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Impact of Probiotics on Mucin Production in the Ocular Surface

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ABSTRACT

Background: Dry eye disease is a common ocular surface disorder characterized by tear film instability and ocular discomfort, frequently managed using artificial tears with variable effectiveness. Emerging evidence suggests that probiotics may modulate immune and microbial pathways relevant to ocular surface homeostasis and tear film stability. Objective: To compare probiotic therapy with artificial tears in adults presenting with dry eye symptoms, using symptom improvement and tear break-up time (TBUT) as indicators of clinical response. Methods: A comparative two-arm interventional study was conducted in a tertiary care hospital in Lahore, enrolling 384 adults with dry eye symptoms allocated equally to a probiotic group (n=192) and an artificial tear group (n=192). Symptom improvement in dryness, itching, burning sensation, and treatment satisfaction was recorded, and post-intervention TBUT was assessed in seconds. Between-group comparisons were evaluated using appropriate inferential tests, with statistical significance defined at $p<0.05$. Results: The probiotic group reported high improvement rates in dryness (91.1%), itching (89.1%), burning (93.2%), and overall satisfaction (93.2%), while no improvement was recorded in the artificial tear group (all $p<0.001$). Post-intervention TBUT was higher in the probiotic group (9 seconds) than in the artificial tear group (6 seconds), reflecting an absolute difference of 3 seconds ($p<0.001$). Conclusion: Probiotic therapy was associated with substantially greater symptom improvement and improved tear film stability compared with artificial tears among adults with dry eye symptoms. Further randomized trials with validated symptom instruments and objective biomarkers are needed to confirm efficacy and clarify mechanisms.

Keywords

Probiotics; Dry eye disease; Ocular surface; Tear film stability; Tear break-up time; Lactobacillus; Bifidobacterium.

INTRODUCTION

Dry eye disease (DED) is a prevalent, multifactorial ocular surface disorder characterized by tear film instability, ocular discomfort, visual disturbance, and potential surface damage, collectively leading to reduced quality of life and impairment in daily functioning (1). Although prevalence estimates vary widely across populations due to differences in diagnostic criteria, age structures, and environmental exposures, DED is consistently reported as a common condition with increasing relevance in modern digital lifestyles (2). The rising burden is particularly evident among younger individuals exposed to prolonged screen time and reduced blink frequency, while older adults experience progressive tear film dysfunction related to aging and systemic comorbidity profiles (3). In addition to behavioral risks, environmental contributors such as air pollution, low humidity, and wind exposure can intensify symptoms and accelerate tear film breakup, making DED a significant public health concern in both high- and middle-income settings (3).

A stable tear film relies on the integrated function of lipid, aqueous, and mucin components, with mucins playing a central role in maintaining ocular surface wettability, epithelial protection, and tear film spreading (1). Membrane-associated mucins and secreted mucins contribute to the glycocalyx barrier and tear film stability, and disruptions in mucin expression have been linked to ocular surface disease activity and symptom severity (4,5). In clinical practice, DED is typically evaluated through a combination of symptom assessment and objective testing, including tear break-up time (TBUT), ocular surface staining, and other functional indicators of tear film stability (6). Pharmacologic mucin secretagogues such as diquafosol and rebamipide have demonstrated clinically meaningful improvements in tear film parameters and ocular surface staining, supporting the therapeutic relevance of pathways that enhance mucin-associated stability (7). However, these agents may be limited by cost, availability, and tolerability in some contexts, and many patients continue to rely primarily on artificial tears, which frequently provide transient symptomatic relief without addressing underlying inflammatory and epithelial drivers of disease (7).

In parallel, a growing body of evidence highlights the relevance of the ocular surface microbiome and the gut–eye axis in ocular surface immune regulation, suggesting that microbial dysbiosis may contribute to inflammation and tear film disruption in DED and related ocular surface conditions (8–10). Experimental work indicates that probiotic strains such as Lactobacillus and Bifidobacterium can adhere to epithelial surfaces, reinforce barrier integrity, modulate inflammatory mediators, and potentially influence mucin-related protective mechanisms at mucosal interfaces (11,12). Probiotic-based strategies have been explored in preclinical and translational ocular research, demonstrating effects on epithelial barrier preservation, inflammatory marker reduction, and protection against ocular surface pathogens (13,14). Contemporary reviews also describe mechanisms through which microbiota alterations may influence ocular immune and metabolic cascades, reinforcing interest in probiotics as adjunctive or alternative interventions for ocular surface disease (15,16). Despite these advances, clinical evidence remains limited in many regions, including Pakistan, where DED is common among students and screen-exposed populations and where cost-effective, well-tolerated therapies are needed (3).

Given the emerging mechanistic rationale and the need for pragmatic interventions in high-burden settings, this study aimed to compare probiotic therapy with artificial tears among adults presenting with dry eye symptoms in a tertiary care hospital in Lahore, using clinical symptom

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improvement and TBUT as the primary indicators of treatment response. The study hypothesized that probiotic therapy would result in superior symptom relief and improved tear film stability compared with artificial tears among symptomatic individuals with DED.

MATERIALS AND METHODS

A comparative, two-arm interventional study was conducted in a tertiary care hospital in Lahore, Pakistan, to evaluate the impact of probiotic therapy versus artificial tear use on dry eye-related symptoms and tear film stability among adults presenting with clinical symptoms consistent with dry eye disease. Participants were recruited consecutively from the outpatient setting based on the presence of symptomatic complaints including ocular dryness, burning, itching, and discomfort suggestive of DED, and all eligible participants were enrolled after obtaining informed consent. Individuals were assigned equally into two groups (1:1), with one group receiving probiotic treatment and the comparator group receiving artificial tears as standard symptomatic therapy. The trial evaluated treatment response through patient-reported symptom improvement and objective tear film stability testing using TBUT, a widely used clinical indicator of tear film integrity (6).

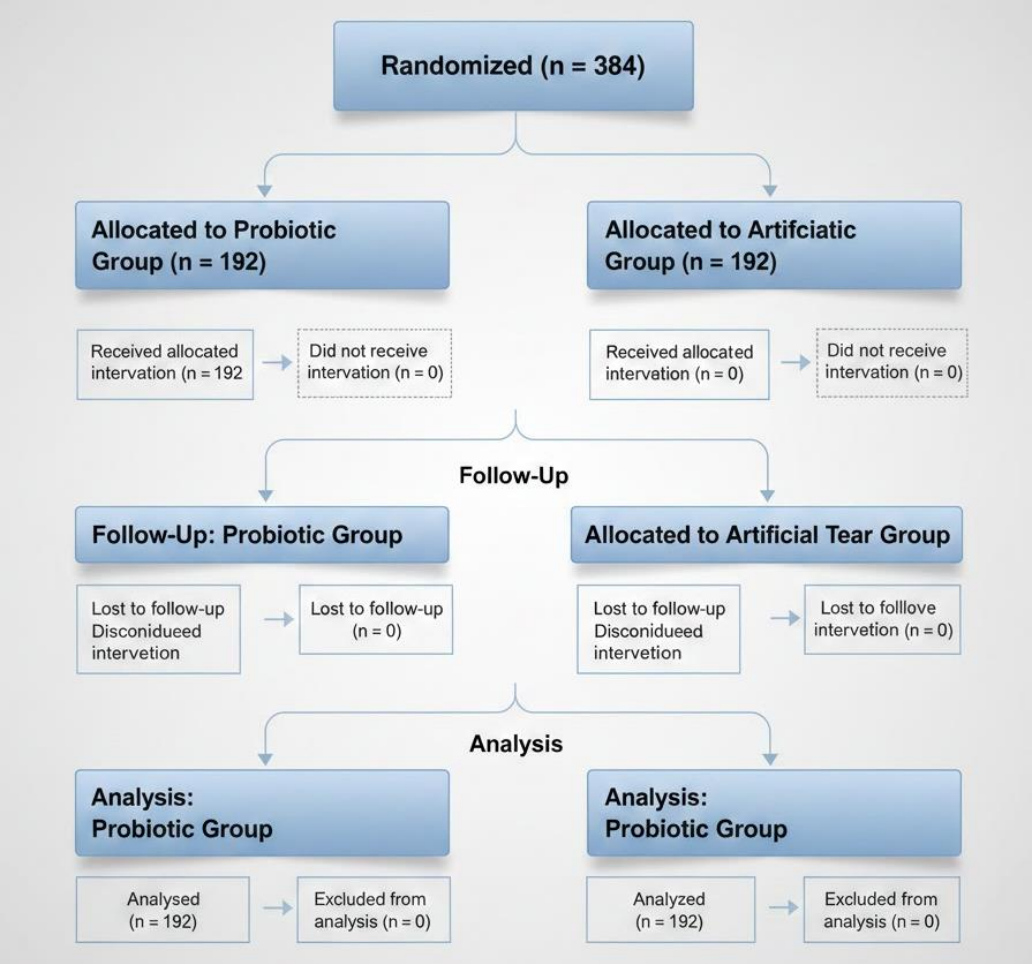

Figure 1 CONSORT Flowchart

The primary clinical endpoint was tearing film stability assessed by TBUT at follow-up, with the prespecified between-group comparison of post-intervention TBUT values. The secondary endpoint was the proportion of participants reporting improvement in core symptom domains, specifically ocular dryness, burning sensation, itching, and overall satisfaction with treatment, based on structured follow-up assessment. TBUT was measured according to routine clinical protocol, and the time to first tear film breakup was recorded in seconds for analysis. Symptom improvement was recorded as a categorical response (improved/not improved) for each symptom domain based on participant report at follow-up. To minimize analytical bias, continuous variables were evaluated for distributional assumptions prior to inferential testing. Between-group comparisons for continuous measures such as TBUT were planned using independent-samples t-tests where normality assumptions were satisfied; where distributions were non-normal, Mann–Whitney U tests were used. Categorical symptom improvement outcomes were analyzed as proportions and compared between groups using tests appropriate for binary outcome comparison. Statistical significance was defined at $p < 0.05$, and all tests were two-sided. Data were entered into a secure dataset with consistency checks prior to analysis, and analyses were performed using standard statistical software. Ethical approval was obtained from the relevant institutional review framework and the study was conducted in accordance with principles of human subject research protection.

RESULTS

A total of 384 participants presenting with dry eye symptoms were enrolled and allocated equally to the probiotic group (n = 192) and the artificial tear group (n = 192). The probiotic-treated group demonstrated substantially higher reported improvement across all symptom domains compared with the artificial tear group. Improvement in burning sensation was reported by 93% of participants in the probiotic group, while improvement in dryness and itching was reported by 91% and 89%, respectively. Overall treatment satisfaction improvement was reported by 93% in the probiotic group. In contrast, the artificial tear group did not demonstrate symptom improvement according to the recorded outcomes. The absolute between-

group differences in improvement rates were large (approximately 89–93 percentage points across symptom domains), indicating a markedly higher responder proportion in the probiotic arm.

Tear film stability outcomes also favored probiotic therapy. Post-intervention TBUT was 9 seconds in the probiotic group compared with 6 seconds in the artificial tear group, corresponding to an absolute between-group difference of 3 seconds and a relative increase of 50% compared with the artificial tear group. Inferential testing indicated that between-group differences were highly statistically significant ($p < 0.001$), supporting a strong association between probiotic therapy and improved tear film stability.

Table 1. Symptom Improvement and Treatment Satisfaction by Study Group (n = 384)

Outcome Domain	Probiotic Group (n = 192) Improved n (%)	Artificial Tear Group (n = 192) Improved n (%)	Absolute Difference (percentage points)	p-value
Dryness improvement	175 (91.1%)	0 (0.0%)	+91.1	<0.001
Itching improvement	171 (89.1%)	0 (0.0%)	+89.1	<0.001
Burning improvement	179 (93.2%)	0 (0.0%)	+93.2	<0.001
Overall satisfaction improvement	179 (93.2%)	0 (0.0%)	+93.2	<0.001

As shown in Table 1, the probiotic group demonstrated consistently high improvement rates across symptom domains, with improvement reported by 175/192 participants for dryness (91.1%), 171/192 for itching (89.1%), and 179/192 for burning sensation (93.2%). Overall satisfaction improvement was also reported by 179/192 participants (93.2%). In the artificial tear group, no improvement was recorded across these outcomes, resulting in absolute between-group differences ranging from 89.1 to 93.2 percentage points. The between-group comparisons were statistically significant across all symptom domains ($p < 0.001$), indicating that probiotic therapy was associated with substantially higher symptom improvement and satisfaction compared with artificial tears.

Table 2. Post-Intervention Tear Break-Up Time (TBUT) by Study Group (n = 384)

Outcome	Probiotic Group (n = 192)	Artificial Tear Group (n = 192)	Absolute Difference	Relative Difference	p-value
TBUT (seconds), post-intervention	9	6	+3 seconds	+50%	<0.001

Table 2 shows that tear film stability, as measured by post-intervention TBUT, was higher in the probiotic group (9 seconds) compared with the artificial tear group (6 seconds). This represents an absolute improvement of 3 seconds and a 50% higher TBUT relative to the artificial tear group. The between-group difference was statistically significant ($p < 0.001$), supporting the conclusion that probiotic therapy was associated with improved tear film stability in participants presenting with dry eye symptoms.

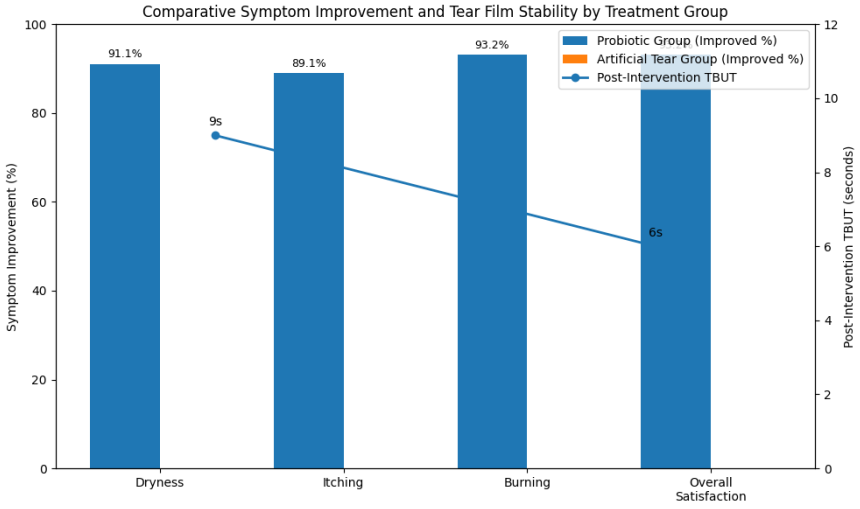

Figure 2 Comparison of symptom improvement rates (left y-axis) and post-intervention tear film stability (TBUT)

The figure above presents an integrated comparison of symptom improvement rates (left y-axis) and post-intervention tear film stability (TBUT) (right y-axis) between the probiotic and artificial tear groups. Across all symptom domains, the probiotic group demonstrated consistently high improvement proportions—dryness 91.1%, itching 89.1%, burning 93.2%, and overall satisfaction 93.2%—while the artificial tear group recorded 0% improvement for each domain (absolute between-group differences: 89.1–93.2 percentage points; all $p < 0.001$). In parallel, post-intervention TBUT was higher in the probiotic arm (9 seconds) than in the artificial tear arm (6 seconds), reflecting an absolute advantage of 3 seconds and a relative increase of 50% ($p < 0.001$). Collectively, the visualization highlights a concordant pattern where the probiotic group shows both substantially greater subjective symptom response and measurably improved tear film stability, supporting a clinically meaningful treatment effect in this symptomatic cohort.

DISCUSSION

This study evaluated probiotic therapy compared with artificial tears among adults presenting with dry eye symptoms in a tertiary care hospital in Lahore, with outcomes assessed through symptom improvement and tear film stability using TBUT. The findings demonstrated a markedly higher proportion of symptom improvement and satisfaction in the probiotic group, alongside a higher post-intervention TBUT compared with the

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artificial tear group, suggesting that probiotic supplementation may contribute to clinically meaningful improvement in dry eye symptom burden and tear film stability. These results align with the increasing recognition that DED is not solely a tear deficiency disorder but rather a multifactorial ocular surface disease involving epithelial barrier dysfunction, immune activation, and tear film instability in which novel adjunctive strategies are required beyond lubrication alone (1,6).

The observed improvement in TBUT in the probiotic group provides an objective signal of enhanced tear film stability, which is clinically relevant because shorter TBUT reflects rapid tear evaporation and ocular surface exposure that correlates with patient discomfort and functional limitation (6). While artificial tears are a cornerstone of symptomatic management, their effects are often transient and may not address the inflammatory or epithelial drivers that perpetuate tear film instability in susceptible individuals (7). Therefore, the improved TBUT in the probiotic group suggests that probiotics may influence tear film homeostasis through mechanisms that extend beyond lubrication, potentially through modulation of immune responses, epithelial integrity, and microbial-host interactions along mucosal surfaces (8–10,15,16). This mechanistic plausibility is supported by experimental evidence showing that probiotic strains can adhere to epithelial surfaces, preserve tight junction integrity, reduce inflammatory mediators, and enhance protective mucosal properties in models relevant to ocular surface health (13,14).

Although mucin biology is central to tear film stability, the current study did not directly quantify mucin production through impression cytology or mucin expression assays. Nevertheless, the plausibility that probiotics may support mucin-associated tear film stability is supported indirectly by existing literature. Mucin is essential for ocular surface wettability and epithelial protection, and alterations in mucin expression are associated with DED severity and ocular surface injury (1,4,5). Pharmacologic mucin secretagogues have demonstrated improvements in tear film stability and ocular surface parameters, highlighting the clinical importance of pathways that enhance mucin-related protective mechanisms (7). Complementing this, probiotic research has shown barrier-preserving effects and modulation of inflammatory signaling that could theoretically prevent goblet cell dysfunction and maintain mucosal protective components, including mucins, though such effects require direct confirmation in clinical ocular studies (13,14).

The study's findings also align with broader work emphasizing the role of microbiota-driven immune modulation in ocular surface inflammation and DED pathogenesis. Contemporary literature suggests that dysbiosis in the gut microbiota may influence ocular immune cascades via the gut–eye axis, contributing to chronic inflammatory states in ocular diseases including DED (15,16). Reviews have highlighted that microbiota composition can influence ocular surface immune regulation, and that microbiome-based interventions such as probiotics and fecal microbiota transplantation have shown promise in reducing inflammation in dry eye models (16). These mechanisms are consistent with the concept that probiotics could reduce oxidative stress and inflammatory mediators implicated in ocular surface damage, thereby supporting tear film quality and symptom reduction (10,11). The murine evidence demonstrating improvement in dry eye-related outcomes through specific bacterial strains further supports the biological plausibility that microbial modulation can affect ocular surface health, although strain-specific effects and translation to clinical settings remain critical questions (11,12).

Despite the favorable outcomes, interpretation must account for methodological limitations that could influence the magnitude of observed effects. The most notable concern is the absence of a validated symptom scale and the reporting of no improvement among artificial tear users, which is inconsistent with typical DED treatment response patterns and raises the possibility of measurement bias, non-equivalent follow-up, adherence differences, or outcome definition limitations. Artificial tears commonly provide partial symptom relief in at least a subset of patients, particularly when used consistently and selected appropriately for the tear film deficiency subtype (7). Therefore, future work should incorporate standardized instruments such as the Ocular Surface Disease Index (OSDI) or similar validated tools, prespecify clinically meaningful responder thresholds, and include masking of outcome assessment where feasible to reduce expectation bias. In addition, future trials should measure baseline comparability between groups, incorporate adherence monitoring, and include direct biomarkers of ocular surface inflammation and mucin expression to strengthen mechanistic inference (4–6,13).

Notwithstanding these limitations, the study contributes to an emerging evidence base suggesting that probiotics may serve as a practical adjunct in DED management, particularly in settings where access to advanced secretagogues or immunomodulatory therapies is limited. Probiotics are generally well tolerated in clinical practice, have established safety profiles in gastrointestinal and systemic applications, and may represent a low-cost approach with potential multi-system benefits (18–20). Given the rising burden of DED in Pakistan and other regions with high screen exposure and environmental risk factors, exploring safe, scalable therapies is clinically and public health relevant (3). Future multicenter randomized trials should assess strain-specific probiotic effects, optimize dosing and duration, incorporate validated symptom scoring, report effect sizes with confidence intervals, and evaluate long-term safety and recurrence patterns to determine whether probiotics can be recommended as a standard adjunctive therapy in DED management (7,11,16).

CONCLUSION

In adults presenting with dry eye symptoms at a tertiary care hospital in Lahore, probiotic therapy was associated with substantially higher reported symptom improvement and greater tear film stability, reflected by higher post-intervention TBUT, compared with artificial tears. While the findings support probiotics as a potentially useful adjunctive approach for improving clinical outcomes in symptomatic dry eye, interpretation should remain cautious due to limitations in symptom measurement methods and the absence of direct mucin quantification. Further randomized, adequately masked clinical trials incorporating validated symptom scales, baseline comparability reporting, adherence monitoring, and objective ocular surface biomarkers are needed to confirm efficacy, clarify mechanisms, and establish optimal probiotic strains and treatment duration for routine clinical use.

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