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by Fitrikasari Alifiati

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Probiotic supplementation for reducing psychological symptoms in cancer patients on chemotherapy: A pilot trial

Alifiati Fitrikasari [a,*], Innawati Jusup [a], Titis Hadiati [a], Widodo Sarjana [a], Salytha Ivana Ardiningrum [b], Cindy Kurniawati Chandra [b], Damai Santosa [c]

[a] Department Psychiatry, Faculty of Medicine, Diponegoro University/Dr. Kariadi General Hospital, Semarang, Indonesia
[b] Faculty of Medicine, Diponegoro University/Dr. Kariadi General Hospital, Semarang, Indonesia
[c] Division of Hematology-Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Diponegoro University/Dr. Kariadi General Hospital, Semarang, Indonesia

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ABSTRACT

Background: Psychological disorders, including depression, anxiety, and stress, are prevalent among cancer patients undergoing chemotherapy. Probiotics have been investigated as a potential supplement to modulate the gut–brain axis and improve psychological symptoms, possibly through mechanisms such as serotonin regulation. However, studies on the effects of probiotics on psychological symptoms in chemotherapy patients are limited.
Methods: This randomised, double-blinded, placebo-controlled pilot trial was conducted at the outpatient clinic of dr. Kariadi Hospital, Semarang, in 2023. Sixty-one cancer patients undergoing chemotherapy were enrolled and randomised into an intervention (n = 30) and control (n = 31) group. The intervention group received probiotics (*Lactobacillus rhamnosus* Rosell-11 and *Lactobacillus helveticus* Rosell-52) twice daily for eight weeks. The primary outcomes were changes in depression, anxiety, and stress levels measured by the Depression, Anxiety, and Stress Scale 42 (DASS-42). The secondary outcome was serum serotonin levels.
Results: The intervention group showed a significant decrease in total DASS-42 scores ($p = 0.001$), indicating an overall reduction in psychological distress. However, changes in the scores of the subscales (depression, anxiety, and stress) were not statistically significant ($p > 0.05$). Serum serotonin levels increased in the intervention group, but this was not statistically significant ($p = 0.38$). The findings should be interpreted cautiously due to small sample size and potential confounding factors.
Conclusion: This pilot study suggests that eight weeks of probiotic supplementation may reduce overall psychological symptoms in cancer patients undergoing chemotherapy. Larger trials with rigorous controls and longer interventions are needed to confirm these preliminary findings.

1. Introduction

Psychological disorders are becoming increasingly prevalent among patients diagnosed with cancer, with conditions such as delirium, depression, adjustment disorders, anxiety, sexual dysfunction, and sleep disorders affecting 30 %–40 % of this population (Mastan et al., 2024; Ostovar et al., 2022). The incidence of psychiatric disorders is even higher among those at advanced cancer stages. Anxiety was more common (varying from 7 % to 88 %) than depression (ranging from 3 % to 65.5 %) among cancer patients with diverse forms residing in different Southeast Asian nations (Ostovar et al., 2022). Additionally, a study in one Indonesian hospital reported that 23 % of patients undergoing chemotherapy experienced depression, 40 % suffered from anxiety, and 21 % had stress (Mastan et al., 2024). Despite the significant impact of these conditions on patients' quality of life, psychiatric disorders in cancer patients are often underdiagnosed and inadequately treated, leading to further deterioration in their overall wellbeing (Mastan et al., 2024; Ostovar et al., 2022; S et al., 2018).

Chemotherapy has been shown to disrupt the balance of gut microbiota, a condition known as gut dysbiosis (Deleemans et al., 2019). This disruption can lead to a reduction in the diversity and number of commensal bacteria, which, in turn, can negatively affect mood and

* Corresponding author at. Department of Psychiatry, Faculty of Medicine, Universitas Diponegoro, Jl. Prof. H. Soedarto, SH, Tembalang, Semarang 50275 Indonesia.
E-mail address: fitrisutomo@yahoo.com (A. Fitrikasari).

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cognitive function (Deleemans et al., 2019; Maddern et al., 2023). Research has demonstrated that changes in microbiota composition can influence the development of the psychological symptoms of conditions including depression and anxiety (Deleemans et al., 2019; Maddern et al., 2023). Animal studies have further demonstrated that gut microbiota play a critical role in regulating the pathway associated with depression (Deleemans et al., 2019), suggesting that gut microbiota may be a promising therapeutic target for psychological disorders among cancer patients.

Since psychological disorders are linked to low serotonin levels—a condition that can be exacerbated by gut dysbiosis—targeting the gut microbiota through oral probiotics presents a promising therapeutic approach (Merkouris et al., 2024; Zhang et al., 2023). Probiotics have traditionally been used to mitigate the gastrointestinal side-effects of chemotherapy, such as nausea and vomiting (Vivarelli et al., 2019). Recent studies have suggested that probiotics may additionally improve psychological wellbeing by influencing neurotransmitter pathways, including serotonin pathways, which are closely associated with mood regulation (Merkouris et al., 2024; Zhang et al., 2023). Specifically, probiotics containing *Lactobacillus rhamnosus* and *Lactobacillus helveticus* have been shown to reduce symptoms of depression, enhance cognitive function, and balance key neurochemicals, including serotonin, epinephrine, and brain-derived neurotrophic factor (BDNF), in animal studies (Deleemans et al., 2019; Ye et al., 2022).

Despite these promising findings, existing researches have predominantly focused on the effects of probiotics on the physical side-effects of cancer and chemotherapy, with limited studies specifically evaluating their efficacy in managing psychological conditions in chemotherapy patients. In addition, the influence of the combination of probiotics used in this study (*Lactobacillus rhomnosus* Rosell-11 and *Lactobacillus helveticus* Rosell-52) on psychological disorders in a human sample has never been studied. Therefore, this pilot study aims to assess the feasibility and acceptability of probiotic supplementation to reduce psychological symptoms in cancer patients undergoing chemotherapy. The primary outcome was a change in depression, anxiety, and stress levels, measured using the Depression, Anxiety, and Stress Scale 42 (DASS-42) and the secondary outcome was a change in serum serotonin levels.

2. Methods

This study was a randomised, double-blinded, placebo-controlled pilot trial conducted in the outpatient clinic of Kasuari Ward of Dr. Kariadi Hospital, Semarang in 2023. The trial was designed to assess the effect of probiotic supplementation on depression, anxiety, and stress in cancer patients undergoing chemotherapy, using serum serotonin levels as a biomarker.

2.1. Participants

Participants included cancer patients who were undergoing chemotherapy in Dr Kariadi Hospital. The only inclusion criterion was that patients had to be aged between 18 and 76 years. Exclusion criteria were patients who smoked or had used antibiotics during the week prior to our intervention. Notably, the optimal abstinence period for antibiotics before participating in a study assessing probiotics and gut microbiota can vary depending on the type of antibiotic used and the patient's metabolism. Therefore, the abstinence period is usually calculated based on the drug's half-life. Most antibiotics have a half-life ranging from a few hours to a few days (Armstrong, 2020). Hence, a one-week abstinence period preceding this study seemed reasonable to minimise the potential impact of residual antibiotics on gut microbiota and the study outcomes.

2.2. Sample size

The sample size was determined using the minimum sample for a pilot clinical trial (Julious, 2005). A total of 61 patients were enrolled and randomised into the intervention ($n = 30$) and control ($n = 31$) groups, with an allocation ratio of 1:1.

2.3. Randomisation and blinding

Patients were randomly allocated to either the intervention or control group using block randomisation, with a block size of four (ABAB, BABA, AABB, BBAA) and an allocation ratio of 1:1. The block order was stored in a sealed envelope and was only opened after the study was completed. The treatment code was also included in the envelope and was numbered according to the block order. Blinding was maintained by ensuring that the probiotic and placebo capsules were identical in appearance (colour, size, and shape), packaging, and administration. The placebo capsules were manufactured by the pharmaceutical laboratory of Medical Faculty, Diponegoro University. The placebo capsule contained the same additional substances as the probiotic capsule, namely maltodextrin, magnesium stearate, and ascorbic acid. These substances did not interfere with the research results. Both patients and investigators were blinded to the group assignments; only the pharmacist knew the group assignments.

2.4. Intervention

The treatment was given to the patient upon their arrival. The intervention group received probiotics (*Lactobacillus rhomnosus* Rosell-11 and *Lactobacillus helveticus* Rosell-52 at a dose of 2×10^9 CFU) twice a day for eight weeks.

2.5. Outcomes

The primary outcome was a change in depression, anxiety, and stress levels, measured using the Depression, Anxiety, and Stress Scale 42 (DASS-42) at baseline and after the eight-week intervention. The secondary outcome was a change in serum serotonin levels after the eight weeks, measured using an enzyme-linked immunosorbent assay (ELISA).

2.6. Research instruments

To assess the primary outcomes, the following instrument was used:

1) DASS-42
The DASS-42 is a 42-item questionnaire used to measure the severity of depression, anxiety, and stress in participants. The questionnaire consists of 42 assessment statements (supplementary file) to assess depression (14 statements), anxiety (14 statements), and stress (14 statements). Participants were asked to score each statement as 0—*never*, 1—*sometimes*, 2—*often*, or 3—*very often*. Subscale scores were then summed to determine the depression, anxiety, and stress scale scores (supplementary file).

Meanwhile, to assess the secondary outcome, the following instrument was used:

2) Serotonin measurement

Serum serotonin levels were measured using an ELISA, following the manufacturer's protocol. Blood samples were collected at baseline and after the intervention, and results were read using a microplate reader (EL x 800).

2.7. Statistical methods

This study used SPSS version 20 for statistical analysis. Continuous variables (age, DASS-42 score, and serum serotonin level) were

summarised using mean ± standard deviation, while categorical (nominal and ordinal) variables (gender, marital status, highest educational, jobs, history of psychiatric illness, history of psychiatric treatment, and duration of cancer diagnosis) were presented as frequencies and percentages.

For nominal variables (gender, marital status, and jobs), between group comparisons were conducted using chi-square test. Meanwhile, Mann-Whitney test was used for ordinal variables (highest education and duration since cancer diagnosis).

For continuous variables, Shapiro–Wilk test was used to assess the normality of data distribution. Between-group comparisons were conducted using independent *t*-test if the data was normally distributed and Mann–Whitney U test if the data was not normally distributed. Within-group comparisons were conducted using paired *t*-test if the data was normally distributed and using Wilcoxon signed rank test if the data was not normally distributed. A p-value < 0.05 was considered statistically significant.

An intention-to-treat (ITT) analysis was also performed to assess the effect of the intervention on several outcomes, including the total DASS score, it's subscales (depressions, anxiety, and stress), and serotonin level. All participants were analyzed based on control and intervention groups regardless of whether they completed the study or not. The intended outcomes were the decrease in total DASS score and it's subscales, and increase in serotonin levels. The calculated metrics were control event rate (CER), experimental event rate (EER), absolute risk reduction (ARR), relative risk reduction (RRR), and number needed to treat (NNT).

2.8. Ethics

The study was registered at the Indonesian Clinical Research Registry (INA-CRR) with registration number 042024030706474KRGNHZ, and it was approved by the Health Research Ethics Committee of Dr. Kariadi Hospital, Semarang (No. 1496/EC/KEPK-RSDK/2023). All participants provided written informed consent prior to participation. The trial was conducted according to the principles of the Declaration of Helsinki.

3. Results

3.1. Sample characteristics

This study included 61 cancer patients who met the inclusion and exclusion criteria. The study sample was divided into two groups via randomisation, namely an intervention group and a control group. The baseline characteristics of the participants in the intervention ($n = 30$) and control ($n = 31$) groups are shown in supplementary file. There were no significant differences between the two groups for any of the baseline characteristics (age, cancer diagnosis, duration since cancer diagnosis, baseline DASS scores, and baseline serotonin level).

The primary reasons for dropout included unresponsiveness to contact attempts (45.7 %), hospitalisation (20 %), failure to attend control visits (20 %), and death (11.4 %) (supplementary file). Those who were unresponsive were participants whom the research team was unable to contact, despite repeated follow-up attempts. As a result, the intervention group comprised 13 subjects, so did the control group (Fig. 1).

Table 1 shows the characteristics of the study sample for each group.

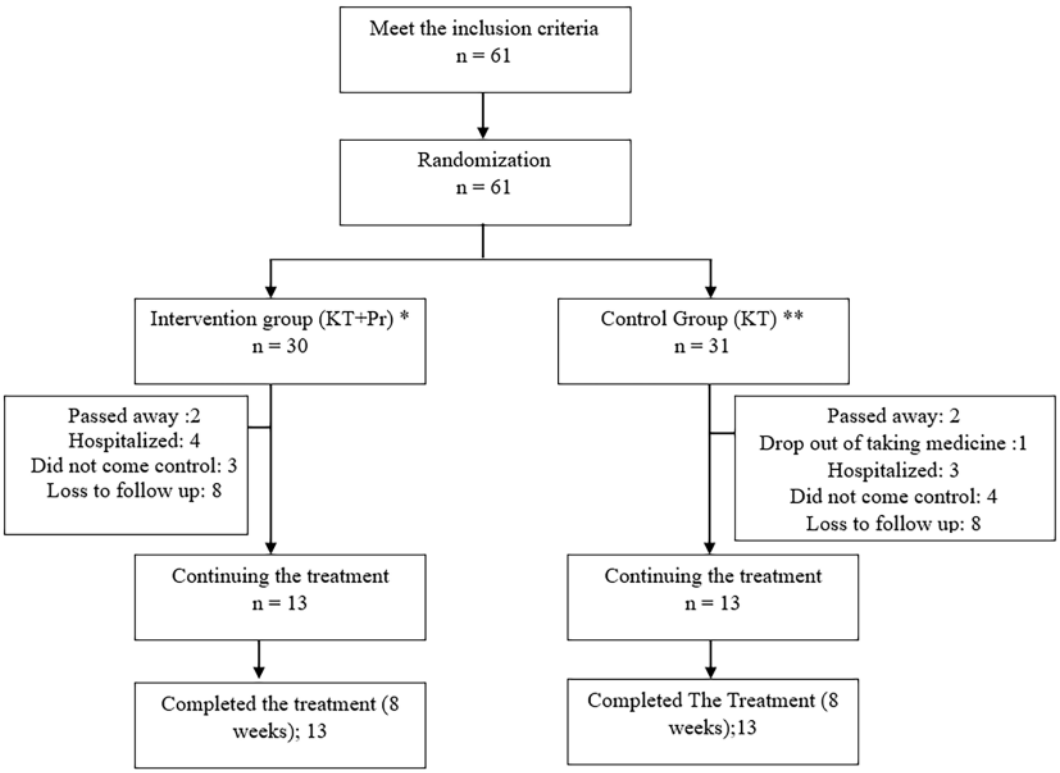

Fig. 1. CONSORT diagram. This study included 61 cancer patients, randomised into an intervention group and a control group.
Description:
*KT + Pr = Chemotherapy + probiotics
**KT = Chemotherapy + placebo.

Table 1
Characteristics of the research sample.

Variables	Intervention (n = 13)	Control (n = 13)	p-value *
Age			
Mean ± SD	54 ± 7.88	49 ± 17.06	0.08‡
Median (min–max)	54 (43–68)	54 (23–76)	
Variables	**Frequency (%) Intervention (n = 13)**	**Control (n = 13)**	**p-value**
Gender			
Male	7 (53.8 %)	6 (46.2 %)	1.00¥
Female	6 (46.2 %)	7 (53.8 %)	
Marital status			
Not married	1 (7.7 %)	2 (15.4 %)	0.70¥
Married	11 (84.6 %)	11 (84.6 %)	
Divorced	1 (7.7 %)	0 (0 %)	
Highest education			
Elementary school	1 (7.7 %)	1 (7.7 %)	0.71‡
Junior high school	2 (15.4 %)	4 (30.8 %)	
Senior high school	5 (38.5 %)	3 (23.1 %)	
Bachelor	4 (30.8 %)	4 (30.8 %)	
Did not attend school	1 (7.7 %)	1 (7.7 %)	
Jobs			
Working	8 (61.5 %)	9 (69.2 %)	0.50¥
Not working	5 (38.5 %)	4 (30.8 %)	
History of psychiatric treatment (including benzodiazepine)			
Yes	0	0	.e
No	13 (50 %)	13 (50 %)	
Psychiatric diagnosis			
Yes	0	0	.e
No	13 (50 %)	13 (50 %)	
Duration of psychiatric treatment			
Yes	0	0	.e
No	13 (50 %)	13 (50 %)	
Duration since cancer diagnosis			
3–6 months	2 (15.4 %)	4 (30.8 %)	0.52‡
6 months–1 year	5 (38.5 %)	4 (30.8 %)	
1–5 years	5 (38.5 %)	4 (30.8 %)	
> 5 years	1 (7.7 %)	1 (7.7 %)	

‡ Mann–Whitney;.
§ independent t;.
¥ chi-square;.
e not measurable because $n = 0$,.
* $p < 0.05$ was considered statistically significant.

In this study sample, the mean ages in the intervention and control groups were 54 and 49 years, respectively. The number of male and female patients was approximately equal in the intervention and control groups. Most of the study sample was married (84.6 %), had high school as their highest level of education (30.7 %), and worked (65 %). All samples had no history of psychiatric treatment or previous psychiatric diagnoses. There were also no significant differences in their age, gender, marital status, educational level, employment status, and duration of cancer, either.

3.2. The effect of probiotics on depression, stress, and anxiety

The results showed an insignificant decrease in depression (p = 0.32), anxiety (p = 0.91), and stress (p = 0.58) scores, while there was a significant decrease in total DASS-42 scores (p = 0.001), in the intervention group after receiving probiotics for eight weeks (Table 2). When comparing the control group with the intervention group, there were insignificant differences in depression, anxiety, and stress scores, but total DASS-42 scores significantly differed between the two groups (p = 0.048; Table 2).

3.3. The effect of probiotics on serotonin

We found an increase in serotonin levels in the intervention group, but it was not statistically significant (p = 0.38; Table 3).

Table 2
Comparison of depression scores for the intervention and control groups before and after the intervention.

DASS-42	Group		p
	Intervention	Control	
Pre-intervention	19.00 ± 7.10	13.69 ± 7.06	0.07‡ (95 % CI −0.42, 11.04)
Post-intervention	17.38 ± 6.48	11.15 ± 6.83	0.048‡*
P	0.001¶* (95 % CI 0.78, 2.45)	0.002†*	0.21†
Depression			
Pre-intervention	5.69 ± 3.20	6.31 ± 3.77	0.658§ (95 % CI −3.4, 2.2)
Post-intervention	5.46 ± 3.05	4.69 ± 2.78	0.508§ (95 % CI −1.6, 3.1)
P	0.32†	0.01†*	0.06‡
Anxiety			
Pre-intervention	5.23 ± 3.86	5.15 ± 8.16	0.188‡
Post-intervention	5.46 ± 4.05	3.54 ± 4.82	0.055‡
P	0.91†	0.02†*	0.08‡
Stress			
Pre-intervention	6.15 ± 3.02	9.15 ± 5.54	0.099§ (95 % CI −6.6, 0.6)
Post-intervention	6.46 ± 2.33	6.92 ± 4.27	0.735§ (95 % CI −3.2, 2.3)
P	0.58†	0.007†*	0.003‡

* Statistically significant ($p < 0.05$);.
‡ Mann–Whitney;.
§ independent t;.
¶ paired t;.
† Wilcoxon.

3.3. Intention-to-Treat (ITT) analysis

As presented in supplementary file, the CER, EER, ARR, RRR, and NNT provide early indicators of the intervention's potential impact. The results demonstrate a beneficial effect of probiotics in reducing overall psychological symptoms, as evidenced by increasing of total DASS-42 scores. However, the effect sized for the depression, anxiety, and stress subscales, as well as serotonin levels, were smaller and not statistically significant. The NNT value, despite exploratory, suggest that approximately nine patients would need to be treated with probiotics to achieve a reduction in total psychological symptoms in one patient.

4. Discussion

This pilot study investigated the preliminary effects of probiotic supplementation on psychological symptoms and serotonin levels in cancer patients undergoing chemotherapy. Cancer patients undergoing chemotherapy frequently experience significant psychological distress, including depression, anxiety, and stress, which adversely affects their

Table 3
Comparison of serotonin levels between the intervention and control groups before and after the intervention.

Serotonin	Group		p
	Intervention	Control	
Pre-intervention	98.85 ± 125.22	145.77 ± 199.78	0.80‡
Post-intervention	104.15 ± 195.69	161.38 ± 175.37	0.01†*
P	0.38†	0.09†	
Difference	5.31 ± 77.48	15.62 ± 66.20	0.048‡*

* Statistically significant ($p < 0.05$);.
‡ Mann–Whitney;.
† Wilcoxon.

quality of life (Ostovar et al., 2022). Probiotic supplementation has been explored for its potential to modulate gut microbiota and influence the psychological symptoms of depression, anxiety, and stress via the gut–brain axis (Sabit et al., 2023). A systematic review also reported the beneficial effects of probiotic supplementation measured using the Hamilton Depression Rating Scale in patients with psychiatric disorders (Amirani et al., 2020). However, the effects of probiotics on these outcomes have shown variability across studies (Merkouris et al., 2024; Potter et al., 2023; Ye et al., 2022; Zhang et al., 2023).

While probiotics have been shown to influence the gut-brain axis and improve psychological symptoms in other contexts, their effects on cancer patients undergoing chemotherapy are not well-established. Thus, this study provides preliminary insights into the feasibility and potential efficacy of probiotics in reducing psychological symptoms in this population.

The intention-to-treat (ITT) analysis was crucial in this pilot study to account for all randomized participants, including those who did not complete the study. The ITT approach provides a more realistic estimation of the treatment effect, especially in the study which has high dropout rate (Ahn & Kang, 2023).

The results indicate that the administration of probiotics over eight weeks caused a significant decrease in total DASS-42 scores ($p = 0.001$), suggesting an overall reduction in psychological distress. However, as a pilot study, these findings are exploratory and should be interpreted with caution. The observed number needed to treat (NNT) of 9 for total DASS-42 score reduction demonstrates that the intervention may have clinical relevance, but this needs confirmation in larger trials.

In terms of the specific DASS subscales (depression, anxiety, and stress), the decreases in the scores for each subscale were not statistically significant ($p > 0.05$). The most notable effect was seen in the stress subscale, with an NNT of 5, showing that probiotics may have a more positive effect on stress symptoms in cancer patients. However, the larger NNTs for the depression (8) and anxiety (17) subscales exhibit the need for further investigation with larger sample sizes to determine the true effect of probiotic supplementation on these specific psychological symptoms.

Chemotherapy, radiotherapy, and immunotherapy have toxic effects that can lead to changes in gut microbiota, a reduction in gut commensal bacteria, and inflammation of the gastrointestinal tract (Deleemans et al., 2019; Fernandes et al., 2024). Gut dysbiosis, a disruption in the gut microbiota, can lead to increased gut permeability, allowing toxins to enter the bloodstream and activating pro-inflammatory cytokines (IL-6, Il-1β, TNF-a, and C-reactive protein), while it may cause the hyperactivation of the hypothalamic–pituitary axis (HPA-axis) (Deleemans et al., 2019). These inflammatory conditions then lead to decreased levels of serotonin (5-HT) and BDNF (Deleemans et al., 2019). Both of these can, in turn, cause psychological and cognitive changes such as anxiety and depression, fatigue, memory impairment, and decision-making impairment (Lu et al., 2022; Maddern et al., 2023; Merkouris et al., 2024; Sabit et al., 2023).

The mechanism of psychological disturbance discussed in our study is related to chemotherapy-induced gut dysbiosis, with serum serotonin as a biomarker. In this study, while the intervention group receiving probiotic supplementation showed an increase in serum serotonin levels, this change was not statistically significant ($p = 0.38$) and the NNT of 7 should be viewed as an exploratory finding. The control group, which did not receive probiotics, demonstrated more pronounced changes in serum serotonin levels. Hence, there are certain external factors that may have influenced these results. One such factor is the potential consumption of ondansetron. Ondansetron, a commonly used antiemetic in chemotherapy patients, is known to influence serotonin levels by blocking serotonin 5-HT3 receptors (Gupta et al., 2014). This pharmacological action can lead to fluctuations in circulating serotonin levels (Gupta et al., 2014), potentially explaining the more pronounced changes observed in the control group.

In addition, a diet that includes amino acids such as tryptophan, a precursor of serotonin, can contribute to variations in serotonin levels (Jenkins et al., 2016; Mohajeri et al., 2015) since tryptophan-rich foods can increase serotonin synthesis. However, dietary habits were not controlled for in this study, even though differences in diets among participants might have affected the results. Future studies should thus control for the medications and diets of their participants more rigorously.

An increase in serotonin is one of several mechanisms involved in the improvement of depression, anxiety, and stress symptoms from probiotic use. In addition to serotonin production, probiotics may reduce symptoms of depression and anxiety by decreasing stress-induced HPA responses, decreasing cortisol levels, increasing neurotransmitter synthesis (GABA, dopamine, noradrenaline, melatonin, histamine, and acetylcholine), stimulating the production of gut neuropeptides (glucagons like peptide-1 and tyrosine), improving the gut barrier, increasing BDNF production, decreasing the release of pro-inflammatory cytokines, and increasing anti-inflammatory cytokines (Lu et al., 2022; Sabit et al., 2023; Zhang et al., 2023).

Overall, the gut–brain axis and serotonin production are influenced by numerous factors beyond just probiotic supplementation, including stress levels, diet, and physical activity (Lou et al., 2023; Madison & Kiecolt-Glaser, 2019; Mohajeri et al., 2015). The influence of these variables might have differed between the control and intervention groups, contributing to the outcomes seen in our study.

4.1. Limitations

This pilot study has several limitations that must be considered when interpreting the findings. First, although the intention-to-treat (ITT) analysis helped mitigate the impact of dropouts, the high dropout rate weakens the robustness of the findings. The high dropout rate was primarily driven by factors such as unresponsiveness, hospitalization, and death. Most of the dropout patients comprised individuals who were unresponsive to follow-up attempts (45.7 %). Despite repeated attempts to contact them by telephone or messengers, participants could not be reached. Given that the comparison data of baseline characteristics between dropout and completer groups showed no significant differences, the risk of selection bias is minimized. However, the high dropout rate still poses a limitation to the statistical power, because the small sample size and homogeneity of the study population may limit the generalizability of the findings. Further larger-scale study should aim to implement strategies to improve participant retention, such as a more flexible follow-up options or using alternative contact methods, and include more diverse population to increase the generalizability of the findings.

Another major concern is the use of serum serotonin as a biomarker. While the direct impact of central nervous system (CNS) serotonin on the pathophysiology of depression, anxiety, and stress is well-recognised, the direct measurement of CNS serotonin is invasive and not feasible in a clinical trial setting. We acknowledge that serum serotonin can be influenced by various peripheral factors, and it may not accurately reflect CNS serotonin concentration. Although this was a limitation of our methodology, it is considered a feasible and ethical non-invasive sampling method for human subjects. Thus, many studies have already used this biomarker to investigate the systemic effects of probiotic supplementation (Jenkins et al., 2016; Merkouris et al., 2024; Potter et al., 2023; Yano et al., 2015). However, chemotherapy can induce serotonin release from enterochromaffin cells in the gut (Cubeddu et al., 1995). This drug-induced serotonin release could have confounded the effects of probiotics. To mitigate this in future studies, alternative biomarkers should be utilized and other potential confounders such as chemotherapy type, anti-emetic use, and dietary factors should be controlled.

Another important limitation is that we did not apply any statistical correction to control for the potential inflation of Type I error because we conducted multiple comparisons. In future studies, statistical corrections should be applied when analyzing multiple outcomes.

Additionally, the duration of the intervention may have not been sufficient to detect meaningful changes in all outcomes. Studies have suggested that gut microbiota exist in a complex and dynamic ecosystem that may require longer probiotic interventions to undergo significant alterations (Ng et al., 2023). Another study also reported the beneficial effects of probiotic supplementation on symptoms of depression after 12 weeks among patients under methadone maintenance treatment programmes (Molavi et al., 2022). Thus, extending the duration of probiotic supplementation in future trial could determine whether longer-term treatment will give more pronounced effects.

Finally, we did not control for other external factors, such as physical activity, dietary habits, medication use, and other lifestyle factors that may influence the gut microbiota, serotonin levels, and psychological disorders of cancer patients. Controlling for these variables in future research is crucial to better understanding the direct effects of probiotics on psychological symptoms in cancer patients.

5. Conclusions

This pilot study provides preliminary evidence that eight weeks of probiotic supplementation may have a potential role in reducing overall psychological symptoms in cancer patients undergoing chemotherapy, as shown by changes in total DASS-42 scores. However, the results should be interpreted carefully due to the small sample size, high dropout rate, and limitations associated with other factors that may influence the gut microbiota, serotonin levels, and psychological disorders of cancer patients. Future larger trials with more rigorous controls and longer intervention periods are needed to confirm these preliminary findings and to further explore the therapeutic potential of probiotics on psychological symptoms in cancer patients undergoing chemotherapy.

CRediT authorship contribution statement

Alifiati Fitrikasari: Conceptualization, Methodology, Data curation, Writing – original draft. **Innawati Jusup:** Methodology, Validation. **Titis Hadiati:** Formal analysis, Project administration. **Widodo Sarjana:** Data curation. **Salytha Ivana Ardiningrum:** Writing – review & editing. **Cindy Kurniawati Chandra:** Writing – review & editing. **Damai Santosa:** Writing – original draft, Resources.

Declaration of competing interest

We have no known conflicts of interest to disclose.

Declaration of generative AI in scientific writing

During the preparation of this work, the authors used ChatGPT 4.0 to improve the grammar and clarity of the manuscript, as English is not the authors' first language. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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Supplementary materials

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