



CASE REPORT

Effect of probiotic administration in adult atopic dermatitis patients: an evidence-based case report

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Abstract

Introduction: Atopic dermatitis (AD) is a chronic skin disease characterized by abnormal skin barrier function and heightened immunologic sensitization. Its incidence has surged recently, with approximately 60% of cases diagnosed within the first year of life. AD can persist or recur, significantly deteriorating the quality of life due to persistent itching and sleep disturbances. Individuals with AD are at increased risk of developing other atopic disorders like asthma and allergic rhinitis. Various dietary approaches, including low carbohydrate, calorie, and fat diets, have been associated with enhanced quality of life by regulating immune responses. Probiotics have been used as adjuvant therapy in allergic conditions, though their effectiveness varies due to the complex nature of allergies.

Method: A literature search was conducted using PubMed, Cochrane Library, and Google Scholar. MeSH terms, advanced search strategies, and predefined eligibility criteria were employed to identify relevant studies. Duplicate studies were excluded, and critical assessment tools and levels of evidence were defined per Oxford Center for Evidence-based Medicine standards.

Results: One systematic review and meta-analysis of randomized controlled trials (RCTs) met the PICO and eligibility criteria. The meta-analysis demonstrated that probiotics significantly decreased AD severity in adults, enhancing their overall quality of life. Other meta-analyses and systematic reviews supported that probiotics reduce clinical severity and improve life quality in adult AD patients.

Conclusion: Probiotic supplementation is a viable option to improve the quality of life for adult AD patients, offering potential therapeutic benefits in managing this condition.

Keywords: probiotic, allergy, atopic dermatitis

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Case scenario

Ms. TU, 23 years old, has been suffering from AD for the past 3 years. When symptoms arise, the patient often takes cetirizine 1x10 mg. The patient came for treatment due to unbearable itching. In addition to therapy and also allergen and stressor avoidance education by an Ear, Nose, and Throat specialist (ENT), the patient was referred to a

clinical nutrition specialist for nutrition education suitable for the patient's condition. The specialist was also consulted regarding whether probiotic supplementation could help improve the quality of life for the AD patient.

Introduction

Atopic Dermatitis (AD) is a chronic, recurrent inflammatory skin condition that not only disrupts the skin's barrier function but also involves immune dysregulation among other mechanisms.¹ In recent years, the prevalence of AD has increased significantly, with estimates suggesting that 3-10% of adults are affected, which is a notable increase compared to earlier statistics.² Approximately 60% of AD cases start in the first year of life, and while many children experience mild symptoms, the disease can persist into adulthood or recur, impacting life significantly.³ The quality of life for individuals with AD can be severely compromised. The disease often coexists with other atopic disorders such as asthma, allergic rhinitis, and chronic sinusitis, further complicating patients' health scenarios.⁴ The persistent itching and visible rash associated with AD can lead to sleep disturbances, anxiety, social withdrawal, and even asthma, underscoring the profound psychosocial impact of this condition.⁵

Atopic dermatitis can significantly impact the decrease in the quality of life for patients and their families. AD patients have an increased risk of experiencing other atopic disorders, such as asthma, allergic rhinitis, and chronic sinusitis.^{5,6} Similar to other atopic disorders, the dominance of Th2 cells over Th1 cells leads to an imbalance that exacerbates the pathogenesis of AD, increases IgE, and activates interleukin (IL).⁶⁻⁸

Probiotics are living microorganisms administered in sufficient quantities to provide health benefits to the host. Several mechanisms regarding how probiotics reduce atopy have been outlined, including shifting the Th1/Th2 balance towards Th1, inhibiting Th2 cytokines, or increasing the production of regulatory cytokines such as IL-10 through dendritic cell maturation or its receptors.^{9,10}

A systematic review conducted by Lopez et al.,¹

indicates that probiotics have beneficial effects on pediatric patients with AD. Oral probiotics, particularly strains of the *Lactobacillus* genus, help reduce the severity of AD.¹ A clinical trial administering a combination of oral probiotic strains to young patients with moderate AD demonstrates that this oral probiotic administration effectively reduces the SCORAD index and decreases the use of topical steroids in patients with moderate AD.⁹

Clinical Question

P : Adult patients with AD
I : Probiotic supplementation
C : Placebo
O : Quality of life

Clinical question: can probiotic supplementation improve the quality of life in adult patients with AD?

Methods

Literature search was conducted through advanced searching using a combination of MeSH terms and Title/Abstract in the PubMed, and Cochrane Library databases, and advanced search in Google Scholar. The search was performed on June 26, 2023. The keywords used were atopic dermatitis, probiotic, and quality of life. Critical appraisal tools and determination of the level of evidence were created based on the Oxford Centre for Evidence-Based Medicine.

Eligibility Criteria

Inclusion Criteria including subjects aged over 18 years with a diagnosis of AD, receiving probiotic therapy, and has presence of quality of life outcomes, study design was randomized clinical trial (RCT), systematic review, or meta-analysis design, published between year 2019 to 2023 and was written articles are in English. Exclusion criteria studies involving experimental animal subjects, and articles not available in full text.

Results

The author found 7 articles in Pubmed, 12 articles in Cochrane and 2 articles in Google Scholar. Duplicate removal was performed using Zotero. The articles were assessed for eligibility criteria based on PICO, resulting in the selection of four articles as shown in **Figure 1**. One Systematic review and meta-analyses RCT and one Meta-analyses RCT that met the eligibility criteria. The study characteristics of these articles were listed in **Table 2**. The level of evidence for these articles is presented in Table 3, and all the articles were found to be relevant for answering the clinical question (**Table 4**).

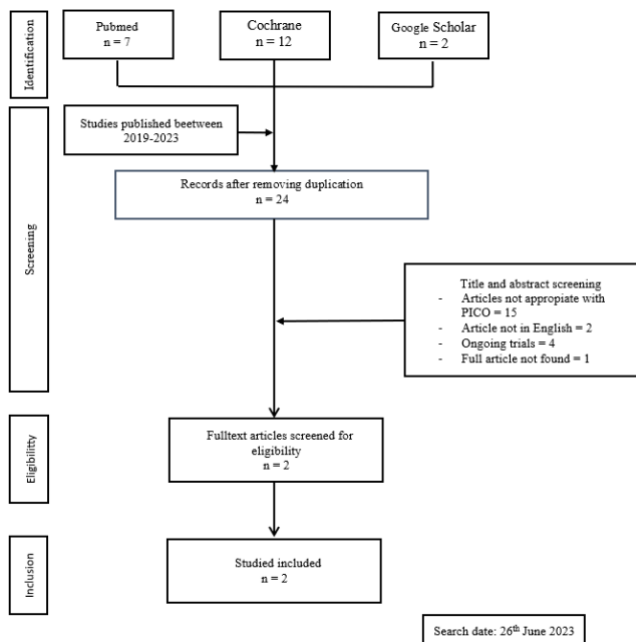


Figure 1. Prisma's flow chart

The literature search was conducted on June 26th, 2023, spanning three databases: PubMed, Cochrane, and Google Scholar. Initially, PubMed yielded 7 studies, Cochrane 12, and Google Scholar 2. After ensuring only studies published between 2019-2023 were considered, all found records were compiled and duplicates removed, resulting in a total of 24 unique records. These 24 records underwent a screening process based on the title and abstract, assessing their relevance to the predefined inclusion criteria (PICO). During this phase, 15 articles were excluded for not aligning

with the PICO criteria, 2 for not being in English, 4 due to being ongoing trials, and 1 because the full article was unavailable. Subsequently, the remaining 2 articles were fully reviewed for eligibility. Both passed the eligibility criteria and were included in the final analysis of the study.

Table 1. Resources and Search Strategy

Database	Terminology	Hits	Eligible
PubMed	((probiotic[Title/Abstract]) AND (atopic dermatitis[Title/Abstract])) AND (quality of life[Title/Abstract]) Filters: Meta-Analysis, Randomized Controlled Trial, Systematic Review	7	2
Cochrane	#1 - (probiotic):ti,ab,kw AND (atopic dermatitis):ti,ab,kw AND (quality of life):ti,ab,kw" with Publication Year from 2019 to 2023, in Trials (Word variations have been searched)	12	0
Google Scholar	allintitle: atopic dermatitis probiotic quality of life	2	0

Table 1 presents the search strategy and outcomes of a systematic literature review focused on the effects of probiotics on quality of life for individuals with atopic dermatitis, utilizing three databases: PubMed, Cochrane, and Google Scholar, with searches conducted from 2019 to 2023. The search terms were specifically designed for each database to capture studies relevant to the predefined criteria. PubMed's search resulted in 7 hits with 2 studies meeting the eligibility criteria, utilizing terms within titles and abstracts along with filters for meta-analysis, randomized controlled trials, and systematic reviews. Cochrane identified 12 studies, but none were eligible, likely due to mismatches in study focus or quality despite using detailed indexing terms. Google Scholar, using a simpler title-focused search, also found 2 articles, but none qualified, pointing to the database's broader and less specialized content scope. The varying outcomes across databases underscore the need for precise and tailored search strategies to effectively identify relevant high-quality studies in systematic reviews.

Table 2 provides a detailed summary of two studies evaluating the effects of probiotics on atopic dermatitis (AD) and quality of life in adult populations. In the first study, Li et al.,²² conducted

a systematic review and meta-analysis involving 402 participants across 9 studies, demonstrating both short-term and long-term reductions in AD

Table 2. Study characteristic

No	Author	Study design	Population characteristics	Number of subjects	Outcomes	Results
1	Li <i>et al.</i> (2022) ²²	Systematic review and meta-analyses RCT	Adult participants with recorded criteria for the diagnosis of atopic dermatitis (AD) and relevant information regarding probiotic administration.	402 (9 studies)	The level of clinical severity and quality of life	The reduction in the severity of AD in the probiotic supplementation group compared to the control occurred in the short term (SMD: 0.63; 95% CI: 0.02-1.25) and long term (SMD: 1.57; 95% CI: 0.66-2.49). There was a significant long-term improvement in quality of life after probiotic supplementation compared to the control (SMD: 0.74; 95% CI: 0.39-1.09). A combination of <i>L. salivarius</i> (LS01) and <i>Bifidobacterium</i> (BR03) was identified as the best supplementation with the highest probability.
2	Umborowati <i>et al.</i> (2022) ²⁰	Meta-analyses RCT	Adult participants of any gender diagnosed with atopic dermatitis or eczema by a doctor.	241 (6 studies)	SCORAD and quality of life	Probiotics have been proven effective in managing AD in adult patients, as evidenced by a reduction in SCORAD (Mean Difference -7.90; 95% CI -7.25 to -6.92; p<0.00001; I2=96%) and an improvement in quality of life (Mean Difference -7.68; 95% CI -14.08 to -1.29; p=0.02; I2=47%), which is statistically significant.

CI, confidence interval; RCT, randomized controlled trial; SCORAD, scoring atopic dermatitis; AD, atopic dermatitis; SMD, standard mean difference; MD, mean difference

severity through probiotic supplementation, with significant long-term improvements in quality of life. Notably, a specific combination of *L. salivarius* (LS01) and *Bifidobacterium* (BR03) was identified as the most effective. The second study by Umborowati et al.,²⁰ included a meta-analysis of 6 studies with 241 participants, showing statistically significant improvements in AD symptoms and quality of life, as evidenced by reductions in SCORAD (scoring atopic

dermatitis) and enhancements in life quality scores. Both studies underscore the therapeutic potential of probiotics in managing AD symptoms and improving the quality of life among adults.

Table 3 evaluates the validity criteria for two systematic reviews and meta-analyses conducted by Li et al.,²² and Umborowati et al.,²⁰ both of which assess the impact of probiotics on atopic dermatitis. Each study was thoroughly analyzed for multiple aspects of research design and

methodology, including study design, number of patients, randomization, comparability in treatment and control groups, blinding, domain-specific considerations, determinant factors, and outcome measurements. Both studies scored

positively across all criteria, indicating robust design and execution. The quality of evidence for each was rated as moderate, and they both achieved a level of evidence classified as 1A

Table 3. Validity criteria

	Study design	Number of patients	Randomization	Similarity treatment and control	Blinding comparable treatment	Domain	Determinant	Measurement of outcomes	Quality of evidence	Level of evidence
Li <i>et al.</i> (2022) ²⁵	+	+	+	+	+	+	+	+	Moderate	1A
Umborowati <i>et al.</i> (2022) ²⁰	+	+	+	+	+	+	+	+	Moderate	1A

* Quality of evidence according to GRADE guidelines, <https://www.ncbi.nlm.nih.gov/pubmed/21208779>

**Level of evidence according to Oxford Center of Evidence-based Medicine (CEBM), <http://www.cebm.net>.

+ clearly mentioned in the article; - not done; ? Not stated clearly

- Systematic review and meta-analysis with troublesome heterogeneity

according to the Oxford Center of Evidence-based Medicine guidelines, suggesting a high standard of reliability in their findings.

Table 4 outlines the relevance criteria assessed for two systematic review studies: Li *et al.*,²² and Umborowati *et al.*,²⁰ Both articles were evaluated on several dimensions to determine

their relevance to the field of study. These dimensions include similarity in population studied, determinants/interventions/indicators used, outcomes measured, and overall importance to the research question. Each study scored positively across all assessed criteria, indicating a high level of relevance.

Table 4. Relevance criteria

Article	Similarity Population	Similarity determinant/intervention/indicators	Similarity outcome	Importance
Li <i>et al.</i> (2022) ²²	+	+	+	+
Umborowati <i>et al.</i> (2022) ²⁰	+	+	+	+

Discussion

Atopic dermatitis can significantly impact the quality of life of affected individuals. The

chronic and relapsing nature of AD has a profound effect on the quality of life of patients and their families. A study involving adolescents with mild-to-moderate AD showed that they had

a lower quality of life, as measured by the Children's Dermatology Life Quality Index.¹² Similar to other atopic disorders, the dominance of Th2 cells over Th1 cells leads to an imbalance that exacerbates the pathogenesis of AD, increases IgE, and activates interleukin (IL).⁷⁻⁹

The prevalence of this disease has increased 2 to 3 times in recent years, with adult AD ranging from 3-10%, while in children, the prevalence of AD can reach 20%.^{3,4} About 60% of AD cases manifest in the first year of life. The onset of AD often occurs at the age of 3 to 6 months. The course of this disease can be continuous over a long period or recurrent.^{1,2} The main complaints of AD patients may include recurring itching, dry skin, and redness. Several therapeutic approaches for AD have been implemented to support skin hydration, such as the use of emollients, allergen avoidance, and the use of antihistamines or corticosteroids during exacerbation phases. Despite these therapeutic approaches alleviating symptoms, their frequent use is often not sufficiently effective, and the recurrence rate remains high.¹³

Several dietary approaches, such as low carbohydrate, low calorie, low fat, and combinations, were related to improved quality of life. Dietary approaches may impact the patient's social interactions, personal satisfaction, economics, physical and psychological. Diet acts as a crucial supplier of nutrients that can affect the cellular microenvironment. Metabolic reprogramming, a significant characteristic linked with disease advancement, can influence both cell metabolism and immune system functionality. Various dietary approaches, such as caloric restriction (CR), fasting-mimicking diets (FMD), and ketogenic diets (KD), have the potential to alter the progression and responsiveness to the treatment of different diseases, including AD. Furthermore, these dietary approaches can modify the composition and functional abilities of the gut microbiome, thus indirectly affecting disease progression and treatment outcomes. These direct and indirect impacts of dietary approaches may affect metabolic changes, regulate immune responses,

and potentially improve the effectiveness of treatments for a range of diseases.^{14,15}

Numerous studies have provided information on the use of probiotics in AD, but the reported results are not consistent, especially in the adult population.¹⁶ Probiotics have been widely used as adjuvant therapy in allergic cases with results that are still inconsistent due to the multifactorial mechanisms of allergy.¹⁷ Probiotics are living microorganisms administered in sufficient quantities to provide health benefits to the host. Several mechanisms regarding how probiotics reduce atopy have been outlined, including shifting the Th1/Th2 balance towards Th1, inhibiting Th2 cytokines, or increasing the production of regulatory cytokines, such as IL-10, through dendritic cell maturation or its receptors.^{9,10}

A systematic review conducted by Lopez *et al.*,¹ indicates that probiotics have beneficial effects on pediatric patients with AD. Oral probiotics, particularly strains of the *Lactobacillus* genus, help reduce the severity of AD.¹ A clinical trial administering a combination of oral probiotic strains to young patients with moderate AD demonstrates that this oral probiotic administration effectively reduces the SCORAD index and decreases the use of topical steroids in patients with moderate AD.⁹

In a comprehensive meta-analysis involving six randomized controlled trials with a total of 241 adult patients suffering from atopic dermatitis (AD), the administration of various probiotic strains demonstrated significant therapeutic benefits. The studies evaluated the effects of different probiotics, including *Lactobacillus plantarum* (2×10^{10} CFU/day for 8 weeks), *Lactobacillus salivarius* (1×10^9 CFU/g twice daily for 16 weeks), a combination of *Lactobacillus salivarius* (LS01 DSM 2275) and *Bifidobacterium breve* (BR03 DSM 11,604) (each with a dose of 1×10^9 CFU/g twice daily for 12 weeks), *Lactobacillus acidophilus* (L-92) (20.7 mg/day in tablet form for 8 weeks), *Lactobacillus paracasei* (K71) (5×100 mg daily for 12 weeks), and *Bifidobacterium animalis subsp. lactis* (LKM 512) (6×10^9 CFU daily for 8 weeks). These probiotics were administered

over periods ranging from 8 to 16 weeks. The primary outcomes measured included the Scoring Atopic Dermatitis (SCORAD) index, quality of life (QoL) assessments, itch severity, skin lesion area, immunological markers such as IgE and various interleukins, and safety assessments. The meta-analysis revealed that probiotics significantly reduced the SCORAD index with a mean difference (MD) of -7.90 (95% CI -7.25 to -6.92; $p < 0.00001$; $I^2 = 96\%$) and improved the quality of life of the patients with a MD of -7.68 (95% CI -14.08 to -1.29; $p = 0.02$; $I^2 = 47\%$). These results indicate that probiotics can effectively decrease the clinical severity of AD and enhance the overall well-being of affected individuals. However, the analysis did not show significant changes in other parameters like serum IgE levels, interleukin-4 (IL-4), and tumor necrosis factor-alpha (TNF- α), suggesting that the impact of probiotics may be more pronounced on clinical symptoms rather than on underlying immunological markers. The clinical improvement in AD is determined by assessing changes in the severity of the disease. The SCORAD assessment index is used to evaluate the severity of AD by combining the extent, severity (intensity) of skin lesions (erythema, edema/papules, crusts, excoriation, lichenification, dryness), and symptomatic patient symptoms (itching, sleep disturbance) in the calculation. The higher the score, the more severe the disease experienced by the patient.¹⁸

Atopic dermatitis patient's quality of life assessment is performed using the Dermatology Life Quality Index (DLQI). The decrease in quality of life in AD patients is related to a decrease in sleep quality and depressive symptoms due to chronic itching, potentially affecting AD therapy. Chronic sleep quality reduction in AD patients contributes to the emergence of emotional and physical fatigue conditions that negatively impact social relationships and social sensitivity. Sleep quality is also inversely related to the severity of the disease in AD patients. The DLQI questionnaire consists of 10 questions with ratings ranging from 0, 1, 2, and 3. Improvement in quality of

life is indicated by a high score, where scores 0-10 are categorized as low DLQI, while scores 11-30 are classified as high DLQI.^{18,19} This questionnaire assesses six aspects: symptoms and feelings, daily activities, leisure time, work and school, personal relationships, and therapy for 7 days. Q1 evaluates itching, Q2 assesses embarrassment, Q3 assesses problems in shopping/house/garden, Q4 assesses clothing choices, Q5 evaluates social activities, Q6 assesses sports activities, Q7 discusses work/learning limitations, Q8 focuses on relationships with partners/close friends/colleagues, Q9 is related to sexual difficulties, and Q10 assesses problems arising from therapy.¹⁹

Prakoeswa et al.,²¹ used the probiotic *Lactobacillus plantarum* IS-10506, isolated from traditional fermented buffalo milk curd in Indonesia, for administration to adults with AD. The study reported a significant increase in Foxp3 and IL-10. *Lactobacillus sp.* serves as an important adjuvant therapy for AD and plays a role in preventing AD recurrence by modulating the Th1 and Th2 cytokine profiles. Probiotics can reduce clinical symptoms by suppressing the Th2 adaptive immune response without enhancing the Th1 adaptive immune response.^{20,21}

Conclusion

The systematic review and meta-analysis offer compelling evidence that probiotic supplementation can significantly enhance the quality of life (QoL) for adult patients with atopic dermatitis (AD). The critical review indicates that probiotics, such as *Lactobacillus plantarum*, *Lactobacillus salivarius*, *Bifidobacterium breve*, *Lactobacillus acidophilus*, *Lactobacillus paracasei*, and *Bifidobacterium animalis subsp. lactis*, administered over periods ranging from 8 to 16 weeks, effectively reduce the clinical severity of AD as measured by the SCORAD index. The improvements in QoL were reflected in several dimensions, including a reduction in itching, better sleep quality, and overall improvement in daily functioning and psychological well-being.

Conflict of interest

The authors declare there is no conflict of interest regarding this article.

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