Physical Functioning			
Pre, median (IQR)	70 (50 – 85)	70 (45 – 90)	0,827*
Post, median (IQR), n=61	90 (75 – 95)	70 (40 – 85)	**0,001***
Delta, median (IQR), n=61	7,5 (0 – 20)	0 (-5 – 0)	**<0,0001***
Physical Role Limitation			
Pre, median (IQR)	25 (25 – 50)	50 (25 – 50)	0,096*
Post, median (IQR), n=61	50 (50 – 75)	50 (25 – 50)	**0,007***
Delta, median (IQR), n=61	0 (0 – 25)	0 (0 – 0)	**<0,0001***
Body pain			
Pre, median (IQR)	38 (23 – 58)	45 (35 – 68)	0,072*
Post, rerata (SD), n=61	65,5 (17,49)	46,09 (15,41)	**<0,0001**
Delta, median (IQR), n=61	22 (10 – 34,5)	0 (-1 – 0)	**<0,0001***
General Health			
Pre, median (IQR)	30 (15 – 45)	40 (25 – 55)	0,068*
Post, rerata (SD), n=61	52,32 (18,43)	40,70 (15,65)	**0,010**
Delta, median (IQR), n=61	30 (12,5 – 36,5)	5 (0 – 15)	**<0,0001***
Vitality			
Pre, rerata (SD)	46,83 (19,14)	47,71 (17,21)	0,839
Post, rerata (SD), n=61	57,68 (19,41)	45,97 (15,05)	**0,010**
Delta, median (IQR), n=61	20 (7,5 – 25,5)	5 (0 – 13)	**0,001***
Social Functioning			
Pre, rerata (SD)	57,77 (21,26)	57,46 (18,74)	0,948
Post, median (IQR), n=61	75 (53,25 – 88)	50 (38 – 63)	**<0,0001***
Delta, median (IQR), n=61	0 (0 – 25)	0 (-6 – 0)	**<0,0001***
Role-Emotional			
Pre, median (IQR)	33 (33 – 67)	67 (67 – 100)	**0,008***
Post, median (IQR), n=61	67 (67 – 100)	67 (33 – 67)	**<0,0001***
Delta, median (IQR), n=61	33 (0 – 34)	0 (-33 – 0)	**<0,0001***
Mental Health			
Pre, rerata (SD)	56,91 (16,72)	58,40 (17,68)	0,719
Post, rerata (SD), n=61	71,14 (15,18)	53,55 (15,78)	**<0,0001**
Delta, median (IQR), n=61	12 (8 – 20)	0 (-10 – 0)	<0,0001*

Independent T Test, * Uji Mann-Whitney

DISCUSSION

In this study, female participants outnumbered male participants in both the intervention and control groups. The gender distribution showed a predominance of females—74.3% in the probiotic group and 71.4% in the placebo group—which aligns with epidemiological data indicating that IBS is more prevalent in women. This finding is consistent with a study by Kim YS et al., which reported that women have a 2–2.5 times higher risk of developing IBS compared to men.[7]

Similarly, a study by Kibune et al. reported that the prevalence of IBS among women was 83%, compared to 17% in men. Another study by Nilsson et al. also showed a gender distribution of 70.3% women and 29.7% men among IBS patients. The median age of subjects in the probiotic group was 43 years (interquartile range [IQR], 35–51), while the placebo group had a median age of 36 years (IQR, 30–43). This age range falls within young to middle adulthood, which corresponds to the age group with the highest global prevalence of IBS. IBS is most frequently diagnosed during the productive years, between the ages of 20 and 50.[7]

Most subjects in both the intervention and control groups had completed senior high school or higher education. A higher level of education is often associated with better disease management and treatment adherence. A study by Asieh et al. suggested that higher education levels may increase susceptibility to IBS through psychological mechanisms. This reflects a trend

where more educated individuals are likely to be more attentive to gastrointestinal symptoms and seek treatment, including alternative therapies such as probiotics.[8]

Several factors may contribute to the development of IBS, including psychological disturbances, altered gut motility, food hypersensitivity, genetic predisposition, imbalances in the gut microbiota, bacterial overgrowth, and disrupted communication between the gut, microbiota, and the central nervous system—commonly referred to as the brain–gut axis.[9]

The results of this study demonstrated that probiotic supplementation significantly reduced depression scores in IBS patients. This finding is consistent with the concept of the gut–brain axis, a bidirectional communication pathway between the gastrointestinal tract and the central nervous system, where gut microbiota play a crucial role in regulating neurotransmitters and stress responses.[10]

The pre-test analysis of Beck Depression Inventory (BDI) scores showed no significant differences between the groups. However, post-test results indicated a significant difference between the intervention and control groups. This finding aligns with a study by Messaoudi et al., which demonstrated a reduction in depression levels after 30 days of probiotic supplementation (Lactobacillus helveticus and Bifidobacterium longum) compared to placebo. Similarly, a study by Akkasheh et al. found that 8 weeks of probiotic supplementation in patients with major depressive disorder led to a significant decrease in BDI scores.[11,12]

Two main hypotheses explain how probiotics may alleviate depressive symptoms: inflammation regulation and enhanced serotonin transmission. Patients with depression often exhibit elevated levels of pro-inflammatory cytokines (IL-1β, IL-6, TNF-α), which activate the HPA axis, disrupt neurotransmitter metabolism, and contribute to depressive symptoms.[13]

Probiotics may help reduce inflammation, improve HPA axis function, and enhance neurotransmitter activity. Furthermore, probiotics influence serotonin production by increasing the availability of free tryptophan in the gut, thereby raising serotonin levels in the central nervous system. These mechanisms support improved stress regulation, mood stabilization, and reduction of depression symptoms associated with neurotransmitter deficiencies.[13]

It is important to note that probiotics are not a substitute for psychotherapy or pharmacotherapy but may serve as a complementary approach in the comprehensive management of IBS accompanied by depression. This aligns with recent recommendations advocating for the integration of microbiota-targeted strategies into the biopsychosocial model of IBS. Thus, in IBS patients who are also receiving psychotherapy and/or antidepressants, probiotic supplementation can be considered a supportive intervention. It carries minimal risk of drug interactions and may even enhance the effectiveness of primary therapies.[13,14]

In this study, quality of life was assessed using the SF-36 instrument, which comprises eight domains: physical functioning, role limitations due to physical problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health. Post-test analysis revealed a significant difference between the intervention and control groups. The significant increase in SF-36 scores in the intervention group indicates that probiotics may contribute to improved quality of life in IBS patients. Based on the SF-36 instrument, all domains of quality of life showed meaningful improvement in the probiotic group compared to placebo, reflecting the broad impact of probiotics on both physical and psychosocial aspects of IBS patients.

These findings are consistent with a randomized clinical trial by Cappello et al., which investigated the effects of a symbiotic mixture in IBS patients. The study reported significant improvements in symptoms such as flatulence, reduced colonic transit time in the rectosigmoid segment, and significantly improved SF-36 quality of life scores. Another study by Pinto-Sanchez et al., involving an 8-week administration of probiotic combinations in IBS patients, also demonstrated symptom improvement and enhanced quality of life (SF-36) compared to placebo.[15]

CONCLUSION

Probiotic administration significantly reduced depressive symptoms in patients with Irritable Bowel Syndrome and significantly improved their quality of life. Routine evaluation of depression risk and quality of life is recommended for patients with IBS. Probiotic supplementation should be considered as an adjunct to standard therapy. Further research on the gut microbiome's genomic profile using fecal samples is needed to better understand dysbiosis patterns in IBS patients.

ACKNOWLEDGMENTS

Thank you to Dr. Cipto Mangunkusumo General Hospital and the Faculty of Medicine Universitas Indonesia, especially those in the Psychosomatic and Palliative Division, Gastroenterology and Hepatology Division, Faculty of Medicine Universitas Indonesia-Cipto Mangunkusumo Hospital.

CONFLICT OF INTEREST

There is no conflict of interest.

FUNDING

This research received no specific grant from any funding agency.

REFERENCES

1. Lacy BE, Mearin F, Chang L, et al. Bowel disorders. Gastroenterology. 2016 May 1;150(6):1393-407.e5.
2. Kopczynska M, Mokros L, Pietras T, Malecka-Panas E. Quality of life and depression in patients with irritable bowel syndrome. Prz Gastroenterol. 2018;13(2):102–8.
3. Kayar Y, Agin M, Unver N, Dertli R, Kirpinar I. The relation between life quality and subtype of the disease in patients with irritable bowel syndrome. Ann Med Res. 2019;(0):1.
4. Widhani A, Djauzi S, Suyatna FD, Dewi BE. Changes in gut microbiota and systemic inflammation after synbiotic supplementation in patients with systemic lupus erythematosus: A randomized, double-blind, placebo-controlled trial. Cells. 2022 Nov 1;11(21).
5. Sarkawi M, Raja Ali RA, Abdul Wahab N, Abdul Rathi ND, Mokhtar NM. A randomized, double-blinded, placebo-controlled clinical trial on Lactobacillus-containing cultured milk drink as adjuvant therapy for depression in irritable bowel syndrome. Sci Rep. 2024 Dec 1;14(1).
6. Simpson CA, Mu A, Haslam N, Schwartz OS, Simmons JG. Feeling down? A systematic review of the gut microbiota in anxiety/depression and irritable bowel syndrome. Journal of Affective Disorders. 2020; 266:429–46.
7. Kim YS, Kim N. Sex-gender differences in irritable bowel syndrome. Journal of Neurogastroenterology and Motility. Korean Society of Neurogastroenterology and Motility. 2018;24:544–58.
8. Mansouri A, Rarani MA, Fallahi M, Alvandi I. Irritable bowel syndrome is concentrated in people with higher education in Iran: an inequality analysis. Epidemiol Health. 2017;39:e2017005
9. Lyra A, Hillilä M, Huttunen T, et al. Irritable bowel syndrome symptom severity improves equally with probiotics and a placebo. World J Gastroenterol. 2016 Dec 28;22(48):10631–42.
10. Gao J, Zhao L, Cheng Y, et al. Probiotics for the treatment of depression and its comorbidities: A systematic review. Frontiers in Cellular and Infection Microbiology. Frontiers Media S.A. 2023;13.
11. Akkasheh G, Kashani-Poor Z, Tajabadi-Ebrahimi M, et al. Clinical and metabolic response to probiotic administration in patients with major depressive disorder: A randomized, double-blind, placebo-controlled trial. Nutrition. 2016;32(3):315–20.
12. Huang R, Wang K, Hu J. Effect of probiotics on depression: A systematic review and meta-analysis of randomized controlled trials. Nutrients. MDPI AG. 2016;18.
13. Theodora RH, Sarjana W, Fitrikasari A, Ss D, Sari P. Differences of BDI-II (Beck Depression Inventory-II) Score before and after Probiotics Administration; 2019.
14. Tetali B, Suresh S. Management of irritable bowel syndrome: a narrative review. Translational Gastroenterology and Hepatology. AME Publishing Company. 2024;9.
15. Pinto-Sanchez MI, Hall GB, Ghajar K, et al. Probiotic bifidobacterium longum NCC3001 reduces depression scores and alters brain activity: A pilot study in patients with irritable bowel syndrome. Gastroenterology. 2017 Aug 1;153(2):448-459.e8.