e-ISSN: 0975-9506, p-ISSN: 2961-6093

Available online on www.ijpqa.com

International Journal of Pharmaceutical Quality Assurance 2025; 16(5); 310-315

Original Research Article

Impact of Probiotic Supplementation on the Incidence and Severity of Antibiotic-Associated Diarrhea in Hospitalized Patients

Nilesh Kumar[1], Manzoor Ahmed Thokar[2]

[1]Assistant Professor, Department of Microbiology, Madhubani Medical College and Hospital, Madhubani, Bihar, India

[2]Professor and HOD, Department of Microbiology, Madhubani Medical College and Hospital, Madhubani, Bihar, India

Received: 17-03-2025 / Revised: 10-04-2025 / Accepted: 26-05-2025

Corresponding Author: Dr. Nilesh Kumar

Conflict of interest: Nil

Abstract:

Background: Antibiotic-associated diarrhea (AAD) is a common complication of antibiotic therapy, particularly in hospitalized patients, resulting from disruption of gut microbiota. Probiotics may help restore microbial balance and prevent AAD.

Aim: To evaluate the role of probiotics in reducing the incidence, duration, and severity of AAD among hospitalized patients receiving antibiotics.

Methodology: A prospective, randomized, controlled trial was conducted at Department of Microbiology, Madhubani Medical College and Hospital, Madhubani, Bihar, India from January 2024 to December 2024.including 80 patients receiving systemic antibiotics. The intervention group (n=45) received *Saccharomyces boulardii* CNCM I-745 alongside antibiotics, while the control group (n=35) received antibiotics alone. Stool frequency and consistency were monitored using the Bristol Stool Form Scale. Data were analyzed using SPSS 27, and relative risk (RR) with 95% CI was calculated.

Results: The incidence of AAD was significantly lower in the probiotic group (11.1%) compared to controls (34.3%; RR = 0.30, p = 0.01). Mean duration of diarrhea was shorter in the intervention group (2.6 ± 0.8 days) versus control (4.1 ± 1.2 days, p = 0.02). Severity differences were not statistically significant. Compliance was high (>93%) in both groups.

Conclusion: Probiotic supplementation significantly reduces the incidence and duration of AAD in hospitalized patients, supporting its use as an effective adjunct to antibiotic therapy.

Keywords: Antibiotic-Associated Diarrhea, Probiotics, *Saccharomyces Boulardii*, Randomized Controlled Trial, Hospitalized Patients.

Introduction

Antibiotic treatment is a fundamental pillar in treatment of bacterial infections and has transformed the modern medicine in terms of increased morbidity and mortality [1]. Nevertheless, the prolific and in many cases extensive use of antibiotics do not pass without ramifications, one of the most prevalent ones being antibiotic-associated diarrhea (AAD). AAD is widely considered as the three or more unformed stools per day that happens as a side effect of antibiotic use and it has a spectrum between mild and self-limiting occurrences to severe colitis especially when triggered by Clostridioides difficile [2]. AAD has been reported to occur in patients taking antibiotics at a rate of between 5 and 30 persons, and the hospitalized patients are more at risk since they take broad-spectrum antibiotics, are aged, have comorbidities, and spend longer hours in hospitals. The condition does not only affect the healing process of the patient but also extends the time spent in hospital, rises the cost of healthcare and, in worst case scenarios, causes some life-threatening complications [3]. Thus, of critical clinical significance is the need to identify viable means by which the risk of AAD in hospitalized patients can be prevented or minimized.

Disruption of normal microbiota in the intestines contributed by the use of antibiotics is one of the major mechanisms underlying AAD [4]. Antibiotics especially the broad-spectrum agents distort the stable composition of gut flora by suppressing normal flora and allowing proliferation of pathogenic organisms like C. difficile, Klebsiella, and other opportunistic pathogens [5]. This microbial imbalance decreases colonization resistance and changes the metabolism of bile acids and decreases the production of short-chain fatty acids, which all lead to the consequences of diarrhea. Moreover, hospitalized patients

particularly those in intensive care unit or surgical units are usually administered several courses of antibiotics, further increasing the chances of destabilizing the microbiome. With this pathophysiological background, interventions targeting to restore or preserve microbial balance have been given growing focus over the past few years. One of them, probiotics, has become a potentially effective and biologically plausible tool to reduce the risk of AAD.

The World Health Organization (WHO) and Food and Agriculture Organization (FAO) define probiotics as live microorganisms that when given in proper quantities, they provide a health benefit to the host. Probiotic strains commonly found are Lactobacillus, Bifidobacterium, Saccharomyces boulardii and Streptococcus thermophilus which have shown effective effects in keeping the gut microbial balance within check [6]. The suggested mechanisms by which probiotics can perform their protective effects are competitive suppression of harmful bacteria, the restoration of gut microbiota diversity, and the improvement of mucosal barrier activity as well as host immune responses. In addition, probiotics are known to secrete antimicrobial factors like bacteriocins and organic acids preventing the colonization of the pathogens and to increase the amount of immunoglobulin A (IgA), which reinforces mucosal immunity [7]. These complex activities present a good biological explanation to the fact that probiotics prevent or minimize AAD in patients under antibiotic treatment.

A number of clinical trials and meta-analyses have examined the effectiveness of probiotics in preventing as well as mitigating occurrence and severity of AAD in hospital patients. There is evidence that probiotics can be used safely alongside antibiotics and that they may help to decrease the risk of diarrhea and also shorten its duration in the event that it occurs [8]. The two most commonly investigated strains include Saccharomyces boulardii and Lactobacillus rhamnosus GG that have been found to be effective in both adult and pediatric populations [9]. Notably, the positive effects of probiotics can be observed during a stay in hospital where inpatient patients have a higher risk of developing AAD because of the frequent use of high-risk antibiotics (clindamycin, cephalosporins, and fluoroquinolones). Moreover, probiotics could be used in the prevention of recurrent C. difficile infections which is a significant global issue because of the high morbidity and cost related to healthcare.

Despite the promising evidence, the use of probiotics in clinical practice is not yet universal, and questions remain regarding the optimal strains, dosages, timing, and duration of administration. Some studies report variability in efficacy, which may be attributed to differences in probiotic preparations, patient populations, and antibiotic regimens. Safety concerns also exist, particularly in immunocompromised or critically ill patients, where probiotic use has occasionally been associated with fungemia or bacteremia. Nevertheless, the overall risk is low, and the potential benefits of probiotics in reducing AAD far outweigh the rare adverse effects when used appropriately. As the burden of antibiotic resistance and healthcare-associated infections continues to grow, probiotics offer a safe, cost-effective, and non-pharmacological adjunct to antibiotic therapy that aligns with the principles of antimicrobial stewardship.

Methodology

Study Design: This study was designed as a prospective, randomized, controlled clinical trial to evaluate the role of probiotics in reducing antibiotic-associated diarrhea (AAD) among hospitalized patients.

Study Area: The study was carried out in the Department of Microbiology, Madhubani Medical College and Hospital, Madhubani, Bihar India from January 2024 to December 2024.

Inclusion and Exclusion Criteria

Inclusion Criteria

- Hospitalized patients aged 18 years and above.
- Patients receiving systemic antibiotic therapy for a minimum duration of 5 days.
- Patients willing to provide written informed consent and comply with study procedures.

Exclusion Criteria

- Patients with pre-existing chronic diarrhea or irritable bowel syndrome.
- Patients with known gastrointestinal malignancy, inflammatory bowel disease, or history of bowel surgery.
- Patients who had consumed probiotics or prebiotics within the past 4 weeks.
- Patients who were critically ill, immunocompromised, or unable to take oral preparations.
- Pregnant and lactating women.

Sample Size: A total of 80 patients were included in the study. Among them, 45 patients were allocated to the intervention group (probiotics + antibiotics) and 35 patients to the control group (antibiotics only).

Procedure: Eligible patients were recruited after initiation of systemic antibiotic therapy. Participants in the intervention group received probiotics in the form of oral capsules containing Saccharomyces boulardii CNCM I-745 (250 mg twice daily) starting within 48 hours of antibiotic initiation and continued for 7 days after completion of antibiotic treatment. The placebo group received identical capsules without live organisms. Patients were followed during hospitalization and up to 4 weeks post-discharge.

Stool frequency and consistency were monitored daily using the Bristol Stool Form Scale, and data were recorded in patient diaries. Antibiotic-associated diarrhea was defined as the passage of three or more loose or watery stools per day for at least two consecutive days, beginning no earlier than 48 hours after antibiotic initiation and up to 2 weeks after antibiotic discontinuation. In suspected cases of Clostridium difficile-associated diarrhea, stool samples were tested for C. difficile toxins using enzyme-linked immunoassay. Compliance with the intervention was assessed by capsule count at follow-up.

Statistical Analysis: Data were analyzed using SPSS version 27.0. Descriptive statistics were used to summarize demographic and clinical variables. Categorical variables were compared using the Chi-square test or Fisher's exact test, and continuous variables were analyzed using Student's t-test or Mann–Whitney U test as appropriate. The incidence of AAD between groups was compared using relative risk (RR) with 95% confidence intervals (CI). A p-value < 0.05 was considered statistically significant.

Result

Table 1 presents the baseline demographic and clinical characteristics of patients in the intervention and control groups. The mean age of patients was comparable between the intervention group (45.6 ± 12.4 years) and the control group (47.3 ± 11.8 years), with no statistically significant difference (p=0.52). Gender distribution was similar, with 24 males and 21 females in the intervention group, and 18 males and 17 females in the control group (p=0.93). The mean duration of hospital stay and antibiotic therapy also showed no significant differences between groups, at 8.2 ± 2.1 versus 8.5 ± 2.3 days (p=0.58) and 7.6 ± 1.3 versus 7.8 ± 1.5 days (p=0.47), respectively. Additionally, the proportion of patients with comorbidities such as diabetes and hypertension were comparable (26.7% vs. 28.6%; p=0.84), indicating that both groups were well-matched at baseline.

Table 1: Baseline Demographic and Clinical Characteristics of Patients

Variable	Intervention Group (n=45)	Control Group (n=35)	p-value
Mean Age (years ± SD)	45.6 ± 12.4	47.3 ± 11.8	0.52
Gender (Male/Female)	24 / 21	18 / 17	0.93
Mean Duration of Hospital Stay (days ± SD)	8.2 ± 2.1	8.5 ± 2.3	0.58
Mean Duration of Antibiotic Therapy (days ± SD)	7.6 ± 1.3	7.8 ± 1.5	0.47
Comorbidities (Diabetes, Hypertension, etc.)	12 (26.7%)	10 (28.6%)	0.84

Table 2 presents the incidence of antibiotic-associated diarrhea (AAD) among patients receiving probiotics alongside antibiotics compared to those receiving antibiotics alone. In the intervention group, out of 45 patients, only 5 (11.1%) developed AAD, whereas 40 patients (88.9%) did not, showing a significantly lower risk compared to the control group, in which 12 of 35 patients (34.3%) experienced AAD. The calculated relative risk for the intervention group was 0.30 (95% CI: 0.12–0.76), indicating that probiotic supplementation reduced the risk of AAD by 70%, and this difference was statistically significant (p = 0.01). These results suggest that probiotics have a protective effect against the development of AAD in hospitalized patients receiving antibiotics.

Table 2: Incidence of Antibiotic-Associated Diarrhea (AAD)

Group	Total Patients (n)	Patients with AAD (n, %)	Patients without AAD (n, %)	Relative Risk (95% CI)	p-value
Intervention (Probiotics + Antibiotics)	45	5 (11.1%)	40 (88.9%)	0.30 (0.12–0.76)	0.01
Control (Antibiotics Only)	35	12 (34.3%)	23 (65.7%)	–	–

Table 3 presents the severity of diarrhea in both groups by the Bristol Stool Form Scale. The vast majority of cases in the intervention group were mild, as there were 3 patients who had a Type 5 stool, 1 patient with a Type 6 stool, and 1 patient with a Type 7 stool. The control group had a slightly larger number of cases, with 4 patients who had a Type 5 stool, 5 patients who had a Type 6 stool, and 3 patients who had a Type 7 stool. Analysis of the data shows there were no meaningful differences between groups for any Type (p= 0.48, p= 0.08, and p= 0.23, for Types 5, 6, and 7, respectively). Overall, severity of diarrhea was comparable between groups.

Table 3: Severity of Diarrhea Based on Bristol Stool Form Scale			
Bristol Stool Form Type	**Intervention Group (n=45)**	**Control Group (n=35)**	**p-value**
Type 5 (Soft blobs)	3	4	0.48
Type 6 (Fluffy pieces)	1	5	0.08
Type 7 (Watery stools)	1	3	0.23

The duration of diarrhea events in patients with antibiotic-associated diarrhea (AAD) is shown in Table 4 for the intervention and control groups. The patient receiving the intervention had shorter mean duration of diarrhea than the control (intervention [2.6 ± 0.8 days] vs control [4.1 ± 1.2 days]); median duration of diarrhea events were 3 days (range 2 - 4 days) for the intervention and 4 days (range 3 - 6 days) for control. The difference was statistically significant (p = 0.02). The intervention was found to be effective in reducing the duration of diarrhea in patients enrolled in the study.

Table 4: Duration of Diarrhea Episodes in Patients with AAD			
Group	**Mean Duration (days ± SD)**	**Median (Range)**	**p-value**
Intervention (n=5)	2.6 ± 0.8	3 (2–4)	0.02
Control (n=12)	4.1 ± 1.2	4 (3–6)	–

Table 5 shows the degree of compliance with the intervention among the participants of the study. In the intervention group (n=45), most of the participants, 42 participants (93.3%), were fully compliant, while 3 participants (6.7%) were partially compliant, and none were non-compliant. In the control group (n=35), there were 33 fully compliant participants (94.3%), 2 partially compliant participants (5.7%), and no non-compliance. A p-value of 0.15 indicates that there was no statistically significant difference in compliance among the groups; therefore, compliance with the study protocol was similarly high among both the intervention and control groups.

Table 5: Compliance with Intervention				
Group	**Full Compliance (n, %)**	**Partial Compliance (n, %)**	**Non-Compliance (n, %)**	**p-value**
Intervention (n=45)	42 (93.3%)	3 (6.7%)	0 (0%)	0.15
Control (n=35)	33 (94.3%)	2 (5.7%)	0 (0%)	–

Discussion

The present research showed that the probiotics significantly decreased the occurrence of antibiotic-associated diarrhea (AAD) in hospitalized patients treated with antibiotics, as 11.1% of patients in the probiotic group versus 34.3% of patients in the control experienced AAD (p = 0.01). The relative risk, which was 0.30, reflects a 70% decreased likelihood of developing AAD among patients taking the probiotics compared to the control patients. Mantegazza et al., (2018) [10] observed that Lactobacillus rhamnosus GG significantly reduced AAD incidence of AAD in both pediatric and adult populations, indicating the strength of probiotic effectiveness among other patients. Our findings are generally congruent with these studies. In conclusion, probiotic supplementation is a clinically relevant method to prevent AAD.

Additionally, the duration of diarrhea in this study was significantly shorter in the probiotic group (2.6 ± 0.8 days) compared to the control group (4.1 ± 1.2 days, p = 0.02). This reduction was similar to what was reported by Guo et al. (2019) [11], who found that probiotic treatment reduced the mean duration of AAD by approximately 1.5 days. Short episodes of diarrhea reduce patient discomfort and risk of dehydration and/or hospitalization-related complications, making probiotics useful in a clinical context. Di Pietro (2020) [12] also reported a reduced duration of AAD in patients receiving Lactobacillus preparation, supporting the notion that probiotics help to restore the gut microbiota homeostasis following antibiotic-associated dysbiosis.

In terms of both the frequency and length of AAD, there was a notable decline in the probiotic group; however, there were no significant differences in severity of diarrhea scored by the Bristol Stool Form Scale, although there was a trend towards less severe stool consistency in the probiotic group. This finding aligns with Guarino's (2015) [13] study in that the main action of probiotics is to reduce frequency and duration rather than eliminate severe diarrhea. Our results suggest that while probiotics do not completely eliminate moderate to severe diarrhea, they do contribute to greater patient comfort and lower symptom burden, which is especially important in hospitalized populations.

Patient adherence to the probiotic protocol in this study was high; more than 93% adherence was demonstrated, and no significant differences between the intervention and control groups were detected. There is already evidence to suggest that

probiotics are well tolerated in delivery, and feasible to incorporate into everyday practice (Szajewska et al., 2016) [14]. Given the high rates of adherence in our study, we have renewed confidence in the benefits we have observed and do not think patient acceptance will be a barrier to future probiotic interventions.

It is worth noting that our research was originally done with a focus on Lactobacillus rhamnosus GG and Bifidobacterium longum BB536, and other reports have documented similar protective effects using coordinated multi-strain probiotic preparations. For example, Mantegazza et al., 2018 [15] documented that a combination of Lactobacillus and Bifidobacterium reduced the incidence of AAD from 25% to 12%, which is comparable to the observed reduction in our cohort. This supports the notion that both single-strain and multi-strain probiotics will be effective, but the magnitude of the benefit will depend partly on strain selection and dosing, and on the types of patients being studied.

Contrastingly, some studies report less pronounced effects of probiotics on severe AAD. Szajewska H. (2005) [16] observed a reduction in diarrhea incidence in children treated with probiotics; however, there was no statistically significant difference in the severity of diarrhea between groups. This partially mirrors our observation regarding diarrhea severity and suggests that while probiotics are effective in preventing AAD and reducing duration, their impact on severe manifestations may be limited. Such variations may be attributed to differences in antibiotic regimens, patient demographics, and underlying health conditions, highlighting the need for individualized approaches to probiotic therapy.

In summary, the current study further supports the role of probiotics as a safe and effective adjunct to antibiotic treatment in the prevention and management of AAD in hospital patients. The substantial reductions in incidence and duration, a high level of adherence among patients and a favorable safety profile all indicate the important clinical value of probiotics. Our findings corroborate other studies (Hickson et al., 2007) [17], and frequent consideration of probiotic supplementation in at-risk patients may improve patient outcomes, decrease length of stay, and reduce the overall health care burden associated with antibiotic treatment. Further studies should examine multi-center studies with larger samples to evaluate optimal strains, doses and duration for clinical benefit.

Conclusion

The findings of this study clearly demonstrate that probiotic supplementation significantly reduces the incidence and duration of antibiotic-associated diarrhea (AAD) in hospitalized patients receiving antibiotic therapy. Patients in the probiotic group experienced a markedly lower incidence of AAD (11.1%) compared to the control group (34.3%), corresponding to a 70% relative risk reduction. Additionally, the duration of diarrhea was significantly shorter in the intervention group, indicating that probiotics not only prevent the onset of AAD but also contribute to faster recovery when diarrhea occurs. While the severity of diarrhea showed only minor differences, the overall clinical benefit, coupled with high patient adherence and a favorable safety profile, highlights probiotics as a practical and effective adjunct to antibiotic therapy. These results support integrating probiotics into routine care to improve patient outcomes and reduce healthcare burden.

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