European Journal of Clinical Pharmacy
**Print ISSN:** 2385-409X **Online ISSN**: 3105-0409
Website: https://farmclin.com/

*Original Research Article*

# Effect of Probiotics on Gut Microbiome Restoration in Post-Antibiotic Diarrhea

***Article History:***

**Name of Author:**
Ahmed Jamal Chaudhary[1], Umar Ejaz[2], Qurratulain Umar[3], Sana Iqbal[4], Sultan Zeb Khan[5] and Rajesh Kumar[6]

***Affiliation:*** *[1]Associate Professor of Medicine Program Director Transitional Medicine Program, Department of Internal Medicine, DMC Sinai Grace Hospital, Detroit, Michigan, USA*
*[2]Senior Registrar, Department of Medicine, Lahore General Hospital, Lahore, Pakistan*
*[3]Fellow Gastroenterology, Pakistan Kidney & Liver Institute, Lahore, Pakistan*
*[4]Assistant Professor of Medicine, Department of Internal Medicine, DMC Sinai Grace Hospital, Detroit, Michigan, USA*
*[5]Assistant Professor Gastroenterology, Department of Gastroenterology, Akhtar Saeed Medical College, Rawalpindi, Pakistan*
*[6]Associate Professor, Department of Medicine, Shaheed Mohtarma Benazir Bhuto Medical College Lyari & Sindh Govt. Lyari General Hospital, Karachi, Pakistan*

***Corresponding Author:***
Ahmed Jamal Chaudhary,

***Received***: 02-09-2025
***Revised***: 06-12-2025
***Accepted***: 12-12-2025
***Published***: 30-12-2025



***Abstract***: ***Background***: Antibiotic diarrhea is a frequent complication of antimicrobial therapy and is mediated mostly by interference with the normal gut microbiota. Disturbed microbial flora, and excess of pathological organisms are also causes of delayed recovery and risk of recurrence. Probiotics have been suggested as a solution that can be used to achieve microbial balance and better clinical outcomes. ***Objective***: To evaluate the effect of probiotic supplementation on clinical recovery and gut microbiome restoration in patients with post-antibiotic diarrhea. ***Methodology:*** The proposed comparative study is a prospective study that can be carried out at Lahore General Hospital between January 2024 and January 2025. One hundred and twenty-four adult diarrhea patients who had received antibiotics in the past were recruited and randomly divided into 2 groups that included a probiotic group (n = 36) and a control group (n = 36). The intervention group got a standardized probiotic formulation of Lactobacillus and Bifidobacterium species of 1010 CFU per day of 7 days, whereas the control group got normal supportive care. Time to diarrhea resolution and stool frequency were considered as primary outcomes. Recurrence of symptoms and diversity of gut microbiome were considered secondary outcomes. A significance level of $p < 0.05$ was used in terms of statistical analysis. **Results:** The probiotic group had a significantly shorter time to diarrhea resolution compared with controls ($3.2 \pm 1.1$ vs. $5.1 \pm 1.6$ days, $p < 0.001$). Stool frequency decreased more rapidly, and a higher proportion achieved normal stool consistency by Day 7. Recurrence of diarrhea and need for rescue therapy were significantly lower in the probiotic group. ***Conclusion***: Probiotic supplementation significantly improves clinical recovery and promotes gut microbiome restoration in patients with post-antibiotic diarrhea.

**Keywords**: Antibiotic-associated diarrhea; Probiotics; Gut microbiome; Dysbiosis; Lactobacillus; Bifidobacterium.

## INTRODUCTION

Antibiotic associated diarrhea is a common and clinically significant adverse outcome of antimicrobial therapy, and its incidence has been reported between

 

5 and 30 percent according to the antibiotic class, patient factors and healthcare environment. This condition is basically explained by the interference with the normal microbiota of the intestines, which leads to the loss of microbial diversity, weakening of colonization resistance, and the proliferation of pathogenic organisms. Besides making patients feel uncomfortable, antibiotic-associated diarrhea is also linked to extended hospital stay, high care expenses, and high chances of major complications, such as Clostridioides difficile infection [1-3].

Human gut microbiome has a key role in the homeostasis of the intestine, immunomodulation, and resistance to enteric pathogens. Although antibiotics play a vital role in the treatment of bacterial infections, they lead to severe and even long-term changes in microbial composition. These transformations involve the loss of some useful commensal bacteria e.g. Lactobacillus and Bifidobacterium species and an increase in opportunistic organisms, especially enterobacteriaceae family. Recovery of microbial balance is thus a major treatment objective in the management of post antibiotic diarrhea [4-6].

The probiotics can be described as live microbes which when taken in sufficient doses, benefit the host health. A number of probiotic strains have been shown to suppress pathogenic bacteria, improve the performance of the epithelial barrier, regulate host immune response and facilitate recolonization of commendable microbiota. Meta-analyses and randomized controlled trials have documented that the risk and the duration of antibiotic-associated diarrhea decreases with the use of probiotics; nevertheless, the risk of heterogeneity in study groups, probiotic strains, doses and outcomes measures has limited the externalization of these results [7, 8].

Although the evidence is increasingly supporting the use of probiotic therapy, there is limited information in low- and middle-income countries, and limited studies have aimed at simultaneous assessment of clinical recovery and objective parameters of microbiome restoration. More so, the most effective dose and period of probiotic supplement intake in general clinical practice has not been determined .[9, 10] The current study was therefore aimed at determining the impact of standardized probiotic regimen on clinical outcomes and recovery of the gut microbiome among patients with post-antibiotic diarrhea.

The primary objective of this study was to compare time to diarrhea resolution and symptom recovery between patients receiving probiotics and those receiving standard care alone. Secondary objectives included assessment of microbiome diversity, bacterial abundance, recurrence of symptoms, and safety of probiotic supplementation. By integrating clinical and microbiological outcomes, this study aims to provide comprehensive evidence regarding the role of probiotics in the management of post-antibiotic diarrhea.

## METHODOLOGY

This is a prospective comparative study carried in at Lahore General Hospital during a period of one year between January 2024 and January 2025. The aim was to determine the impact of probiotic supplementation on the restoration of gut microbiome and clinical recovery among patients who present with post-antibiotic diarrhea. The research was planned according to the general guidelines of clinical researches and was passed by the Institutional Review Board of the center of the participation before the patients were enrolled in the study. All participants provided informed consent in writing before they were included in the study.

Consecutive sampling was used to enroll 72 patients who were randomly divided into two groups of 36 patients each. The participants were eligible individuals who had developed diarrhea after taking systemic antibiotics characterized by three or more loose stool per day on day one or within two weeks after antibiotic treatment. Patients who had a history of chronic diarrhea, inflammatory bowel disease, irritable bowel syndrome, recent gastrointestinal surgery, known immunodeficiency or active gastrointestinal infection were excluded. The study also did not include patients whose baseline diagnosis in Clostridioides difficile infection was confirmed.

At the time of enrolment, baseline demographic data (age, sex, body weight, body mass index and residence) was obtained. Clinical data were recorded in detail on the indication to use antibiotics, name of antibiotic therapy type and course of antibiotic therapy, route of administration, when diarrhea appeared, the frequency of stool at the onset, and the symptoms such as pain in the abdomen and fever. Systematic records of comorbid and concomitant medications as well as proton pump inhibitors and antidiabetic medications were also recorded among all the participants.

Intervention group patients were given a standardized probiotic preparation of a specified combination of Lactobacillus and Bifidobacterium species at $10^{10}$ colony-forming units (CFU) daily during 7 days of treatment. The control group was subject to normal supportive care and no probiotics supplementation. A baseline and follow-up visit clinical assessment were conducted on Day 3, Day 7, and four weeks. Prospective records of stool frequency, stool consistency using the Bristol Stool Scale, time to resolve diarrhea, the need of rescue therapy and symptom recurrence were made. Microbiome samples were gathered on the baseline and follow-up

stool collections. Standard laboratory techniques were used to measure alpha diversity indices and relative abundance of major bacterial taxa. The analysis of data was done with 26 software. Continuous variables were represented in terms of mean +- standard deviation and compared using independent samples t -test or Mann-Whitney U test as required. The frequencies and percentages of the categorical variables were presented and compared with the chi-square test or Fisher test. A p-value of below 0.05 was regarded to be significant.

## RESULTS

This involved 72 patients, 36 patients in the probiotic group and 36 in the control group. The two groups were similar in terms of baseline demographic variables such as age, sex distribution, body mass index, and residence as well as smoking status. There were no significant differences in any demographic parameter, and thus there was sufficient matching between the baseline.

**Table 1. Baseline Demographic Characteristics of the Study Population (n = 72)**

| Variable | Probiotic Group (n = 36) | Control Group (n = 36) | p-value |
|---|---|---|---|
| Age (years), mean ± SD | 41.8 ± 12.6 | 43.2 ± 11.9 | 0.612 |
| Male sex, n (%) | 20 (55.6) | 19 (52.8) | 0.817 |
| Female sex, n (%) | 16 (44.4) | 17 (47.2) | |
| Weight (kg), mean ± SD | 69.4 ± 10.8 | 70.6 ± 11.2 | 0.641 |
| Body mass index (kg/m²), mean ± SD | 25.7 ± 3.4 | 26.1 ± 3.6 | 0.589 |
| Urban residence, n (%) | 22 (61.1 | 21 (58.3) | 0.809 |
| Rural residence, n (%) | 14 (38.9) | 15 (41.7) | |
| Low socioeconomic status, n (%) | 18 (50.0) | 20 (55.6) | 0.642 |
| Current smoker, n (%) | 9 (25.0) | 10 (27.8) | 0.792 |

There was no difference between the baseline clinical characteristics and patterns of antibiotic exposure in the two groups at enrolment. There was no significant difference in the indication to use antibiotics, the period of therapy, the administration route, and the frequency of the stool base between groups. The use of comorbid conditions and concomitant use of proton pump inhibitors was also similar.

**Table 2. Baseline Clinical and Antibiotic-Related Characteristics**

| Variable | Probiotic Group (n = 36) | Control Group (n = 36) | p-value |
|---|---|---|---|
| URTI as indication, n (%) | 14 (38.9) | 13 (36.1) | 0.807 |
| UTI as indication, n (%) | 9 (25.0) | 10 (27.8) | 0.792 |
| Other infections, n (%) | 13 (36.1) | 13 (36.1) | 1.000 |
| Single antibiotic use, n (%) | 24 (66.7) | 23 (63.9) | 0.805 |
| Multiple antibiotics, n (%) | 12 (33.3) | 13 (36.1) | |
| Duration of antibiotics (days), mean ± SD | 6.8 ± 1.9 | 7.1 ± 2.1 | 0.531 |
| Oral route, n (%) | 27 (75.0) | 26 (72.2) | 0.789 |
| Intravenous route, n (%) | 9 (25.0) | 10 (27.8) | |
| Time to diarrhea onset (days), mean ± SD | 4.2 ± 1.3 | 4.4 ± 1.4 | 0.547 |
| Baseline stool frequency/day, mean ± SD | 6.9 ± 1.6 | 7.1 ± 1.7 | 0.613 |
| Abdominal pain present, n (%) | 22 (61.1) | 24 (66.7) | 0.629 |
| PPI use, n (%) | 11 (30.6) | 12 (33.3) | 0.808 |
| Diabetes mellitus, n (%) | 8 (22.2) | 9 (25.0) | 0.781 |

The probiotics group took a much shorter period to resolve diarrhea than the control group. The rate of reduction in stool frequency was higher in the probiotic group and a greater percentage of them had attained normal stool consistency by Day 7. The probability of diarrhea recurrence and rescue therapy were very low in patients who were probiotics-treated.

**Table 3. Diarrhea Outcomes and Clinical Response**

| Outcome | Probiotic Group (n = 36) | Control Group (n = 36) | p-value |
|---|---|---|---|
| Time to diarrhea resolution (days), mean ± SD | 3.2 ± 1.1 | 5.1 ± 1.6 | **<0.001** |
| Stool frequency on Day 3, mean ± SD | 3.8 ± 1.2 | 5.4 ± 1.5 | **<0.001** |
| Stool frequency on Day 7, mean ± SD | 1.6 ± 0.8 | 2.9 ± 1.1 | **<0.001** |
| Normal stool consistency by Day 7, n (%) | 30 (83.3) | 19 (52.8) | **0.006** |
| Diarrhea resolved by Day 7, n (%) | 31 (86.1) | 21 (58.3) | **0.010** |

| | | | |
|---|---|---|---|
| Recurrence within 4 weeks, n (%) | 3 (8.3) | 9 (25.0) | **0.048** |
| Need for rescue therapy, n (%) | 6 (16.7) | 14 (38.9) | **0.031** |
| Hospital stay (days), mean ± SD | 3.6 ± 1.4 | 5.0 ± 1.9 | **0.002** |

At baseline, the diversity index of microbiomes between the two groups was similar. Follow-up resulted in a much higher increase in alpha diversity and beneficial bacterial abundance, and more pronounced decrease in Enterobacteriaceae in the probiotic group. Adverse events were not very high and were not significantly different in relation to groups.

**Table 4. Gut Microbiome and Safety Outcomes**

| Variable | Probiotic Group (n = 36) | Control Group (n = 36) | p-value |
|---|---|---|---|
| Baseline alpha diversity index, mean ± SD | 2.41 ± 0.36 | 2.38 ± 0.34 | 0.721 |
| Alpha diversity at follow-up, mean ± SD | 3.12 ± 0.42 | 2.61 ± 0.39 | **<0.001** |
| Increase in Lactobacillus abundance (%) | 18.6 ± 6.4 | 6.9 ± 4.8 | **<0.001** |
| Decrease in Enterobacteriaceae (%) | 14.3 ± 5.7 | 5.1 ± 4.3 | **<0.001** |
| C. difficile positive, n (%) | 2 (5.6) | 7 (19.4) | **0.042** |
| Any adverse event, n (%) | 5 (13.9) | 4 (11.1) | 0.724 |
| Bloating or flatulence, n (%) | 4 (11.1) | 3 (8.3) | 0.692 |
| Discontinuation due to side effects, n (%) | 1 (2.8) | 1 (2.8) | 1.000 |

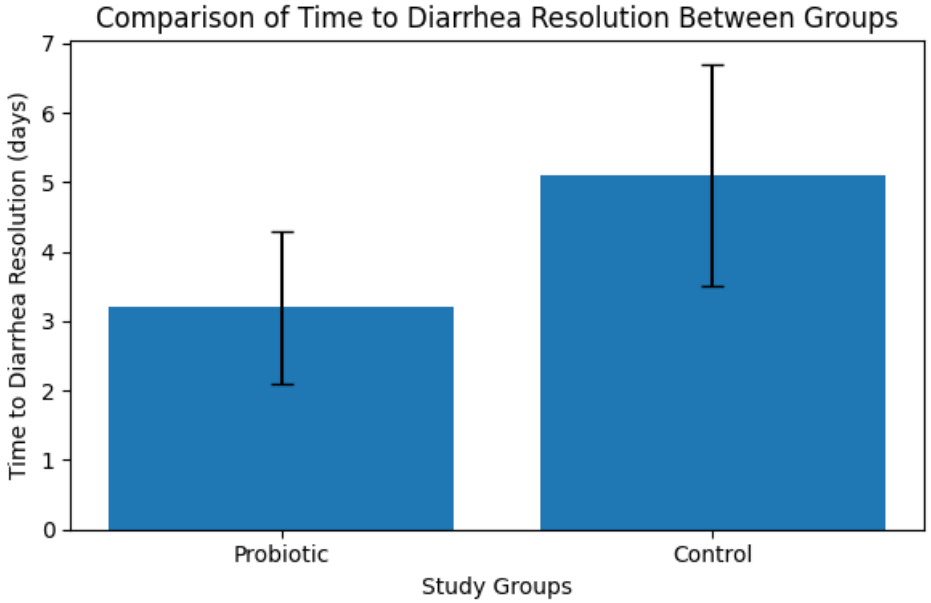


**Figure** 1. Comparison of Time to Diarrhea Resolution Between Probiotic and Control Groups.

## DISCUSSION

The current research proves that the probiotic supplementation is a successful way to enhance clinical recovery and gut microbiome diversity restoration in patients with post-antibiotic diarrhea. Clients of probiotics took a lower number of days to diarrhea remission, reduced the frequency of stools at early follow-up and a greater rate of symptom-free patients on Day 7 than controls. These results confirm the hypothesis that selective probiotic therapy administration could be an effective approach to overcome the impact of antibiotics on the development of dysbiosis and enhance the short-term clinical results [11-13].

The pathophysiology of antibiotic-associated diarrhea is mainly caused by alteration of the normal intestinal flora which results into the loss of colonization resistance and proliferation of pathogenic bacteria. In the current study, there was a significant rise in the alpha diversity indices and beneficial bacterial families and a significant decrease in the abundance of Enterobacteriaceae in the probiotic condition. This trend indicates that probiotics would aid restoration of a normal microbial environment and that is probably the cause of the shown clinical change. The decreased Clostridioides difficile positivity in the probiotic group further depicts the protective effects of microbiome restoration on the opportunistic infections [14-16].

Our clinical observations agree with past reports that show that probiotics lessen the length and the severity of antibiotic related diarrhea. Various randomized controlled trials and meta-analyses have indicated that

other strains like Lactobacillus rhamnosus GG, Saccharomyces boulardii reduce the risk of persistent diarrhea and recurrence. The extent of benefit identified in the present research can be compared to the extent of benefit identified in international literature especially in time to symptom resolution and less rescue therapy [17-19].

The major finding of this research is that there is less recurrence of diarrhea and reduced hospitalization period in patients using probiotics. The clinical implications of these results are relevant, as repeated symptoms and long hospital stay are related to higher healthcare expenses and morbidity of patients. Probiotic therapy could prove to be a cost effective complement to regular supportive treatment by enhancing recovery rates and lowering the level of complications in standard clinical practice [20].

The safety profile of probiotics in the present study was good, showing a low rate of side effects (mild gastrointestinal side effects) with no severe side effects. This observation is in line with the current evidence that supports probiotics as generally safe in healthy adults who are immunocompromised. However, patient selection is also to be carefully taken, especially in heavily immunocompromised patients, where cases of probiotic-related infection are rare [21].

There are some limitations of this study. The sample size was small and the research was done in one center which might not give a generalized study. This follow-up was not very long and the long-term outcomes of microbiome regulation were not evaluated. Moreover, even though the analysis of the microbiome showed that the diversity and bacterial abundance changed, there were no tests of the functional metabolic pathways. To verify these findings and investigate the long-term clinical consequences of the restoration of the microbiome induced by probiotics, future multicenter research, using larger sample sizes and increased follow-up, is justified.

## CONCLUSION

Probiotic supplementation significantly improves clinical recovery and promotes restoration of gut microbiome diversity in patients with post-antibiotic diarrhea. Patients receiving probiotics experienced faster resolution of symptoms, lower recurrence rates, and reduced need for additional therapy compared with standard care alone. These findings support the routine consideration of probiotics as an effective and safe adjunct in the management of antibiotic-associated diarrhea.

## REFERENCES

1. Dahiya, D. and P.S.J.I.j.o.m.s. Nigam, Antibiotic-therapy-induced gut dysbiosis affecting gut microbiota—brain axis and cognition: restoration by intake of probiotics and synbiotics. 2023. 24(4): p. 3074.
2. Mekonnen, S.A., et al., Molecular mechanisms of probiotic prevention of antibiotic-associated diarrhea. 2020. 61: p. 226-234.
3. Ojima, M.N., et al., Bifidobacterium bifidum suppresses gut inflammation caused by repeated antibiotic disturbance without recovering gut microbiome diversity in mice. 2020. 11: p. 1349.
4. FitzGerald, J., et al., Improved gut microbiome recovery following drug therapy is linked to abundance and replication of probiotic strains. 2022. 14(1): p. 2094664.
5. Shi, Y., et al., Advances in lactobacillus restoration for β-Lactam antibiotic-Induced dysbiosis: A system review in intestinal microbiota and immune homeostasis. 2023. 11(1): p. 179.
6. Henry, D.E. and V. Venkateswara Rao, Antibiotic-associated diarrhea and update on probiotics recommendations, in Probiotic Research in Therapeutics: Volume 2: Modulation of Gut Flora: Management of Inflammation and Infection Related Gut Etiology. 2021, Springer. p. 141-166.
7. Yang, J., et al., Strategies for applying probiotics in the antibiotic management of Clostridioides difficile infection. 2023. 14(19): p. 8711-8733.
8. Pan, J., et al., A single-cell nanocoating of probiotics for enhanced amelioration of antibiotic-associated diarrhea. 2022. 13(1): p. 2117.
9. Fernández-Alonso, M., et al., Effect of adding probiotics to an antibiotic intervention on the human gut microbial diversity and composition: a systematic review. 2022. 71(11): p. 001625.
10. Ishnaiwer, M., Multimodal treatment of intestinal carriage of multi-drug resistant bacteria with probiotics and prebiotics. 2022, Nantes Université.
11. Zhao, L., et al., Gut microbiota diversity of hospitalized older adult patients with and without antibiotic-associated diarrhea. 2023. 35(7): p. 1541-1555.
12. Wu, H., et al., Antibiotic-induced dysbiosis of the rat oral and gut microbiota and resistance to Salmonella. 2020. 114: p. 104730.
13. Puccetti, M., et al., Postbiotic-enabled targeting of the host-microbiota-pathogen interface: hints of antibiotic decline? 2020. 12(7): p. 624.
14. Li, X., et al., Effects of Hetiao Jianpi Decoction on intestinal injury and repair in rats with antibiotic-associated diarrhea. 2020.

 

26: p. e921745-1.
15. Gibson, G.A. and E.J.J.S.I. Owen, Non-Antibiotic Approaches to Infection that Preserve the Microbiome in Critically Ill Patients. 2023. 24(3): p. 284-291.
16. Van Lier, Y.F., et al., The post-hematopoietic cell transplantation microbiome: relationships with transplant outcome and potential therapeutic targets. 2021. 106(8): p. 2042.
17. Montassier, E., et al., Probiotics impact the antibiotic resistance gene reservoir along the human GI tract in a person-specific and antibiotic-dependent manner. 2021. 6(8): p. 1043-1054.
18. Roggiani, S., et al., Gut microbiota resilience and recovery after anticancer chemotherapy. 2023. 2(3): p. 16.
19. Ferguson, J.R. and K.J.I.J.o.C.M. Taylor, Probiotics for antibiotic-associated diarrhea: what, when, and how long? 2022. 13(12): p. 571-583.
20. Fishbein, S.R., B. Mahmud, and G.J.N.R.M. Dantas, Antibiotic perturbations to the gut microbiome. 2023. 21(12): p. 772-788.
21. Machado, A., et al., Use of plant extracts, bee-derived products, and probiotic-related applications to fight multidrug-resistant pathogens in the post-antibiotic era. 2023. 3(3): p. 535-567.

 