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Review

A Meta-analysis of the Effect of Probiotic *Lactobacillus* sp. as Immunomodulating Inflammatory Responses

Probiyotik Lactobacillus sp.'nin İmmünomodülatör Enflamatuvar Yanıtlar Üzerindeki Etkisinin Meta-analizi

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ABSTRACT

Lactobacillus sp. is considered an indispensable probiotic, and this probiotic has an effective role in maintaining the immune system. We evaluated the effect of the probiotic *Lactobacillus* sp. on modulating inflammation in several cases. In collecting the literature, we used databases from the Web of Science, the Cochrane Central Register of Controlled Trials, PubMed, and Embase. Studies that met the inclusion criteria were analyzed using Review Manager (version 5.4). A p-value of <0.05 of the total effect is considered statistically significant. Finally, 1895 references were retrieved and 20 were included in the meta-analysis. This meta-analysis suggested that most cases in this study were healthy elderly who received treatment with *Lactobacillus* sp. *Lactobacillus* sp. has a positive effect on B cells, eosinophils, IgE, NK cells, TNF-α, and IL-10. *Lactobacillus* could regulate the immune system by modulating inflammation in the healthy elderly.

Keywords: Good health and well-being, inflammation response, immune system, *Lactobacillus* sp.

ÖZ

Lactobacillus sp. vazgeçilmez bir probiyotik olarak kabul edilimektedir ve bağışıklık sisteminin korunmasında etkili bir role sahiptir. Çalışmamızda probiyotik *Lactobacillus* sp.'nin çeşitli vakalarda enflamasyonu modüle etme üzerindeki etkisini değerlendirdik. Literatür taramasında Web of Science, Cochrane Central Register of Controlled Trials, PubMed ve Embase veri tabanlarını kullandık. Dahil edilme kriterlerini karşılayan çalışmalar Review Manager (versiyon 5.4) ile analiz edildi. Toplam etkinin p-değerinin <0,05 olması istatistiksel olarak anlamlı kabul edildi. Son olarak, toplam 1895 referansa ulaşıldı ve 20 tanesi meta-analize dahil edildi. Bu meta-analiz, bu çalışmadaki olguların çoğunun *Lactobacillus* sp. ile tedavi gören sağlıklı yaşlılar olduğunu göstermiştir. *Lactobacillus* sp. B hücreleri, eozinofiller, IgE, NK hücreleri, TNF-α ve IL-10 üzerinde olumlu bir etkiye sahiptir ve sağlıklı yaşlılarda enflamasyonu modüle ederek bağışıklık sistemini düzenleyebilir.

Anahtar kelimeler: İyi sağlık ve iyilik hali, enflamasyon yanıtı, bağışıklık sistemi, *Lactobacillus* sp.

INTRODUCTION

Many studies have shown that probiotics, especially *Lactobacillus* sp., play an effective role in maintaining the immune system. This role is evidenced by the interaction between probiotics and commensal organisms in modulating mucosal immune cells or epithelial cells. The number of *Lactobacillus* sp. in the small intestine in adults is small, but this number can be increased through food fermentation assisted by short-chain fatty acids. The amount of microbiota found in feces is small, ranging from 0.01% to 0.6% of total counts[1]. Some *Lactobacilli*, such as *Ligilactobacillus salivarius*, *Lactobacillus rhamnosus*, and *Lacticaseibacillus paracasei*, were also

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detected in infants with amounts ranging from 10^5 to 10^8 CFU/g[2].

Lactobacillus is a genus of rod-shaped, Gram-positive, non-spore forming, facultatively anaerobic bacteria from the phylum *Firmicutes*[3]. In March 2020, 261 *Lactobacillus* species had been identified and reclassified into 25 genera (including 23 new genera); this was due to their high genotypic, phenotypic, and ecological diversity[4].

Inflammation occurs not only in diseased conditions but also in aging and obesity. Consuming probiotics can modulate inflammation to balance it. Today, the use of probiotics is becoming popular because many studies have proven the benefits of probiotics in modulating human health. *Lactobacillus* has been widely used in both children and the elderly, and probiotics are not only used as a treatment for disease but also as a prevention. One of the probiotics that is often used in research is *Lactobacillus* sp. and *Bifidobacterium* however this study limits the effectiveness of *Lactobacillus* sp. on the immune system, and the mechanism of *Lactobacillus* sp. in modulating the immune system through the gut microbiome is still unknown.

There have been many studies on *Lactobacillus* probiotics with different strains, proving that *Lactobacillus* has great potential for use in human and murine models. While some clinical studies have been negative or inconclusive[5], other studies have shown positive results[6-8]. *Lactobacillus* has shown significant and promising results in treating acute infectious diarrhea and in the prevention of antibiotic-associated diarrhea in human clinical trials[6]. Recent research has examined the use of the probiotic *Lactobacillus* in the treatment and prevention of allergic diseases and allergic rhinitis/asthma. There have been many studies proving the role of *L. rhamnosus GG* in the prevention of atopic eczema or dermatitis[9].

Lactobacillus sp. maintains intestinal homeostasis by stimulating regulatory T-cells to produce interleukin (IL)-10 and increasing the expression in a TLR2-dependent manner, thereby inducing B cell production. In some cases of inflammation, *Lactobacillus* sp. has been shown to significantly influence dendritic cells, thereby activating NK cells. *Lactobacillus* sp. plays a dual role, one of which is inhibiting IkB phosphorylation and degradation, thereby preventing NF-κb translocation which results in decreasing tumor necrosis factor alpha (TNF-α) expression. In allergic cases, *Lactobacillus* sp. inhibits Th2 cytokine production, thereby reducing eosinophil infiltration.

The aim of this meta-analysis study was to analyze whether probiotic *Lactobacillus* sp. affects the modulation of the immune system, especially on B cells, eosinophils, immunoglobulin (Ig)E, NK cells , TNF-α, and IL-10, under inflammatory conditions. This study provides more reliable evidence for clinical decisions.

MATERIALS and METHODS

Study Strategy

Four databases serve as reference sources for this analysis: Cochrane Library , Web of Science, Embase, and PubMed. All basic research from this source takes *Lactobacillus* sp. probiotic intervention against the immune system taken from 1992 to 2022. The keywords used for the literature search are "*Lactobacillus*", "Probiotic", "Immune System", and "Immunity".

Inclusion criteria: (1) clinical study of *Lactobacillus* sp. administered to humans; (2) research using immunological parameters; (3) the data have a mean, standard deviation, and total of samples. Exclusion criteria: (1) meta-analysis studies, reports, reviews, and meeting conclusions; (2) tests on experimental animals, *in vitro* tests, and research other than clinical trials; (3) research without original data; (4) research using prebiotics or other ingredients; (5) non-randomized controlled trials; (6) no measure of immune outcome; (7) not relevant to *Lactobacillus* sp. probiotics and immune system.

Publication bias uses the value from Egger's test; if $p>0.05$, then there is no publication bias. The determination of publication bias fulfills the following requirements: (1) Random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessments; (5) incomplete outcome data; (6) selective reporting.

Data Collection

The supporting PRISMA 2019 checklist for this study is available as supporting information[10]. Data extracted from journals filtered based on inclusion and exclusion criteria. Some authors independently extracted data, made decisions, and compared their conclusions with those of other studies. If there is a disagreement between studies, a third person (a member of the writing team) is needed to solve the problem through discussion and consultation. During the extraction process of the original data, authentication and reliability are required to avoid bias. Bias caused by the subject will be evaluated as soon as possible. To ensure the reliability of data

extraction and minimize bias and error, the authors conducted systematic training of the experts. The information data obtained from this study were as follows: the type of *Lactobacillus* sp. obtained, the type of disease, and the dose used *Lactobacillus* sp. effect on B cells, NK cells, eosinophils, IgE, IL-10, and TNF-α.

Data Organization and Analysis

Before conducting the meta-analysis, several indicators were standardized. The meta-analysis used Review Manager 5.4 (Cochrane Collaboration Network, London, UK). This study used the Cohen's method, and the effect measure was std. Mean difference. Forest plots were used to detect heterogeneity from the collection of journals obtained. Funnel plots are used for possible publication bias. Sample size, mean difference, and 95% confidence interval (CI) were calculated to analyze the results of the acquired immunological parameters. A p-value <0.05 of the total effect was assumed to be statistically significant. I^2 is an indicator that measures the degree of heterogeneity of the total data obtained. If I^2 <50%, the heterogeneity of the total data obtained is low, so the fixed-effects model is used. Conversely I^2>50%, then the heterogeneity of the total data obtained is high so that it uses a random-effects model.

RESULTS

A total of 1895 references were obtained from the four databases shown in Figure 1. A total of 604 references were excluded because they were not relevant =325, duplications =96, and journal reviews =870. Furthermore, several exclusion criteria from references obtained animal trial results =237, no measure immune outcome =160, not randomized clinical trials =187. This meta-analysis study originally used 20 references; however, 10 references have the same authors and title but different parameters of the immune system in Tables 1, 2. Review Manager 5.4 (Cochrane Collaboration Network, London, UK) was used to perform statistical analysis on six indicators: Eosinophils (five studies), B cells (four studies), IgE (seven studies), NK cells (four studies) TNF-α (six studies), and IL-10 (four studies). The mean difference and 95% CI of these indicators are shown in Figures 2-4.

Effect of the Disease

This meta-analysis pooled studies examining several inflammatory diseases and conditions such as atopic dermatitis[11-13], allergic rhinitis[14-16], Japanese cedar pollinosis[17,18], human immunodeficiency virus (HIV)[19], healthy elderly[20-25], inflammatory bowel disease (IBD)[26], and hypercholesterolaemic adults. Our study shows that the most popular reaction to inflammation was in the healthy elderly.

Effect of Probiotic Species

Lactobacillus probiotics have many strains, the most commonly used of which is *Lactobacillus casei Shirota* (*LcS*)[16,25,27]. In addition, the type of strain used to test the effectiveness of *Lactobacillus* probiotics on the immune system was *Lactobacillus plantarum* CJLP133[11], *L. plantarum* YIT 0132[14], *Lactobacillus acidophilus* strain L-92[15], *Lactobacillus GG* and *Lactobacillus gasseri* TMC0356[17], *L. rhamnosus* GR-1[19], *L. casei* DNl14001[20-28], *L. paracasei* NCC 2461[21], *L. gasseri* TMC0356[22], *Lactobacillus reuteri* DSM 17938[23], *L. salivarius* LS01[13], *L. plantarum* HSK201[18], *L. plantarum* L-137[24], *L. plantarum* ECGC 13110402[29], *Lactobacillus pentosus*[12], *L. rhamnosus* GR-1 and *L. reuteri* RC-14[26], and *L. acidophilus*[30].

Effects of Age

The majority of the population in this study was >50 years old and found in healthy elderly cases[20-25,30]. Meanwhile, in other studies, the population was 1-13 years old[11,12] and 18-45 years old[13,15,16,18,27].

Effect of Treatment Length Probiotic was Administered

This study shows that the length treatment of *Lactobacillus* probiotic on the immune system was administered 8 weeks, because it considered effective to modulate eosinophil[14], B cell[20,23], IgE,[15,18,27], NK cell[20], IL-10[23], and TNF-α[23].

Effect of the Probiotic Form

The most popular forms of *Lactobacillus* probiotic was yogurt[11,16,19,20,26,28], and milk[15,17,18,25,27] than other supplement forms such as juice[14], powder[13,21,30], tablet[12,22,23], and capsule[24].

Effect by Country

The results of the meta-analysis of data collection showed that most countries that intervened with the probiotic *Lactobacillus* are Japan[14,15,17,18,22,24,27].

Effect of the Immune System

After an intervention, the 95% CI of eosinophils was -0.50 (the lower limit was <0 and the upper limit was >0). The significant p=0.05 means that *Lactobacillus* has an effect on eosinophils. The mean difference of the total effect was -0.50/mm^3, and its 95% CI was -0.99 to -0.01/mm^3 (Figure 2a), indicating that *Lactobacillus* could effectively decrease the level of eosinophils and regulate host immunity.

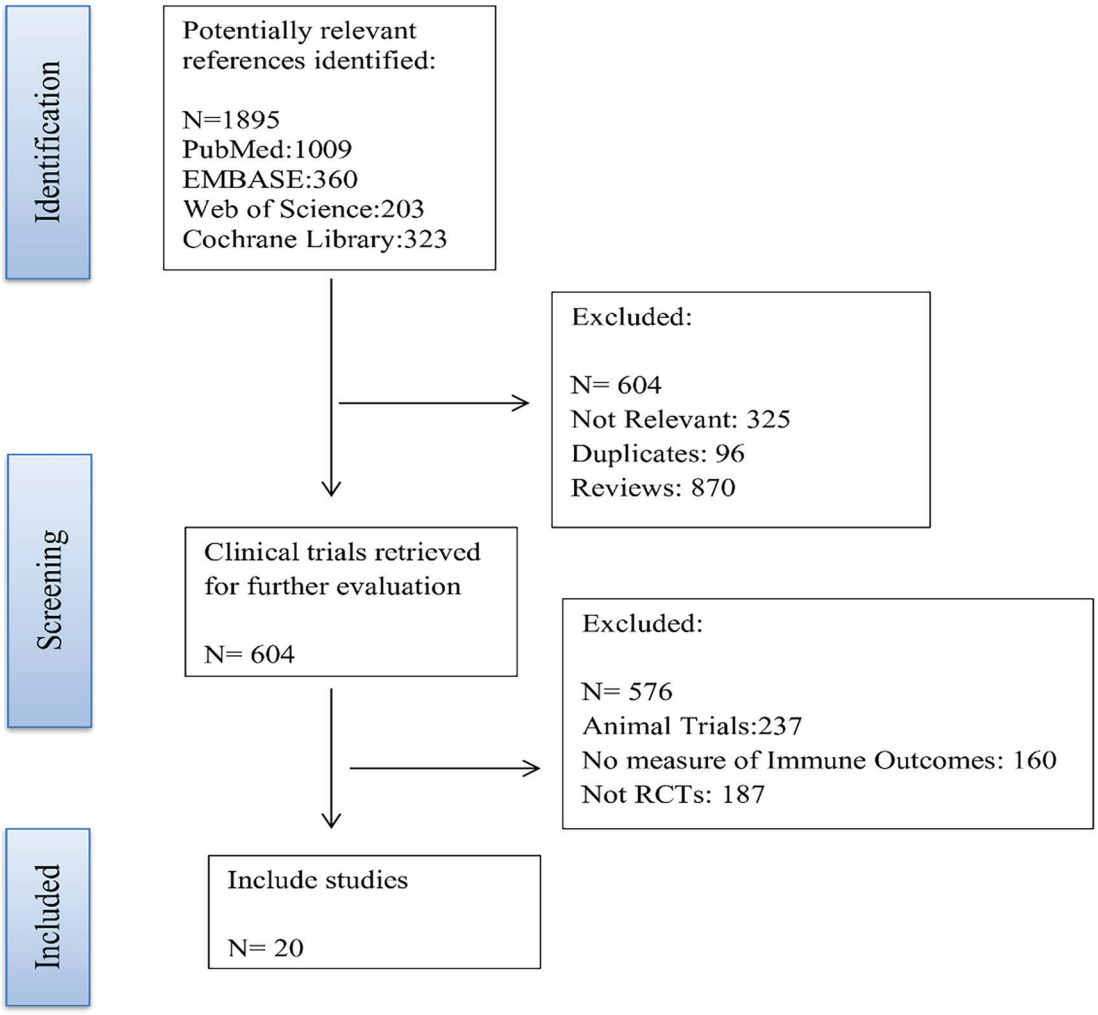

Figure 1. Flowchart of study selection in the meta-analysis.

RCT: Randomized controlled trials

For IgE, the 95% CI of IgE was -0.10 (the lower limit was <0 and the upper limit was >0). A significant p=0.56 means that *Lactobacillus* has no significant effect on IgE. The mean difference of the total effect was -0.10/mm^3, and its 95% CI was -0.42 to 0.23 pg/mL (Figure 2b), indicating that *Lactobacillus* could effectively decrease the level of IgE but not significance.

The forest plot of B cells showed that the significant p=0.02 suggests that *Lactobacillus* has an effect on B cells. The mean difference of the total effect was -0,37/uL, its 95% CI was -0.69 to -0.05/uL in Figure 3a, indicating that *Lactobacillus* could effectively decrease the level of B cells in the treatment group.

The forest plot of NK cells showed that the significant p=0.77 mean that *Lactobacillus* had no significant effect on NK cells, the mean difference of the total effect was -0.04/mm^3, its 95% CI was -0.30 to 0.22/mm^3 in Figure 3b, indicating that *Lactobacillus* could effectively decrease the level of NK cells in the treatment group but not significant.

IL-10, the 95% CI was -0.25 (the lower limit was <0 and the upper limit was >0). The significant p=0.10 indicates that *Lactobacillus* has no significant effect on IL-10. The mean difference of the total effect was -0.25 pg/mL, and its 95% CI was -0.55 to 0.05 pg/mL (Figure 4a), indicating that *Lactobacillus* could effectively increase the level of IL-10 in the treatment group, but the difference was not significant.

After the intervention, the 95% CI of TNF-α -0.12 were -0.50 (the lower limit was <0 and the upper limit was >0). The significant p=0.39 means that *Lactobacillus* has no significant effect on TNF-α. The mean difference of the total effect was -0.12 pg/mL, and its 95% CI was 0.40 to 0.16 pg/mL (Figure 4b), indicating that

Table 1. Characteristics of the included studies about country, type of disease, form of supplement, age, and duration consumption probiotic.

No	Author (Reference)	Country	Type of disease	Form of supplement	Age (y)	Duration (weeks)
1	Han et al.[11], 2012	Korea	Atopic dermatitis	Yogurts	1-13	12
2	Harima-Mizusawa et al.[14], 2016	Japan	Allergic rhinitis	Juice	16-65	8
3	Ishida et al.[15], 2005	Japan	Allergic rhinitis	Milk	34-36	8
4	Kawase et al.[17], 2009	Japan	Japanese cedar pollinosis	Milk	20-57	10
5	Hummelen et al.[19], 2011	Canada	HIV	Yogurts	>18	4
6	Parra et al.[20], 2004	Spain	Healthy person	Yoghurt	51-58	8
7	Bunout et al.[21], 2004	Switzerland	Healthy eldery	Powder	>70	16
8	Miyazawa et al.[22], 2015	Japan	Healthy eldery	Tablet	50-70	4
9	Mangalat et al.[23], 2012	America	Healthy adults	Tablet	19-60	8
10	Drago et al.[13], 2011	Italy	Atopic dermatitis	Powder	10-46	16
11	Tamura et al.[27], 2007	Japan	Allergic rhinitis	Milk	x=39	8
12	Hasegawa et al.[18], 2009	Japan	Japanese cedar polinosis	Milk	x=35	8
13	Ivory et al.[16], 2008	UK	Allergic rhinitis	Yogurt	18-45	2
14	Hirose et al.[24], 2006	Japan	Healthy subjects	Capsule	40-64	12
15	Seifert et al.[25] 2011	Germany	Healthy individuals	Milk	18-60	4
16	Meyer et al.[28] 2007	Austria	Healthy young women	Yogurt	22-29	2
17	Costabile et al.[29], 2017	UK	Hypercholesterolaemic	Capsular	30-65	12
18	Ahn et al.[12], 2020	Korea	Atopic Dermatitis	Tablet	2-13	12
19	Baroja et al.[26], 2007	Canada	Inflammatory bowel disease	Yogurt	26-63	4
20	Ouwehand et al.[30], 2008	Finland	Healthy elderly	Powder	>65	2

x= mean of age. HIV: Human immunodeficiency virus

Table 2. Characteristics of the included studies about gebus of *Lactobacillus*, dose, and outcome.

No	Author (Reference)	Genus of Lactobacillus	Dose	Type of immune
1	Han et al.[11], 2012	*L. plantarum*CJLP133	$1x10^{10}$ CFU	Eosinophil & IgE
2	Harima-Mizusawa et al.[14],2016	*L. plantarum* YIT 0132	100 mL	Eosinophil
3	Ishida et al.[15], 2005	*L. acidophilus* strain L-92	$3x10^{10}$ CFU	Eosinophils & IgE
4	Kawase et al.[17], 2009	*L.GG* and *L. gasseri* TMC0356	$1.4×10^{8}$ CFU and $1.0×10^{7}$ CFU	Eosinophils & IgE
5	Hummelen et al.[19], 2011	*L. rhamnosus* GR-1	$15.38×10^{10}$ CFU	Eosinophils
6	Parra et al.[20], 2004	*L. casei* DNl14001	$10^{8}x10^{10}$ CFU	B cell & NK cell
7	Bunout et al.[21], 2004	*L. paracasei* NCC 2461	10^{9} CFU	B cell & NK cell
8	Miyazawa et al.[22], 2015	*L. gasseri* TMC0356	$1.0×10^{9}$ CFU	B cell
9	Mangalat et al.[23], 2012	*L. reuteri* DSM 17938	$5x10^{8}$ CFU	B cell, IL-10 & TNF-α
10	Drago et al.[13], 2011	*L. salivarius* LS01	$1 x 10^{9}$ CFU	IgE
11	Tamura et al.[27], 2007	*L. casei* strain *Shirota*	$4x10^{10}$ CFU	IgE
12	Hasegawa et al.[18], 2009	*L. plantarum* strain HSK201	$6x10^{10}$ CFU	IgE
13	Ivory et al.[16], 2008	L. casei Shirota	$6.5x10^{9}$ CFU	IgE & TNF-α
14	Hirose et al.[24], 2006	*L. plantarum* L-137	10 mg	NK cell
15	Seifert et al.[25], 2011	L. casei Shirota	$1.95x10^{10}$ CFU	NK cell
16	Meyer et al.[28], 2007	*L. casei* DN114 001	$3.7x10^{8}$ CFU	IL-10 & TNF-α
17	Costabile et al.[29], 2017	*L. plantarum* ECGC13110402	$2x10^{9}$ CFU	IL-10 & TNF-α
18	Ahn et al.[12], 2020	L. pentosus	$1.0×10^{10}$ CFU	IL-10
19	Baroja et al.[26], 2007	*L. rhamnosus* GR-1 and *L. reuteri* RC-14	$1x10^{3}$ CFU and $2x10^{7}$ CFU	TNF-α
20	Ouwehand et al.[30], 2008	L. acidophilus	$2x10^{9}$ CFU	TNF-α

x=mean of age, IL-10: Interleukin 10, TNF-α: Tumor necrosis factor alpha, IgE: Immunoglobulin E

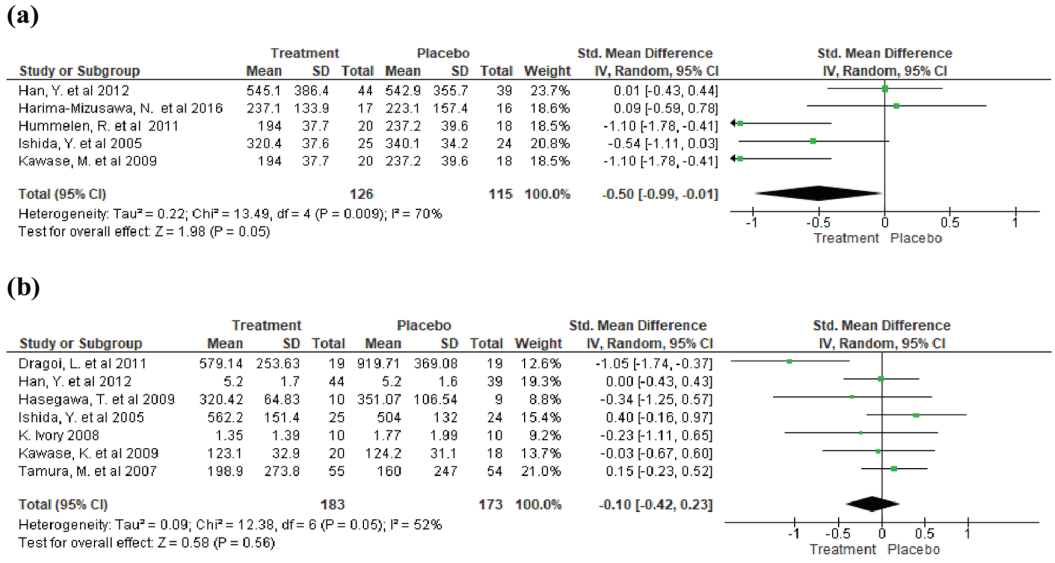

Figure 2. Forest plot effect of *Lactobacillus* supplementation on (a) eosinophils and (b) IgE comparing between *Lactobacillus* group (treatment) and placebo group. The statistical method used was Cohen'd, the effect measure was standard mean difference, and the analysis method was the random effects model.

SD: Standard deviation, CI: Confidence interval, *IgE: Immunoglobulin E*

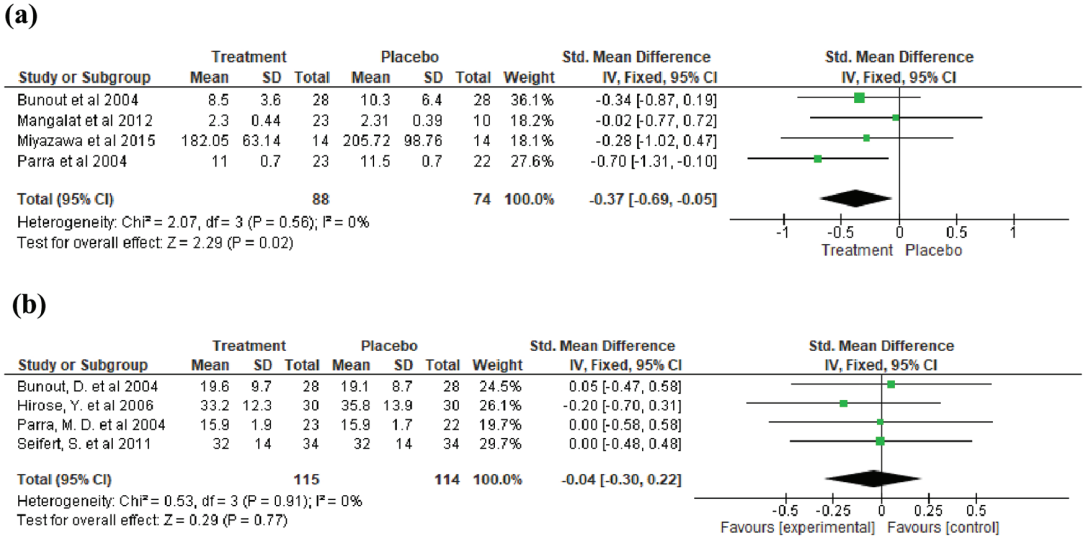

Figure 3. Forest plot effect of *Lactobacillus* supplementation on (a) B cells and (b) NK cells comparing between *Lactobacillus* group (treatment) and placebo group. The statistical method used was Cohen'd, the effect measure was standard mean difference, and the analysis method was the fixed effects model.

SD: Standard deviation, CI: Confidence interval

Lactobacillus could effectively decrease the level of TNF-α and regulate host immunity. Only 20 studies met the requirements of Egger's test. Overall, these studies have a low risk of bias due to the incomplete outcome requirements in Figure 5.

DISCUSSION

In recent years, probiotics have attracted extensive attention for treatment because of their low cost and minimal adverse reactions. However, previous studies regarding probiotics have shown limitations such as a small sample size, lack of medical evidence, and

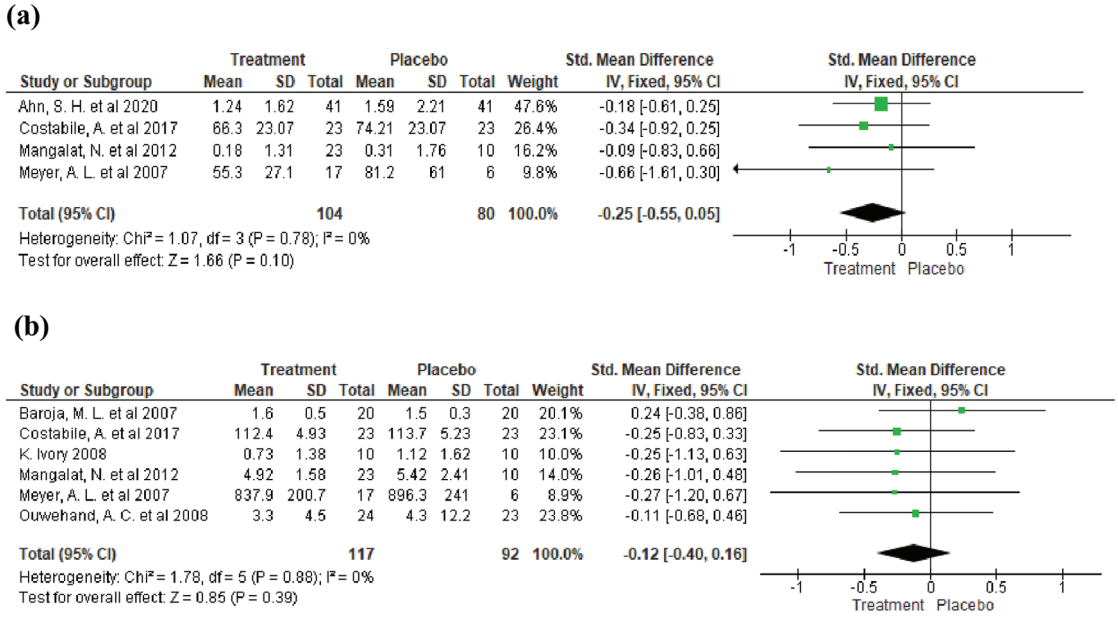

Figure 4. Forest plot effect of *Lactobacillus* supplementation on (a) IL-10 and (b) TNF-α comparing between *Lactobacillus* group (treatment) and placebo group. The statistical method used was Cohen'd, the effect measure was standard mean difference, and the analysis method was the fixed effects model.

SD: Standard deviation, CI: Confidence interval, IL-10: Interleukin 10, TNF-α: Tumor necrosis factor

Figure 5. Risk of bias. Quality evaluation of included trials.

incomplete evaluation indicators. Our meta-analysis study mainly focused on the systematic evaluation of the efficacy of *Lactobacillus* on the immune system. This study gathered 20 studies, 10 of which have the same references but different immune cells that have proven the effect of *Lactobacillus* on the immune system, such as B cells, eosinophils, IgE, NK cells, TNF-α, and IL-10. Currently, research proves the immunomodulatory effect of *Lactobacillus* on several diseases such as allergies, IBD, and atopic dermatitis.

Lactobacillus probiotic strains improve the integrity of intestinal defenses, thereby maintaining immune cell tolerance, reducing translocation of bacteria across the intestinal mucosa, and causing disease-coding phenotypes such as gastrointestinal infections, IBD, and irritable bowel syndrome[31]. Probiotics have a significant influence on the intestinal microbiota, which has been proven in experimental animal studies and clinical trials in humans. *Lactobacillus* also plays a significant role in the modulation and production of B cells, eosinophils, IgE, NK cells, TNF-α, and IL-10.

Many studies have proven that consumption of *Lactobacillus* has a good effect on the body. The probiotic effect is commonly accepted with daily consumption of a minimum of 10^6 CFU/mL or gram of probiotics[32]. Consumption of probiotics has different effects on each individual. The effect was based on immunological reactions and symptomatic parameters caused by the amount of *Lactobacillus* probiotic consumption. Probiotics can be administered orally in the form of capsules[33,34], yoghurt[35,36], dairy drinks or milk[15,16,37,38], and tablets[39,40]. Our data suggest that the majority of *Lactobacillus* probiotics are administered in the form of milk. Factors that influence the effectiveness of probiotic consumption are the duration and timing of intake. Moreover, the duration of *Lactobacillus* consumption in human trials differed from 2 to 12 weeks, and 8 weeks is the most popular time for *Lactobacillus* treatment. *LcS* is the most popular strain used for *Lactobacillus* treatment.

Our data show that age is the inflammatory reaction that triggers the activation of immunological cells. The majority of them are >50 years old. In several studies, aged >50 years, there has been an inflammatory reaction such as activation of TNF-α and IL-6[41-43]. This study proves the effect of *Lactobacillus* probiotics can modulate inflammatory reactions in healthy 50-year-olds. It showed that *Lactobacillus* probiotics could modulate the activity of B cells, eosinophils, IgE, NK cells, TNF-α, and IL-10.

B cells play a role in eliminating incoming bacteria. On the other hand, B cells can also cause autoimmune and allergic diseases[44]. This study proves that *Lactobacillus* impacts reducing the number of B cells. This decrease in B cells is necessary because antibodies can damage the intestinal mucosa. In some cases, such as allergies and autoimmune diseases, B cell activation is very high and can attack other immune cells. The results of our meta-analysis prove that a decrease in *Lactobacillus* plays a role in reducing the activation of B cells.

Several studies using probiotics have proven effective in increasing NK cell activity. Studies have shown that the administration *of L. rhamnosus* HN001 supplements for 3 weeks shows the activity of NK cells in middle-aged and elderly populations[45]. Our analysis proves that *Lactobacillus* positivity increases NK cell activation, which means that NK cells are effective for the treatment group. One probiotic that is often used in research trials is the lactic acid bacteria strain, *LcS*, which is currently manufactured in Japan as a commercial beverage. Many studies have shown the immunomodulatory effects of *LcS* on the gut immune system, particularly NK cell activity within the innate immune system[46].

Our analysis also showed that *Lactobacillus* had a positive result on TNF-α which means that *Lactobacillus* acts as an immunomodulator to decrease TNF-α cells. Probiotics such as *Lactobacillus* can inhibit TNF-α expression, generating an immunosuppressant and anti-inflammatory effect as a response; this statement has been widely reported by other studies. A study showed that the probiotic *Lactobacillus* can reduce TNF-α expression, and treat colitis symptoms[47].

Like TNF-α, we proved that *Lactobacillus* downregulates IgE. This effect is essential in patients with food allergies because it avoids clinical manifestations with vital consequences for allergic patients. IgE is an amply recognized antibody (immunoglobulin) associated with allergic responses. In different cases, IgE antibodies can bind to allergens and increase host resistance against parasites (helminths and protozoans). Mechanism of IgE as a defense through binding to allergen products and FcεRI on basophils and mast cells, antigen and IgE-induced aggregation of FcεRI can trigger the release of histamine, proteases, prostaglandins, leukotrienes, chemokines and cytokines[48].

IL-10 plays a central role in downregulating inflammatory cascades by suppressing the secretion of proinflammatory cytokines. *Lactobacillus* was positive for IL-10 expression. Some studies have revealed the positive effect of *Lactobacillus* sp. in stimulating IL-10.

Current research has demonstrated that administering *L. casei* can modify intestinal microbiota composition and TLR expression and increase IL-10 levels in the colonic mucosa of patients with mild ulcerative colitis[49].

The strength of this study was that the probiotic *Lactobacillus* sp. is highly effective in the elderly who are >50 years old through modulation of eosinophils and B cells. The limitations of this study: (1) Many studies have examined the effects of *Lactobacillus* sp. probiotics but did not include the mean, standard deviation, and the number of samples, so that studies were excluded from this study; (2) There is little evidence of the effect of probiotic *Lactobacillus* sp. on anti-inflammatory parameters; (3) Only collects a few cases (atopic dermatitis, allergic rhinitis, Japanese cedar pollinosis, HIV, healthy eldery, hypercholestrolaemic, and IBD), so the role of probiotic *Lactobacillus* sp. in other cases is not known.

CONCLUSION

In conclusion, our meta-analysis demonstrated that most cases in this study were healthy elderly patients who received treatment with *Lactobacillus* sp. *Lactobacillus* sp. positively affects B cells, eosinophils, IgE, NK cells, TNF-α, and IL-10. This means that *Lactobacillus* could regulate the immune system by modulating inflammation in the healthy elderly.

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Ethics

Author Contributions

Concept: W.F.E., S.P.M., I.D.S., D.S., R.E.P., S.Z., Design: W.F.E., S.P.M., I.D.S., D.S., R.E.P., S.Z., Data Collection and/or Processing: W.F.E., I.D.S., D.S., Analysis and/or Interpretation: W.F.E., S.P.M., D.S., R.E.P., Literature Search: W.F.E., R.E.P., Writing: W.F.E., S.P.M., I.D.S., D.S., R.E.P., S.Z.

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