Bali Medical and Wellness Journal
bmw-journal.com

Article

Systematic Review: Effectiveness of Probiotic Giving as Additional Therapy in Atopic Dermatitis Patient

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ABSTRACT

Background: Atopic dermatitis (AD), also known as eczema, is a chronic inflammatory skin condition affecting the epidermis and dermis. It is triggered by a combination of environmental and genetic factors, leading to symptoms such as polymorphic rashes and intense itching.

Objective: This systematic review aims to evaluate the effectiveness of oral probiotic supplementation as an adjunct therapy for individuals with atopic dermatitis.

Methods: The literature was reviewed by searching two electronic databases, Google Scholar and PubMed, resulting in the inclusion of eight studies that collectively involved 347 AD patients.

Results: The findings indicate that probiotic supplementation can significantly reduce the severity and incidence of atopic dermatitis. This effect is attributed to the inhibition of Th2 cell activity and a reduction in pro-inflammatory cytokines, including TNF-α and IgE, which are known contributors to the pathophysiology of AD.

Conclusion: Probiotics present a promising alternative for the prevention and management of atopic dermatitis, potentially enhancing patient outcomes.

Keywords: probiotics, atopic dermatitis, eczema, Th2 cells, inflammation

Citation: Pangkahila, E.M.; Dewi, M.Y.A.; Harimawan,A. I W. Systematic Review: Effectiveness of Probiotic Giving as Additional Therapy in Atopic Dermatitis Patient. Bali Medical and Wellness Journal **2024**, 1 (2), 41-50.

Submitted: October 16, 2024
Revised: October 24, 2024
Accepted: October 30, 2024
Published: November 1, 2024

INTRODUCTION

Atopic dermatitis, commonly referred to as eczema, is a chronic inflammatory condition affecting the epidermis and dermis. It is triggered by both external and internal factors, leading to symptoms such as rashes and itching. This condition typically presents in specific areas of the body, most notably the face in infants and the flexural regions in children (Djuanda A, 2016). The causes of atopic dermatitis are multifaceted, involving genetic factors that lead to skin barrier dysfunction, immunological issues, and environmental influences (Rusu E, 2019). The condition is marked by a dominant Th2 immune response and is often associated with a family or personal history of other allergic conditions. Currently, there is no definitive cure for atopic dermatitis, and ineffective treatment can significantly impact the quality of life for both patients and their families. Recent studies have highlighted the potential benefits of probiotics, particularly mixed bacterial strains, in the treatment and prevention of atopic dermatitis (Rusu E, 2019; Huang R, 2017). With an estimated 230 million cases worldwide, atopic dermatitis is considered one of the most common chronic diseases, affecting 15% to 30% of children and 5% to 10% of adults

(Torres T, 2019; Saini S, 2019; Christopher PM, 2020; Tsai TF, 2019; Mayba JN, 2017).

Probiotics are live microorganisms that can positively affect health when consumed in adequate amounts. They help protect the intestinal lining and epithelium, preventing harmful pathogen invasion. Common probiotics include species from the Lactobacillus (e.g., L. acidophilus, L. reuteri), Bifidobacterium (e.g., B. longum, B. bifidum), and Streptococcus (e.g., S. thermophilus) genera (Rusu E, 2019). When taken in sufficient quantities, probiotics can benefit not only the gastrointestinal system but also the brain and skin. Several studies have indicated that oral probiotics can help prevent, reduce risks, and alleviate symptoms of atopic dermatitis (Huang R, 2017).

Long-term use of corticosteroids to manage atopic dermatitis is discouraged due to potential side effects, which may include skin problems, electrolyte imbalances, neuropsychological issues, and congenital malformations (Fishbein AB, 2020; Buchman AL, 2020). In a randomized, double-blind, placebo-controlled trial involving 50 children aged 4 to 17, those who received mixed probiotics (including Bifidobacterium lactis and Lactobacillus casei) showed a greater reduction in the SCORAD index than the control group, along with a decreased reliance on topical corticosteroids (Rusu E, 2019).

Probiotics may work through two main immunological mechanisms. First, they may enhance the growth and activity of beneficial lactic acid bacteria like bifidobacteria and lactobacilli, leading to increased intestinal IgA production, reduced inflammatory cytokines from Th2 cells, and increased regulatory cytokines such as IL-12, IFN-γ, and IL-10. Second, the fermentation of prebiotics by lactic acid bacteria can produce short-chain fatty acids (SCFAs) like acetate, propionate, and butyrate, which promote the production of IFN-γ and IL-10 (Van der Aa L, 2010). Increasing the levels of Lactobacillus in the intestines through oral probiotic supplementation could thus provide a new strategy for preventing and managing atopic dermatitis (Laura C, 2022; Dinicola C, 2013). This literature review aims to assess the effects of probiotics on atopic dermatitis, including the appropriate dosage, frequency, and duration of supplementation. Additionally, it will evaluate the outcomes of probiotic use in reducing symptom severity and enhancing the quality of life for individuals with atopic dermatitis.

METHODS

This systematic review was completed in 2024, with results reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The review focused on randomized controlled trial (RCT) designs to evaluate the effectiveness of probiotics as an additional therapy for atopic dermatitis.

Information Sources and Search Strategies

This literature review employed a systematic review approach focused on randomized controlled trial (RCT) designs. A comprehensive literature search was conducted according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The search was performed in two electronic

databases: Google Scholar and PubMed. Keywords used in the search included "probiotics" and "atopic dermatitis."

Eligibility Criteria

Inclusion criteria for this review encompassed journal articles published between 2014 and 2024, written in either English or Indonesian. Eligible studies were required to be observational primary literature or RCTs that specifically examined the use of probiotics as additional therapy for atopic dermatitis. Exclusion criteria were as follows: articles that did not align with the research topic, studies lacking available full texts, and publications not in English or Indonesian.

Critical Appraisal of Risk of Bias

To assess the quality of the included studies, a critical appraisal focusing on the risk of bias was performed. Each article was evaluated for methodological rigor, including randomization, blinding, and control measures, ensuring a reliable assessment of the efficacy of probiotics in managing atopic dermatitis.

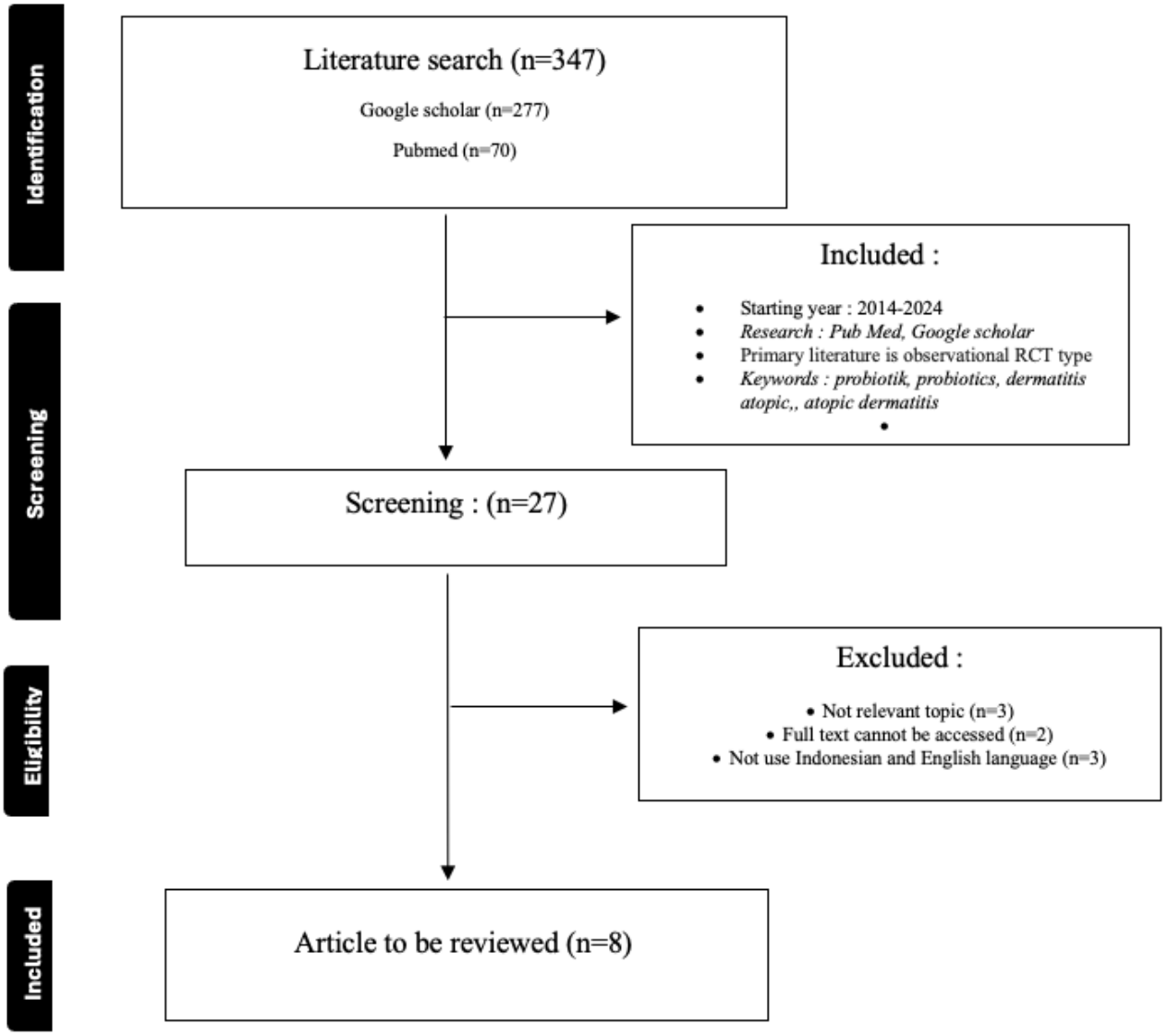

Figure 1. PRISMA flowchart

Data Extraction

Data was systematically extracted from the selected articles, focusing on relevant outcomes, study characteristics, sample sizes, and methodologies. This information included the effectiveness of probiotic intervention, types of probiotics used, and the severity of atopic dermatitis measured through standardized scales.

Synthesis Methods

The synthesis of the reviewed studies was conducted through a qualitative analysis that summarized the findings of each article. Trends and patterns in the effectiveness of probiotics as an additional therapy for atopic dermatitis were identified and discussed, providing a comprehensive overview of current research in this field. Ultimately, eight articles were selected based on the defined criteria to evaluate the effectiveness of probiotics in patients with atopic dermatitis.

RESULTS

The results of the identification process from the search conducted on Google Scholar and PubMed revealed 27 articles that matched the search criteria, containing one or more of the specified keywords in their titles. From these, 8 articles were selected for review after excluding those with inappropriate titles. The details of each reviewed article are presented in Table 1.

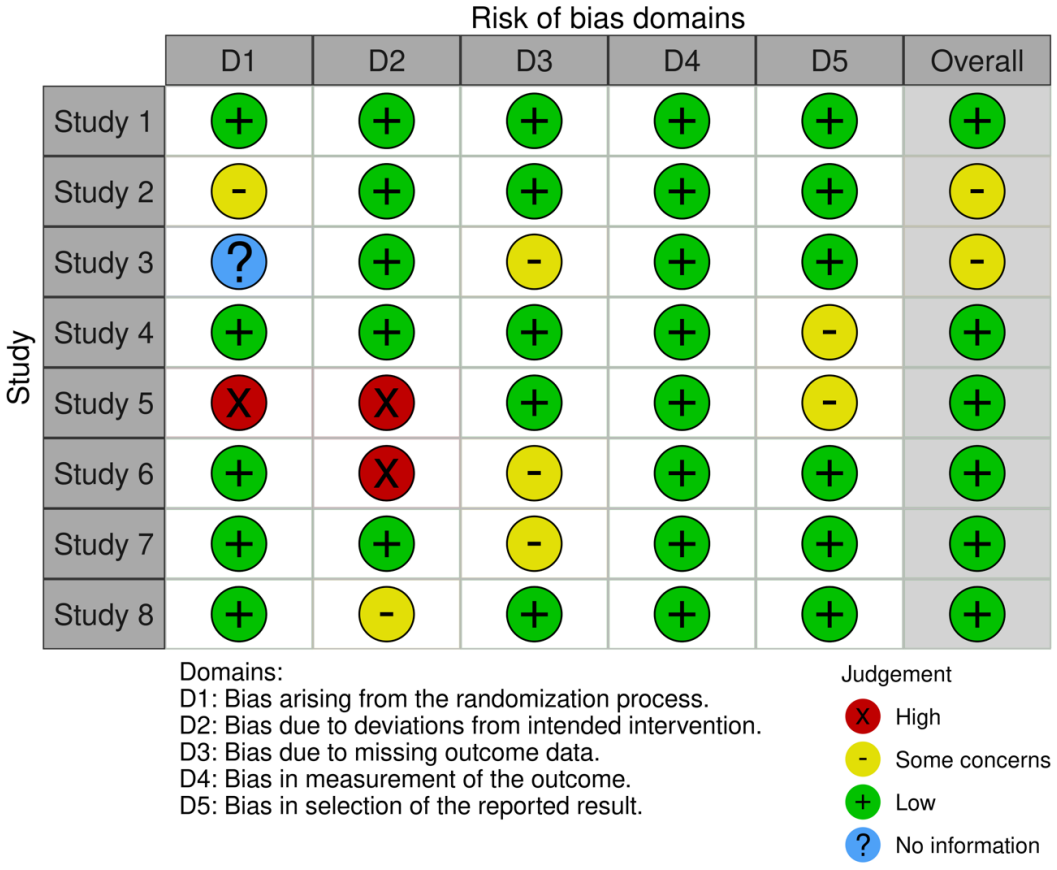

Figure 2. Risk of Bias assessment

Table 1. Overview of included studies

Author(s); Year; Country	Methods and Samples	Intervention	Results
Bonita Laissa et al; 2019; Indonesia	RCT DB, 30 patients AD patients aged >14 years, total serum IgE levels >100 IU/L	Lactobacillus plantarum IS-10506 therapy used in this study was given in the form of powder at a dose of 2x 1,120 grams ($2x10^{10}$ CFU) for 8 weeks.	- The decrease in SCORAD was significantly greater in the probiotic group (p=0.006) - The large difference in changes in total IgE levels: - IgE Pre: (p=0.340) - Post IgE: (p=0.350)
Ardentry et al; 2017; Indonesia	RCT DB, 48 AD patients aged 9-15 years	Treatment was given for 2 weeks using 3x1 sachet dose of probiotics and placebo.	Decreased total IgE levels in the Probiotic group (p=0.010) Probiotics: -89.76 + 357.66 Placebo: 91.53 + 474.75
Cukrowska Bozena et al; 2021; Polandia	RCT DB, 151 patients aged <2 years	A mixture of 3 probiotics: 50% of *Lactobacillus casei* ŁOCK 0919 25% of *Lactobacillus rhamnosus* ŁOCK 0908 25% of *Lactobacillus rhamnosus* ŁOCK 0900 ($1x10^{9}$) selama 3 bulan	A significantly greater decrease in SCORAD occurred in the probiotic group (p 0.034) • Probiotics: 522,713 ± 832,648 • Placebo: 260,793 ± 206,098
Wu et al; 2017; Taiwan	RCT DB, 66 patients 4-48 months AD	L. rhamnosus (MP108) 350 mg once a day for 8 weeks	The SCORAD index decreased significantly in both groups, with an average decrease of: • Probiotics: -23.20 ± 15.24 • Placebo: -12.35 ± 12.82 Significant change between groups (p=0.002) The IDQOL value decreased but there was no significant difference between groups (p 0.65) with an average decrease: •Probiotics: -3.58 • Placebo: -3.38

Author(s); Year; Country	Methods and Samples	Intervention	Results
Jeong et al; 2020; Korea Selatan	RCT DB, 66 patients AD	L. rhamnosus IDCC 3201 tyndallizate (RHT3201) 1.0 x 10^{10} CFU/d once daily for 12 weeks	A significantly greater decrease in SCORAD occurred in the probiotic group (p 0.0283) • Probiotics: -13.89 ± 10.05 • Placebo: -8.37 ± 9.95
Angela et al; 2021; Italia	RCT DB, 80 mild to moderate AD patients aged 18 and 50 years	Food supplements containing a mixture of probiotics were given as follows: 1 × 10^9 CFU L. plantarum PBS067, 1 × 10^9 CFU L. reuteri PBS072 and 1 × 10^9 CFU L. rhamnosus LRH020, once per day for 56 days	The SCORAD index decreased significantly in the probiotic and placebo groups ($p < 0.001$) • Probiotic mix: 14.6 ± 1.3 • Placebo: 12.8 ± 1.1 A significantly greater decrease in SCORAD occurred in the probiotic group
Laura Carucci et al; 2022; Italy	RCT DB, 100 AD patients aged 6-36 months	Isocolor and isosmell capsules 1 x 10^{10} CFU LGG once daily for 12 weeks	The SCORAD index decreased significantly in the probiotic and placebo groups ($p < 0.001$) • Probiotics: 0.63 ± 0.77 • Placebo: 0.24 ± 0.37 A significantly greater decrease in SCORAD occurred in the probiotic group (p 0.5) The resulting median IDQOL (IQR) values were significantly lower in the Probiotic group compared with Placebo [3(6) vs. 2 (5) $p < .05$].
So Hyung; 2020; Korea Selatan	RCT DB, 41 AD patients aged 2-13 years	L. pentosus (1.0×10^{10} CFU) twice daily for 12 weeks	A significantly greater decrease in SCORAD occurred in the probiotic group (p 0.040) • Probiotics: 30.4 ± 8.6 • Placebo: 34.3 ± 8.3

DISCUSSION

This review examined eight studies that explored the effects of probiotics on atopic dermatitis. Of these studies, only two evaluated changes in the quality of life of patients, with one reporting an improvement in quality of life. Seven studies indicated significant differences between the probiotic group and the placebo group. Additionally, two studies analyzed total IgE levels, while one study noted a decrease in the Infant Dermatology Quality of Life Index (IDQOL) without significant differences. Overall, the systematic review suggests that oral probiotic supplementation positively impacts the SCORAD index and quality of life as measured by the relevant indices, with all studies demonstrating significant reductions in the SCORAD index among patients.

Atopic dermatitis is characterized by symptoms such as itching, which can severely affect a patient's quality of life. Other symptoms include dry skin, redness, papule formation, and lichenification. Scratching can disrupt the epidermal skin barrier, leading to inflammation and the migration of activated antigen-presenting cells to the lymph nodes and naive T cells to T helper 2 (Th2) cells. This process increases the levels of Th2 cytokines, as well as Tumor Necrosis Factor α (TNF-α) and IFN-γ, which further compromise the skin barrier by inducing apoptosis in keratinocytes and impairing tight junction function, making patients more susceptible to infections (Rather IA, 2016).

Research has linked changes in skin microbiota to immune modulation resulting from skin barrier dysfunction. Recently, attention has shifted toward understanding the relationship between gut microbiota and immune modulation in the context of atopic dermatitis (Kim J, 2021). Probiotics can alter the gut microbiota, leading to therapeutic effects through immune modulation by balancing pro- and anti-inflammatory cytokines (Dinicola C, 2013).

In a randomized controlled trial (RCT) by Bonita et al. (2019), the probiotic group exhibited a significant reduction in symptoms compared to the placebo group; however, there was no significant difference in total serum IgE levels between the adult patients in the two groups. This lack of difference in IgE levels may be attributed to the short evaluation period after treatment (Bonita laissa, 2019). Conversely, a study by Ardentery et al. (2017) involving participants aged 9-15 years found differences in total IgE levels, with the probiotic group showing a greater decrease than the placebo group. This decrease in IgE is likely related to an increased IFN-γ:IL-4 ratio, which indicates an enhanced Th1 immune response.

Furthermore, the combination of probiotics acts as a strong activator of the innate immune system due to specific peptidoglycan and lipoteichoic acid molecules in the probiotic cell walls. These molecules interact with toll-like receptors (TLR) 2 and TLR4, resulting in the activation of T cells and a polarization toward Th1 and regulatory T cells (Treg). This stimulation of Th1 cells by cytokines such as IFN-γ suppresses the Th2 immune response by decreasing IL-4 synthesis, corroborated by findings showing higher levels of IFN-γ and lower IL-4 levels in the induced group compared to the control group (Iwasaki A, 2019).

Cukrowska et al. (2021) conducted an RCT involving 151 patients under 2 years old with atopic dermatitis and cow's milk protein allergy. They found that a probiotic combination of Lactobacillus rhamnosus strains was safe and beneficial, particularly for allergic patients. Probiotic supplementation over three months led to significant improvements in AD severity as measured by the SCORAD index (Bozena C, 2021). Additionally, Wu et al. (2017) reported that administering L. rhamnosus (MP108) at a dosage of 350 mg once daily for eight weeks significantly reduced the SCORAD index, although there was no significant difference in IDQOL scores between the probiotic and placebo groups. In contrast, Laura et al. (2022) reported significant

reductions in both SCORAD and IDQOL scores in the probiotic group after a 12-week intervention.

Variability in the indices used to assess quality of life may stem from the multifaceted impacts on patients, including emotional well-being, social functioning, sleep disturbances, productivity, and family relationships. These effects can vary significantly depending on the patient's age. Quality of life measurements include the Dermatology Life Quality Index (DLQI) for adults, the Children's Dermatology Life Quality Index (CDLQI) for children, and the IDQOL for infants (Koszorú K, 2019).

CONCLUSION

Based on the results of this systematic review, oral probiotic supplementation can serve as an effective adjunct therapy for patients with atopic dermatitis. The optimal dosage of probiotics from the Lactobacillus family ranges from 1 x 10^9 to 1 x 10^10 CFU, with regimens of 350 mg once or twice daily for 8 to 16 weeks, a combination of Lactobacillus at 3 x 10^9 CFU once daily for 56 days, or a mix of Lactobacillus and Bifidobacteria at 1 x 10^9 CFU three times a day for 2 weeks. Research indicates that probiotics can significantly reduce the severity and incidence of atopic dermatitis by inhibiting Th2 cells and decreasing pro-inflammatory cytokines such as TNF-α, IgE, and other inflammatory markers associated with the condition. Several factors can influence the effectiveness of probiotics, including environmental factors, host factors, and intrinsic properties of the probiotics themselves. In summary, the integration of probiotics into the treatment plan for atopic dermatitis may enhance patient outcomes and provide a beneficial strategy for managing this chronic condition. Further research is recommended to explore the long-term effects of probiotics and the mechanisms by which they exert their beneficial impacts on atopic dermatitis and overall skin health.

CONFLICT OF INTEREST

The authors declare no competing interests.

FUNDING

There is no funding support.

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