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ROLE OF MULTI-STRAIN PROBIOTICS IN PRESENTATION OF SEVERITY AND FREQUENCY OF ALLERGIC RHINITIS

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ABSTRACT

Background: *Allergic rhinitis (AR) is a common inflammatory condition characterized by nasal congestion, sneezing, and itching, driven by immune dysregulation. While conventional treatments provide symptom relief, they often fail to address underlying immunological imbalances.* ***Objective:*** *This study aimed to evaluate the efficacy of multi-strain probiotics in improving AR symptoms, quality of life, and immunological markers compared to a placebo.* ***Methods:*** *A randomized, double-blind, placebo-controlled trial was conducted at the Department of Pediatrics, Abbasi Shaheed Hospital during January 2024 to June 2024 with 135 patients diagnosed with AR. Participants received either a multi-strain probiotic formulation or placebo daily for 12 weeks. Outcomes included Total Nasal Symptom Score (TNSS), Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) scores, serum IgE levels, and eosinophil counts. Data were analyzed using intention-to-treat principles.* ***Results:*** *The probiotic group demonstrated a significant reduction in TNSS (46.9%) compared to the placebo group (16.3%), along with greater improvements in RQLQ scores (mean difference: 1.2, $p < 0.001$). Serum IgE levels and eosinophil counts decreased significantly in the probiotic group, highlighting immunological benefits. Adverse events were mild and comparable between groups.* ***Conclusion:*** *Multi-strain probiotics effectively reduce AR symptoms, improve quality of life, and modulate immune markers, offering a safe and valuable adjunct to traditional AR management. Further research is recommended to explore long-term benefits and personalized applications.*

INTRODUCTION

Allergic rhinitis (AR) is a prevalent chronic inflammatory condition of the nasal mucosa, characterized by symptoms such as sneezing, nasal congestion, rhinorrhea, and itching. These symptoms are often triggered by allergen exposure, including pollen, dust mites, mold, and animal dander. Affecting a significant portion of the global population, AR not only impairs quality of life but also imposes substantial healthcare costs and productivity losses. While antihistamines, intranasal corticosteroids, and allergen-specific immunotherapy remain the cornerstone of AR treatment, these conventional interventions primarily provide symptom management [1]. They may not address the root causes of immune dysregulation underlying allergic responses, highlighting the need for alternative or complementary therapies. The immune system's dysregulation in AR involves a skewed Th2 immune response, leading to elevated levels of IgE and the release of pro-inflammatory mediators such as histamine [2]. Increasingly, research has pointed to the critical role of the gut microbiota in maintaining immune homeostasis. A balanced gut microbiota contributes to immune tolerance by regulating the interactions between innate and adaptive immune cells. Conversely,

dysbiosis, or the imbalance of gut microbiota, has been associated with heightened susceptibility to allergic diseases, including AR [3].

Probiotics, defined as live microorganisms that provide health benefits when consumed in adequate amounts, have emerged as a promising adjunctive therapy for allergic conditions. Multi-strain probiotics, which combine various bacterial species and strains, may offer superior benefits compared to single-strain formulations due to their ability to target multiple aspects of immune modulation and gut health [4]. By enhancing microbial diversity, multi-strain probiotics may exert synergistic effects, promoting the restoration of a balanced microbiota and regulating immune function in patients with AR. The potential therapeutic effects of multi-strain probiotics in AR are rooted in their ability to modulate both the gut microbiota and the systemic immune system [5].

Numerous studies have explored the efficacy of multi-strain probiotics in patients with AR, yielding promising results. Clinical trials have reported improvements in AR symptoms such as nasal congestion, sneezing, and itching following probiotic supplementation. These benefits are often accompanied by reductions in markers of inflammation, such as serum IgE and eosinophil counts [6]. Additionally, multi-strain formulations have been shown to enhance quality of life, as measured by validated symptom scores and patient-reported outcomes. Compared to single-strain probiotics, multi-strain formulations appear to provide broader and more robust effects due to their ability to target multiple pathways involved in immune regulation and microbiota restoration [7]. For instance, combinations of Lactobacillus and Bifidobacterium species have demonstrated additive effects in reducing allergic symptoms and modulating immune markers. Multi-strain probiotics are generally well-tolerated, with a favorable safety profile in most populations, including children and adults. However, variations in individual responses underscore the importance of personalized approaches to probiotic therapy [8]. Future research should aim to identify optimal strains, dosages, and treatment durations to maximize therapeutic outcomes in AR. Allergic rhinitis (AR) is characterized by a nasal sensitive inflammation, which is estimated to already affect 10%–40% of the worldwide population. Common symptoms of AR are nasal itching, sneezing, rhinorrhea, and nasal congestion [9]. In addition, some patients experience symptoms of allergic rhino conjunctivitis, such as watery itchy, or red eyes. Severe AR can affect the quality of life, sleep, and work performance. The prevalence of allergic rhinitis (AR) has been rising over the past few decades, and AR is reported to affect up to 30% of the world population, while its incidence ranges from 10% to 20%, leading to impaired quality of life (QoL) [10]. These increasing cases are attributed to the "hygiene hypothesis," which causes skewing of the T helper 1/T helper 2 (Th1/Th2) ratio toward the Th2 lineage, leading to an increase in serum Th2 mediated cytokines and interleukins (ILs), such as IL-3, IL-4, and IL-13. Subsequently, it causes induction of immunoglobin (Ig) E and tissue infiltration by eosinophils. Some authors believe that childhood infections have less to do with AR, but this may be attributed to changes in modern practices [11].

Objective

This study aimed to evaluate the efficacy of multi-strain probiotics in improving AR symptoms, quality of life, and immunological markers compared to a placebo.

Methodology

A randomized, double-blind, placebo-controlled trial was conducted at the Department of Pediatrics, Abbasi Shaheed Hospital during January 2024 to June 2024 with 135 patients diagnosed with AR.

Sample size

The sample size of 135 patients was calculated to provide 80% power to detect a clinically significant difference in TNSS between the probiotic and placebo groups, with a two-tailed alpha of 0.05.

Inclusion Criteria

- Aged between 4 and 12 years.

- Diagnosed with allergic rhinitis based on clinical history and positive results from skin prick tests or elevated serum IgE specific to common allergens.
- Moderate to severe AR symptoms persisting for at least two years.
- Willingness to adhere to the study protocol and attend all follow-up visits.

Exclusion Criteria

- Participants were excluded if they met any of the following criteria:
- Use of systemic corticosteroids, antibiotics, or immunomodulatory drugs within the four weeks prior to enrollment.
- Presence of comorbid autoimmune diseases or severe chronic illnesses such as diabetes or cardiovascular disorders.
- History of gastrointestinal disorders or major gastrointestinal surgery that could affect the absorption or metabolism of probiotics.
- Pregnancy, lactation, or plans to conceive during the study period.

Data collection

Participants were randomly assigned to one of two groups: a probiotic group or a placebo group, using computer-generated randomization. The probiotic group received a multi-strain probiotic formulation consisting of Lactobacillus spp. and Bifidobacterium spp., with a total viable count of 10^{10} CFU per dose. The placebo group received an identical-looking and -tasting capsule containing inert ingredients. Both groups were instructed to take one capsule daily for 12 weeks. Baseline data were collected at enrollment, including demographic information, medical history, and initial symptom scores. Patients were followed up at 4, 8, and 12 weeks to assess adherence to the intervention and record any adverse events. Symptom scores and quality-of-life measures were reassessed at each visit. Laboratory tests, including serum IgE and eosinophil counts, were performed at baseline and at the end of the study. The primary outcome was the improvement in AR symptoms, assessed using the Total Nasal Symptom Score (TNSS), which evaluates nasal congestion, sneezing, rhinorrhea, and itching on a scale of 0 (no symptoms) to 3 (severe symptoms). Secondary outcomes included changes in quality of life measured by the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) and levels of serum IgE and eosinophil counts as markers of allergic inflammation.

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Statistical Analysis

Data were analyzed using SPSS v27. Between-group comparisons were performed using independent t-tests for continuous variables and chi-square tests for categorical variables. Changes over time within groups were analyzed using repeated-measures ANOVA. A p-value of <0.05 was considered statistically significant.

Results

Data were collected from 135 patients. The mean age was 9.4 ± 3.2 years in the probiotic group and 8.25 ± 4.0 years in the placebo group ($p = 0.78$), with a nearly equal gender distribution (52% and 50% female, respectively; $p = 0.82$). Baseline Total Nasal Symptom Scores (TNSS) and Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) scores were similar between groups (TNSS: 8.1 vs. 8.0, $p = 0.65$; RQLQ: 4.5 vs. 4.4, $p = 0.74$).

Table 1: Demographic and Baseline Characteristics

Characteristic	Probiotic Group (n=64)	Placebo Group (n=64)	p-value
Age (years, mean ± SD)	9.4 ± 3.2	8.25 ± 4.0	0.78
Gender (% female)	52%	50%	0.82
Baseline TNSS (mean ± SD)	8.1 ± 1.2	8.0 ± 1.3	0.65
Baseline RQLQ (mean ± SD)	4.5 ± 0.9	4.4 ± 1.0	0.74

Serum IgE (IU/mL)	250 ± 50	245 ± 55	0.63
Eosinophil Count (%)	5.8 ± 1.0	5.7 ± 1.1	0.70

Total Nasal Symptom Scores (TNSS) decreased significantly in the probiotic group (4.3 ± 1.1) versus the placebo group (6.7 ± 1.0), with a between-group difference of 2.4 (95% CI: 1.9–2.9; $p < 0.001$). Similarly, quality of life scores improved markedly, as reflected in a greater reduction in RQLQ scores in the probiotic group (2.1 ± 0.8) compared to the placebo group (3.5 ± 0.9), with a between-group difference of 1.2 (95% CI: 0.9–1.5; $p < 0.001$). Immunological markers also improved, with serum IgE levels decreasing by 60 IU/mL in the probiotic group versus 15 IU/mL in the placebo group (between-group difference: 40, 95% CI: 25–55; $p < 0.001$). Eosinophil counts reduced significantly as well (3.6 ± 0.9 vs. 5.0 ± 1.0), with a between-group difference of 1.4 (95% CI: 1.0–1.8; $p < 0.001$).

Table 2: Primary and Secondary Outcomes

Outcome	Probiotic Group (Mean ± SD)	Placebo Group (Mean ± SD)	Between-Group Difference (95% CI)	p-value
TNSS (Baseline)	8.1 ± 1.2	8.0 ± 1.3	-	-
TNSS (12 Weeks)	4.3 ± 1.1	6.7 ± 1.0	2.4 (1.9–2.9)	< 0.001
RQLQ (Baseline)	4.5 ± 0.9	4.4 ± 1.0	-	-
RQLQ (12 Weeks)	2.1 ± 0.8	3.5 ± 0.9	1.2 (0.9–1.5)	< 0.001
IgE Levels (IU/mL)	250 ± 50 → 190 ± 40	245 ± 55 → 230 ± 45	40 (25–55)	< 0.001
Eosinophil Count (%)	5.8 ± 1.0 → 3.6 ± 0.9	5.7 ± 1.1 → 5.0 ± 1.0	1.4 (1.0–1.8)	< 0.001

Adverse events were mild and comparable between the probiotic and placebo groups, with no statistically significant differences observed. Mild bloating occurred in 7.8% of the probiotic group and 6.3% of the placebo group ($p = 0.75$), while mild diarrhea was reported equally in both groups (4.7%; $p = 1.00$). The overall incidence of any adverse events was slightly higher in the probiotic group (12.5%) compared to the placebo group (10.9%), but this difference was not statistically significant ($p = 0.82$).

Table 3: Adverse Events

Adverse Event	Probiotic Group (%)	Placebo Group (%)	p-value
Mild bloating	7.8%	6.3%	0.75
Mild diarrhea	4.7%	4.7%	1.00
Any adverse event (total)	12.5%	10.9%	0.82
Serious adverse events (total)	0%	0%	-

At 4 weeks, the probiotic group showed a mean TNSS of 6.7 ± 1.1 compared to 7.5 ± 1.2 in the placebo group, with a between-group difference of 0.8 (95% CI: 0.5–1.2; $p < 0.01$). By 8 weeks, the TNSS further decreased to 5.5 ± 1.0 in the probiotic group versus 7.1 ± 1.1 in the placebo group, yielding a between-group difference of 1.6 (95% CI: 1.2–2.0; $p < 0.001$). At the end of the 12-week study, the TNSS in the probiotic group was 4.3 ± 1.1 compared to 6.7 ± 1.0 in the placebo group, with a between-group difference of 2.4 (95% CI: 1.9–2.9; $p < 0.001$).

Table 4: Change in TNSS Over Time

Time Point	Probiotic Group (Mean ± SD)	Placebo Group (Mean ± SD)	Between-Group Difference (95% CI)	p-value
Baseline	8.1 ± 1.2	8.0 ± 1.3	-	-
4 Weeks	6.7 ± 1.1	7.5 ± 1.2	0.8 (0.5–1.2)	< 0.01

8 Weeks	5.5 ± 1.0	7.1 ± 1.1	1.6 (1.2–2.0)	< 0.001
12 Weeks	4.3 ± 1.1	6.7 ± 1.0	2.4 (1.9–2.9)	< 0.001

Serum IgE levels decreased substantially in the probiotic group, from 250 ± 50 IU/mL at baseline to 190 ± 40 IU/mL at 12 weeks, while the placebo group showed a smaller reduction from 245 ± 55 IU/mL to 230 ± 45 IU/mL. The between-group difference was 40 IU/mL (95% CI: 25–55; $p < 0.001$), indicating a notable effect of probiotics on reducing allergic inflammation. Similarly, eosinophil counts dropped significantly in the probiotic group, from 5.8 ± 1.0% at baseline to 3.6 ± 0.9% at 12 weeks, compared to a reduction from 5.7 ± 1.1% to 5.0 ± 1.0% in the placebo group. The between-group difference was 1.4% (95% CI: 1.0–1.8; $p < 0.001$).

Table 5: Change in Biomarkers Over Time

Biomarker	Time Point	Probiotic Group (Mean ± SD)	Placebo Group (Mean ± SD)	Between-Group Difference (95% CI)	p-value
Serum IgE (IU/mL)	Baseline → 12 Weeks	250 ± 50 → 190 ± 40	245 ± 55 → 230 ± 45	40 (25–55)	< 0.001
Eosinophil Count (%)	Baseline → 12 Weeks	5.8 ± 1.0 → 3.6 ± 0.9	5.7 ± 1.1 → 5.0 ± 1.0	1.4 (1.0–1.8)	< 0.001

Discussion

The findings of this study provide compelling evidence for the beneficial role of multi-strain probiotics in the management of allergic rhinitis (AR). By addressing both symptomatic relief and underlying immunological mechanisms, this approach represents a significant advancement in the adjunctive treatment of AR. The discussion focuses on interpreting the results, potential mechanisms, implications for clinical practice, and limitations of the study. The probiotic group demonstrated a substantial reduction in Total Nasal Symptom Score (TNSS) over the 12-week study period compared to the placebo group. This improvement was accompanied by enhanced quality of life, as indicated by the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) scores [12]. Furthermore, the significant reductions in serum IgE levels and eosinophil counts highlight the immunomodulatory effects of multi-strain probiotics. The observed reduction in TNSS aligns with the growing body of evidence suggesting that probiotics can mitigate allergic symptoms by modulating immune responses. The decrease in IgE levels reflects a shift in the immune profile, potentially mediated by regulatory T cells (Tregs) and a rebalancing of the Th1/Th2 cytokine axis. Similarly, the reduction in eosinophil counts underscores the anti-inflammatory effects of probiotics, which may suppress eosinophilic activity in the nasal mucosa, a hallmark of AR [13,14]. These findings have important implications for clinical practice. Unlike traditional pharmacological treatments, which primarily aim to alleviate symptoms, probiotics offer a dual benefit by addressing the root causes of immune dysregulation and improving overall immune health [15]. The favorable safety profile and ease of administration further enhance their suitability for long-term use. Multi-strain formulations, as used in this study, appear particularly promising due to their ability to target diverse pathways and produce synergistic effects. Probiotics could therefore serve as an effective adjunct to conventional therapies such as antihistamines and corticosteroids, potentially reducing the need for these medications over time [16]. Despite these promising results, several limitations of the study must be acknowledged. The 12-week duration of the trial, while sufficient to observe short-term benefits, may not fully capture the long-term efficacy and sustainability of probiotic therapy. The study population was relatively homogeneous, limiting the generalizability of the findings to more diverse groups, including those with comorbidities or varying ages [17,18]. Additionally, individual variations in baseline gut microbiota composition may have influenced the response to probiotics, underscoring the need for future research to explore personalized probiotic interventions. Mechanistic insights were primarily inferred rather than directly measured, and future studies should incorporate advanced tools such as cytokine profiling and microbiome analysis to provide a deeper understanding of how

probiotics exert their effects. Future research should focus on optimizing probiotic formulations by identifying the most effective strains and dosages and evaluating their long-term benefits in larger, more diverse populations.

Conclusion

It is concluded that multi-strain probiotics are an effective and safe adjunctive therapy for allergic rhinitis, offering significant improvements in symptoms, quality of life, and underlying immunological markers. By modulating the immune response and restoring gut microbiota balance, probiotics address both symptomatic relief and the root causes of AR. These findings support their integration into comprehensive AR management strategies.

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