MAGNA MEDIKA
Berkala Ilmiah Kedokteran dan Kesehatan

e-ISSN 2774-2318
p-ISSN 2407-0505

Literature Review
MAGNA MEDIKA
Berkala Ilmiah Kedokteran dan Kesehatan
Journal Page: https://jurnal.unimus.ac.id/index.php/APKKM

The effectiveness of *Lactobacillus plantarum* administration in patients with atopic dermatitis

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Article Info

Article history:

Received 26 March 2021
Revised 15 October 2021
Accepted 15 October 2021
Available online 01 February 2022

Keywords:

Atopic dermatitis, probiotic, *Lactobacillus plantarum*

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How to cite this article:

Ismatu Aghni Fatwa Izzati, Ratih Pramuningtyas, Rochmadina Suci Bestari, Nurhayani. The effectiveness of *Lactobacillus plantarum* administration in patients with atopic dermatitis. MAGNA MEDIKA Berk Ilm Kedokt dan Kesehat. 2022;9(1):43-50

Abstract

Background: Atopic dermatitis is a chronic and residual inflammatory skin disease with increased prevalence every year. The medications that are often given can cause serious side effects if it is given in the long term. The treatment of *Lactobacillus plantarum* is expected to be a safer long-term treatment option for a patient with atopic dermatitis.

Objective: To determine the effective treatment of *Lactobacillus plantarum* in patients with atopic dermatitis

Method: The research design was a Systematic Review with a qualitative approach using meta-synthesis analysis type.

Results: The search was conducted on three databases: PubMed, Science Direct, and Google Scholar. Total articles obtained were 239 with 16 duplicate data. Two hundred eleven articles were included in the exclusion criteria, and five articles were interventions with combination probiotics. So there are seven articles included in the research with clinical trials, open trials, pilot studies, and four research using the randomized controlled trial Double-Blind design. All results showed improvement in symptoms with the SCORAD index or Skindex-16. Several studies also measured IgE, IL-4, IL-10, IL-13, IL-17, the percentage of Th1, Th2, Treg, TGF-β, IFN-γ and obtained different results.

Conclusion: Treatment of Lactobacillus plantarum in patients with atopic dermatitis is effective in reducing symptoms and as an immunomodulator.

e-ISSN 2774-2318
p-ISSN 2407-0505

INTRODUCTION

Atopic Dermatitis (AD) is a chronic, residual inflammatory skin disease that is related to another allergic disease such as bronchial asthma and allergic rhinoconjunctivitis. The complaints can be in the form of unusual itchiness, erythema, edema, vesicles, and acute stage wound; then, the patient will undergo excoriations and lichenifications in the chronic stage[1]. According to the Indonesian Pediatric Dermatology Study Group (KSDAI), the prevalence rate of AD cases is in the first rank of children's skin diseases top 10, which is about 611 cases or 23,67%[2]. There are about 70% - 80% of AD patients with extrinsic type; in this form, there is environmental allergen sensitization accompanied with IgE serum increase[3].

Although AD does not cause death, it causes a variety of problems such as health issues, physical issues, social relationship issues, environmental issues, and psychological issues. Besides, the need for long-term therapies can affect the economic condition of patients and their family[4]. AD therapy is intended to minimize the relapse frequency and reduce the duration and the degree of severity in relapse. Topical corticosteroids can be added to pharmacological therapy. However, for long-term treatments, corticosteroids therapy causes side effects, it leads to systemic effects even further[5]. Patients can use moisturizers for skin barrier function improvement and for decreasing topical steroid usages. Nevertheless, one of the frequently used moisturizers is *Sodium Lauryl Sulfate* (SLS), which is reported as irritant[6]. Another therapy that can be used is probiotic therapy; it has a unique role in AD treatments or preventions[7].

Moreover, probiotics are used to help the host from pathogenic bacteria, and the usage of probiotics for children's diseases is increased[8,9]. The role of probiotics toward atopic dermatitis disease is supported by some researches that showed a variety of results[10]. As in Navarro-Lopez et al. and Wang and Wang, the administration of probiotics is able to decrease the SCORAD index and decrease the topical steroid usage on AD patients[11,12]. While, in Gore et al., there are no significant SCORAD differences in all group[13]. Some lactic acid bacterial species are suitable probiotics; some of those are from *Bifidobacterium* genera, *Lactobacillus genera, Bacillus coagulans,* etc[7]. In addition, one of them is *Lactobacillus plantarum.* The *Lactobacillus plantarum* growth will produce antibacterial substances such as *hydrogen peroxide*, organic acids, and bacteriocin. Many types of research about the effect of *Lactobacillus plantarum* administration in AD patients is experimental research. Therefore, this research wants to do analytical review studies toward the previous studies that have been done with assessing the effectiveness of *Lactobacillus plantarum* administration in AD patients.

METHODS

This research design is a Systematic Review with a qualitative approach using a meta-synthesis type of analysis which aims to answer research questions by summarizing various research results (meta-aggregation). This research has been approved by the Health Research Ethics Committee Faculty of Medicine of Universitas Muhammadiyah Surakarta

e-ISSN 2774-2318
p-ISSN 2407-0505

with No. 3155 / C.1 / KEPK-FKUMS / XI / 2020.

The search was conducted on three databases: PubMed, ScienceDirect, and Google Scholar using the keywords "*Lactobacillus plantarum*" AND "atopic dermatitis" with a limit of 2005-2020 and in Indonesian and English. The process of searching for articles was carried out on Friday, December 4th, 2020, and data synthesis to be used was carried out on Saturday, December 5th, 2020, using the Mendeley application. In the initial search, a total of 239 results were obtained from several databases, namely PubMed (n=31), Science Direct (n=69), Google Scholar (n=139). After the process of deleting duplicated articles, 223 articles were obtained. A total of 211 articles were excluded because they did not meet the criteria and five articles used a combination probiotic supplement as an intervention, so that there are seven articles that, according to the inclusion criteria for data analysis.

RESULTS

There are seven clinical trials listed at table 1 that are required with several research designs, namely *clinical trials, open trials,* and *pilot studies*. Furthermore, there are four types of research that used *randomized controlled trial double-blind* research design, and 3 of them are from Indonesia. There are six types of research that used SCORAD as an AD measuring instrument, and one research used Skindex-16 for assessing patients' life qualities in terms of skin diseases. In addition, there are six types of research that measured the IgE levels, and there is only one research that took measurements with SCORAD. Measurements of IL-4 levels were found in 3 studies, measurement of IFN-γ in 2 studies, measurement of IL-10, IL-13, IL-17, percentage of Th1, Th2, Treg, TGF-β, each in 1 study.

All studies resulted in a significant reduction in symptoms based on the SCORAD index and Skindex-16 in the *Lactobacillus plantarum* group. Some studies show meaningless results toward total IgE levels decrease, but there are symptom improvements in patients with high IgE levels in the experimental group and placebo group.

e-ISSN 2774-2318
p-ISSN 2407-0505

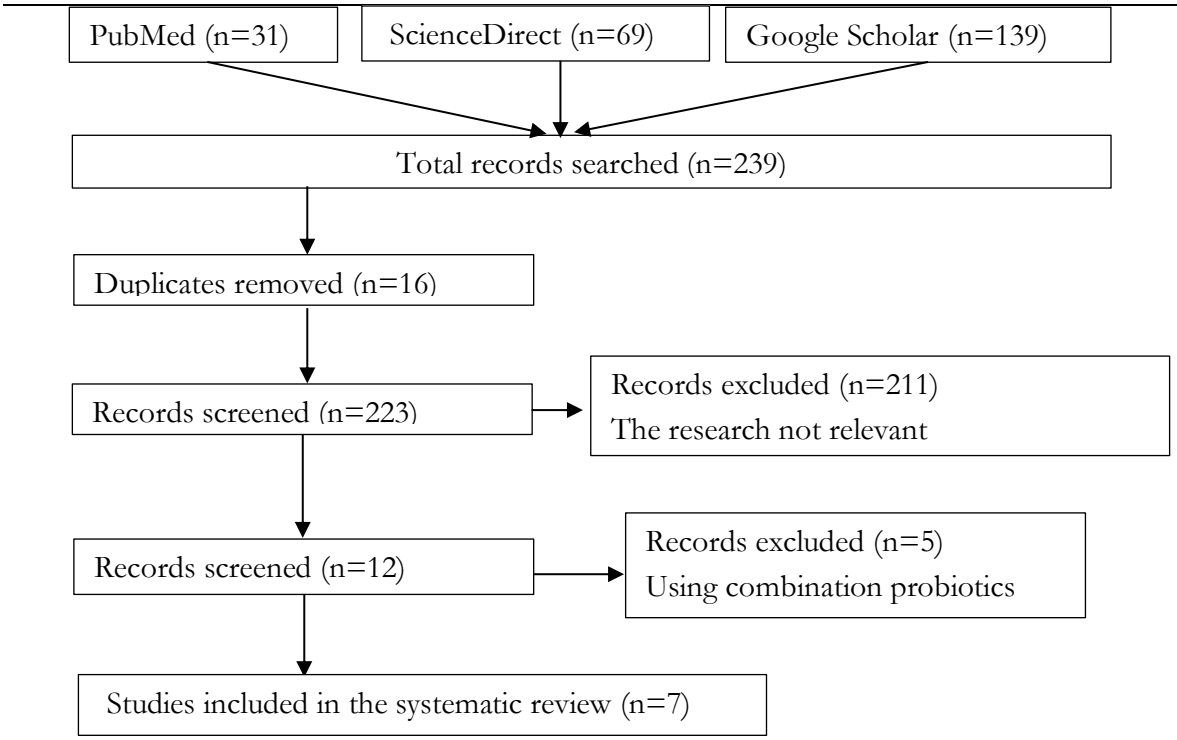

Figure 1. PRISMA flowchart (Source: personal data, 2020)

DISCUSSION

This research is systematic review research with seven types of research results from many countries. Even though all researches are from experimental studies, but there are different methods used for identifying the effects, measurements results, criteria of samples, types, doses, and the duration of *Lactobacillus plantarum* administration. The researches subjects in some of these trials were more women than men. It is in line with the previous research that AD frequently occurs in women than men with the ratio of 1,3:1. It states that the ratio of AD patients for women and men is 2,6:1. The differences in every country are caused by the differences in environmental interactions, genetics, and immunological factors. Most of the researches subjects are acute exacerbation of chronic AD patients; it is appropriate with research that mentioned that AD is chronic residual, so the patients often relapse[1].

Lactobacillus plantarum growth in the digestive tract will produce organic acids (acetic acid and lactic acid), hydrogen peroxide, and bacteriocin that will give protection effects because they are antibacterial. Their roles in immune status can be modulated by intestinal barrier increase. It can be responsible for decreasing allergic events and the severity of AD[18]. Moreover, there are glycoprotein isolates from *Lactobacillus plantarum* isolation that has anti-inflammatory effects and anti-allergy[19]. *Lactobacillus plantarum* can reduce inflammation with pro-inflammatory cytokines, IL-4, IL-6, TNF α, INF- γ decrease, high sensitivity C reactive protein (hsCRP); and increase IL-10 expression[18]. AD patients are dominated by Th2 cells that secrete IL-4 and increase IgE production. Those play an essential role in skin allergen presentation in the Th2. *Lactobacillus plantarum* can help the gut microbiota stimu-

e-ISSN 2774-2318
p-ISSN 2407-0505

lation with modulating toll-like receptors (TLR) and introducing proteoglycan protein in enterocytes; it can activate dendritic cells and Th1 response and will suppress the Th2[11]. It can increase Th1 cytokines regulation such as INF- γ, IL-2, and IL-12. Besides, it can suppress the Th2 cell's production, especially cytokine IL-4[20]. Those can produce the balance between the Th1 cells and Th2 cells. Therefore, *Lactobacillus plantarum* administration in AD patients shows symptoms and immunological improvements.

Table 1. The Results of Data Extraction

Author (year)	Study Design	Population	Intervension (Dose/duration)	Result
Karim,A., et al. (2019)[14]	RCT DB	Adult	LP IS-10506 ($2x10^{10}$ cfu/day, 8 week)	They are reducing the SCORAD index in the LP group more significantly.
Bonita, L., et al. (2019)[15]	RCT DB	Adult	LP IS-10506 ($2x10^{10}$ cfu/day, 8 week)	They are reducing the SCORAD index in the LP group more significantly and no significant difference in decreasing IgE level serum.
Prakoeswa, C.R.S., et al. (2017)[16]	RCT DB	Children	LP IS-10506 (10^{10} cfu/day, 12 week)	Reduce clinical symptoms by a decrease in SCORAD index, IL-4, IL-7, and IgE but not significant. Increase Foxp3+ to IL-10 level ratio.
Han, Y., et al. (2012)[17]	RCT DB	Children	LP CJLP133 ($0.5x10^{10}$ cfu, twice daily, 12 weeks)	They are reducing the clinical severity, SCORAD score, total eosinophil count, IFN-γ, and IL4.
Kim, J., et al. (2017)[18]	CT	Children	LP CJLP133 ($1x10^{10}$ cfu/day, 12 week)	Reducing SCORAD index, eosinophilia, high total IgE levels, increased TGF-β mRNA, and a high proportion of $CD4^+CD25^+Foxp3^+$ in Treg cells (associated with good clinical response).
Harima Mizusawa, N., et al. (2016)[19]	2 OT	Adult	LP0132- *fermented juice* ($6x10^{10}$ *cells*/ 100 ml, eight weeks)	Reducing Skindex-16 in both trials, ECP, total IgE, specific IgE (Japanese cedar and cypress pollen) significantly attenuated in Trial 2, with no significant changes in the percentage of Th1, Th2, Th1/Th2, Treg during the trials.
Fang, Z., et al. (2019)[20]	PS	Adult	LP CCFM8610 (10^9 cfu/day, eight weeks)	Decreased SCORAD index, improved DLQI index, upregulation of IL-10 expression, not showed any significant differences in IgE, IL-4, and IL-13.

RCT DB=Randomized Controlled Trial Double-Blind, CT=Clinical Trials, OT=Open Trials, PS=Pilot Study, LP=*Lactobacillus plantarum*, cfu=colony forming unit, SCORAD=SCORing Atopic Dermatitis, IgE=Immunoglobulin E, IL=interleukin, IFN=interferon, TGF=transforming growth factor, DLQI=Dermatology Life Quality Index, ECP=eosinophil cationic protein. *Source: Personal data, 2020*

e-ISSN 2774-2318
p-ISSN 2407-0505

Atopic dermatitis is divided into two types there are intrinsic and extrinsic types. A patient of intrinsic type or non-allergenic AD is marked with normal specific IgE levels and does not have any correlation with respiratory disease. While, in extrinsic type, there is specific IgE serum increase toward environmental allergen or foods. However, both types can be accompanied by eosinophilia. From the obtained results, there is research that encloses eosinophil measurements; Han et al. show a significant decrease at the end of intervention at the LP CJLP133 $0.5x10^{10}$ cfu twice a day for 12 weeks administrated group[14]. Moreover, in Harima-Mizusawa et al., there are specific IgE measurements in the *Japanese cedar and cypress pollen*, mites, and house dust that are not decreased significantly[16]. Normal levels of IgE vary in a population that is affected by many factors, such as genetic factors. For example, there is polymorphism, environment interaction, age, race (American-African and Filipino descent have higher IgE levels), gender (which can be higher in men), and seasons (allergy sufferers will have higher IgE levels in autumn). In dominant researches results, there is no change in total IgE levels both in adults and children. There can cause by the short time intervention.

In the extrinsic AD, the memory T cells express *the skin-homing receptor*, *cutaneous lymphocyte-associated antigen* (CLA), so there is Th2 cytokines increase as IL-4 and IL-13 that induce IgE synthesis, also IL-5 that has a role in eosinophil development and resistance. Research conducted by Prakoeswa et al. and Han et al. shows the IL-4 levels decrease significantly in the experimental group[13,14]. Meanwhile, in research by Fang et al., there is no significant change in IL-4 levels. It is because of the different types of *Lactobacillus plantarum*, doses, and the duration of administration[17].

Most clinical trials results used the SCORAD index for assessing clinical symptoms in patients. People with severe AD were rarely sampled because severe AD patients still got standard therapy in the form of systemic corticosteroids that can confound variables in research. All research results mentioned that patients who got topical corticosteroid, antihistamines, systemic immunosuppressive, phototherapy, and another probiotic for four weeks were excluded because they can increase bias that might happen in the research.

All results did not mention the side effects caused by *Lactobacillus plantarum* administration. However, in Harima-Mizusawa, N. et al., it is mentioned that there are no listed subjects that undergo harmful effects or have a change in their diet or lifestyle during the trial[16]. A similar thing is mentioned in Bonita, L. et al., there are no side effects in all treatments during monitoring and evaluation. In some RCT studies, some side effects happened after consuming probiotics such as flatulence, abdominal discomfort, nausea, and diarrhea, which those effects can improve on their own[12]. This study used a research sample that controlled confounding factors such as administration of systemic corticosteroids, antihistamines, and emollients. However, it has not been able to provide results regarding the effective dosage and side effects that can occur due to the administration of *Lactobacillus plantarum*. This research is expected to be the reference for further research with uses similar dose and duration of administration, sample

e-ISSN 2774-2318
p-ISSN 2407-0505

criteria, and measurement of results to determine the effective dose.

CONCLUSION

Lactobacillus plantarum is effectively given to AD patients for symptomatic or immunological improvement. It is hoped that further research can use the same for types of *Lactobacillus plantarum*, dosage, and duration of administration.

REFERENCES

1. Djuanda A. Ilmu Penyakit Kulit dan Kelamin, Edisi 7. 2017.
2. Keles FF, Pandaleke HEJ, Mawu FO. Profil dermatitis atopik pada anak di Poliklinik Kulit dan Kelamin RSUP Prof. Dr. R. D. Kandou Manado periode Januari 2013 – Desember 2015. e-CliniC. 2016;4(2).
3. Widaty S, Soebono H, Nilasari H, Listiawan Y, Siswati AS. Panduan Praktik Klinis Bagi Dokter Spesialis Kulit dan Kelamin di Indonesia. Vol. 74, Journal of Organic Chemistry. Jakarta: PERDOSKI; 2017. 1–420 p.
4. Wong ITY, Tsuyuki RT, Cresswell-Melville A, Doiron P, Drucker AM. Guidelines for the management of atopic dermatitis (eczema) for pharmacists. Can Pharm J. 2017;150(5): 285–97.
5. Febrina D, Hindritiani R, Ruchiatan K. Laporan Kasus : Efek Samping Kortikosteroid Topikal Jangka Lama pada Wajah Pendahuluan Laporan Kasus. Syifa' Med. 2018;8(2):68–76.
6. Holt J, Krieg N., Sneath PH., Al E. Bergey's Manual of Determinative Bacteriology. 2000.
7. Kusuma KB. Probiotik dan Peranannya pada Penyakit Alergi Anak. 2017;44(6): 441–4.
8. Mizock BA. Probiotics. Disease-a-Month. 2015;61(7):259–90.
9. Fuchs-Tarlovsky V, Marquez-Barba MF, Sriram K. Probiotics in dermatologic practice. Nutrition [Internet]. 2016;32(3):289–95. Available from: http://dx.doi.org/10.1016/j.nut.2015.09.001
10. Huang R, Ning H, Shen M, Li J, Zhang J, Chen X. Probiotics for the Treatment of Atopic Dermatitis in Children: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Front Cell Infect Microbiol. 2017;7:392.
11. Karim A, et al. Efek Pemberian Lactobacillus plantarum IS-10506 terhadap Indeks Scoring Atopic Dermatitis (SCORAD) Pasien Dermatitis Atopik Dewasa Derajat Ringan. Periodical of Dermatology and Venereology. 2019;31(3):85-92.
12. Bonita L, et al. Efektivitas Lactobacillus plantarum terhadap Serum Imunoglobulin E Total dan Indeks Scoring Atopic Dermatitis (SCORAD) Pasien Dermatitis Atopik Dewasa. Berkala Ilmu Kesehatan Kulit dan Kelamin. 2019;31(3):78-84.
13. Prakoeswa CRS, Herwanto N, Prameswari R, Astari L, Sawitri S, Hidayati AN, et al. Lactobacillus plantarum IS-10506 supplementation reduced SCORAD in children with atopic dermatitis. Benef Microbes. 2017 Oct;8(5):833–40.
14. Han Y, Kim B, Ban J, Lee J, Kim BJ, Choi BS, et al. A randomized trial of Lactobacillus plantarum CJLP133 for the treatment of atopic dermatitis. Pediatr Allergy Immunol Off Publ Eur Soc Pediatr Allergy Immunol. 2012 Nov;23(7):667–73.
15. Kim J, Lee BS, Kim B, Na I, Lee J, Lee JY, et al. Identification of atopic dermatitis phenotypes with good responses to probiotics (Lactobacillus plantarum CJLP133) in children. Benef Microbes. 2017 Oct;8(5):755–61.
16. Harima-Mizusawa N, Kamachi K, Kano M, Nozaki D, Uetake T, Yokomizo Y, et al. Beneficial effects of citrus juice fermented with Lactobacillus plantarum YIT 0132 on atopic

e-ISSN 2774-2318
p-ISSN 2407-0505

dermatitis: results of daily intake by adult patients in two open trials. Biosci microbiota, food Heal. 2016;35(1):29–39.
17. Fang Z, Lu W, Zhao J, Zhang H, Qian L, Wang Q, et al. Probiotics modulate the gut microbiota composition and immune responses in patients with atopic dermatitis: a pilot study. Eur J Nutr. 2020 Aug;59(5):2119–30.
18. Rusu E et al. Prebiotics and probiotics in atopic dermatitis (Review). Exp Ther Med. 2019;926–931.
19. Song S, Bae DW, Lim K, Griffiths MW, Oh S. Cold stress improves the ability of Lactobacillus plantarum L67 to survive freezing. Int J Food Microbiol. 2014;191:135–43.
20. Park M-S, Song N-E, Baik S-H, Pae H-O, Park SH. Oral administration of lactobacilli isolated from Jeotgal, a salted fermented seafood, inhibits the development of 2,4-dinitrofluoroben-zene-induced atopic dermatitis in mice. Exp Ther Med. 2017 Jul;14(1):635–41.