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THE EFFECT OF PROBIOTIC ADMINISTRATION ON THE GUT–LUNG AXIS IN REDUCING THE INCIDENCE OF PNEUMONIA: A SYSTEMATIC REVIEW

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Abstract

Introduction: Pneumonia is a major cause of illness and death, especially in critically ill patients. Probiotics have been proposed as a supportive intervention to enhance immune function, maintain gut microbial balance, and strengthen the intestinal barrier against inflammation. **Research objectives:** The aim of this review is to systematically identify relevant evidence regarding the relationship between probiotics and pneumonia. **Methods**: The article employs a systematic review as its methodology. A comprehensive literature search was conducted across PubMed, Google Scholar, and Scopus. The selection of articles for the review was based on established inclusion and exclusion criteria, adhering to the guidelines set forth by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). **Results:** Based on 50 articles, 10 articles were filtered that met the inclusion criteria. The reviewed studies indicated that probiotic supplementation may reduce the severity of pneumonia, particularly ventilator-associated pneumonia (VAP), and improve immune response in critically ill patients. Other research supports that probiotic administration can reduce ICU stays and improve overall good immunity. However, other studies have shown that probiotic administration does not affect the length of stay or therapy in the ICU for pneumonia patients. **Conclusion**: The administration of probiotics in pneumonia patients provides multiple benefits, particularly by enhancing immunity through the modulation of macrophages within the gut–lung axis.

keywords : immune system, pneumonia, probiotik, systematic review

Introduction

Pneumonia is an acute inflammation of the lung alveoli caused by a bacterial, viral, or fungal infection. According to reports from the Centers for Disease Control and Prevention (IVAC) and Johns Hopkins University, pneumonia remains a global health crisis, particularly among children and the elderly. A November 2024 report showed that pneumonia was the leading cause of death among infectious diseases, accounting for 2.2 million deaths in 2021 alone, with 726,000 of these deaths among children under 5 years of age. (1). According to the 2023 Indonesian Health Profile, pneumonia is one of the leading causes of post-neonatal death in Indonesia. Pneumonia cases in Indonesia fluctuated significantly from 2013 to 2023. The 2023 report found a decline in pneumonia cases, from 38.8% in 2022 to 36.95% in 2023.(2).

One of the efforts undertaken to prevent and improve patient health is the implementation of IMCI (*Integrated Management of Childhood Illness*). Such cases are often associated with poor nutritional status or classified as severe

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malnutrition. (2). In efforts to strengthen the immune system, pneumonia patients are often recommended to take probiotics. Probiotics help enhance immune function, maintain microbial balance, and protect the intestinal barrier against inflammation. Several studies have also indicated that probiotics may reduce the severity of pneumonia, particularly ventilator-associated pneumonia (VAP) in critically ill patients. (3).

Based on this background, the authors conducted a systematic review on the effect of probiotics supplementation on the gut-lung axis in reducing the incidence of pneumonia. The aim of this review is to systematically identify relevant evidence regarding the relationship between probiotics and pneumonia.

Methods

The method used in this study was a systematic review, a research approach aimed at systematically identifying and evaluating relevant studies. This review was conducted in accordance with the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) guidelines. The retrieved articles were systematically selected by the researchers based on the predefined inclusion and exclusion criteria. Subsequently, the eligible studies were analyzed in a systematic and transparent manner following the systematic review approach to obtain comprehensive and reliable information.

The inclusion criteria for this systematic review covered quantitative studies (cross-sectional, cohort, RCT, and others), published between 2015 and 2025, and available in full text. The exclusion criteria included studies that did not specifically address pneumonia, studies focusing only on pneumonia or only on probiotics without linking both, duplicate articles, and inaccessible publications. Articles that met the inclusion and exclusion criteria were then analyzed and reviewed further, and the findings are presented in the results and discussion section.

Tables and Figures

The initial article collection yielded 50 articles, consisting of 25 from PubMed, 18 from Google Scholar, and 7 from Scopus. During the initial screening, 16 articles were excluded due to the unavailability of full text, leaving 34 articles. Further eligibility assessment excluded 24 articles because they were not related to pneumonia or did not employ quantitative methods. Ultimately, 10 articles met the inclusion criteria.

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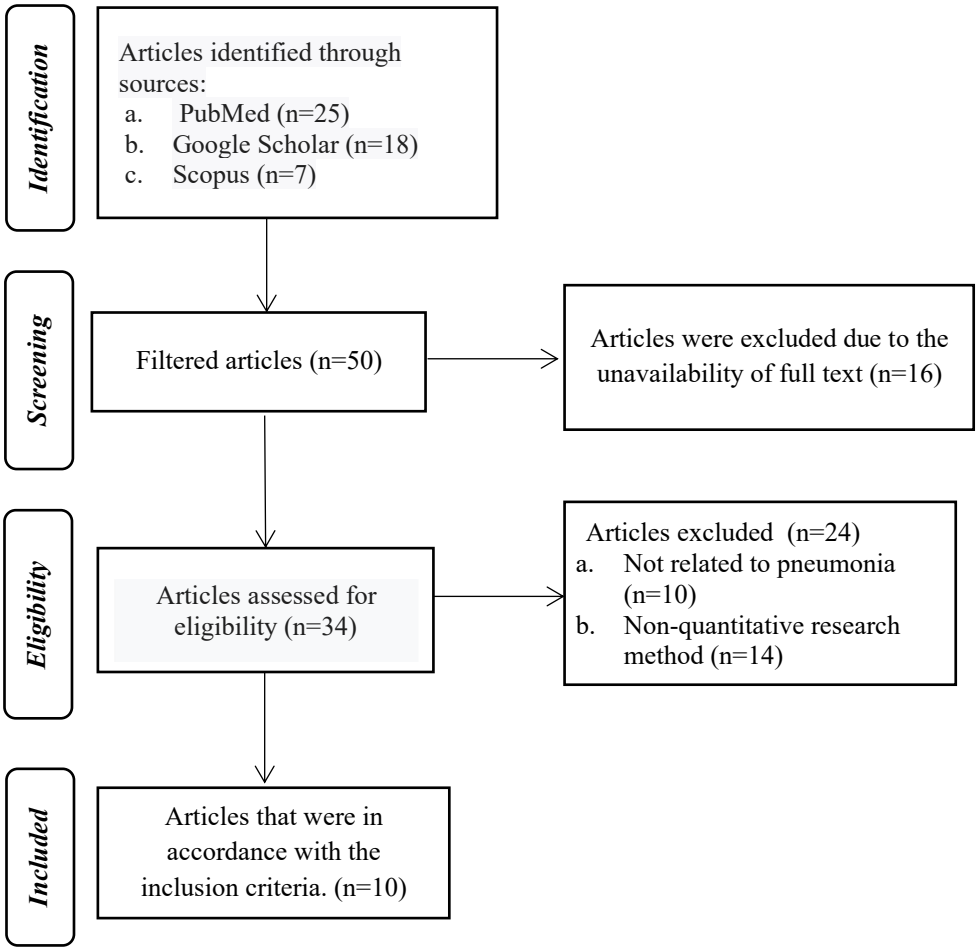

Figure 1 Diagram *Preferred Reporting Items for Systematic Review and Meta-analyses* (PRISMA)

Table 1, The Effect of Probiotic Administration on Pneumonia

No.	Author (s)	Year	Title	Methods	Aspect of Probiotic Administration in Pneumonia
1.	Chang Hun Lee, Yunjung Choi, Seung Young Seo, Seonghun Kim, In hee Kim, Sang Woo Kim, Soo Teik Lee, Seung Ok Lee	2021	Addition of probiotics to antibiotics improves the clinical course of pneumonia in young people without comorbidities: a randomized controlled trial	RCT	This simple randomized controlled trial was conducted among pneumonia patients at Pohang Naval Hospital, South Korea, between May 2016 and January 2017. The study evaluated the effects of probiotics in patients diagnosed with pneumonia, showing that the probiotic group experienced a faster reduction in body temperature and demonstrated more favorable inflammatory biomarker outcomes.

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2.	Jieni Fu, Xiangmei Liu, Zhenduo Cui, Yufeng Zheng, hui Jiang, Yu Zhang, Zhaoyang Li, Yanqin Liang, Shengli Zhu, Paul K Chu, Kelvin Wai Kwok Yeung and Shuilin Wu	2022	Probiotic-based nanoparticles for targeted microbiota modulation and immune restoration in bacterial pneumonia	Experimental study	This study showed that the probiotic formulation OASCLR increased microbiota diversity and beneficial bacterial populations while reducing pathogenic species. OASCLR is a nanoparticle-based probiotic to effectively increase body immunity. It also enhanced macrophage phagocytic activity from 2.61% to 12.3%. These findings suggest that, through interactions with $CD44^{+}$ macrophages, OASCLR may activate host immunity and stimulate fibroblast responses in immunocompetent pneumonia.
3.	Tim J Schuijt, Jacqueline M Lankelma, Brendon P Scicluna, Felipe de Sousa e Melo, Joris J T H Roelofs, J Daan de Boer, Arjan J Hoogendijk, Regina de Beer, Alex de Vos, Clara Belzer, Willem M de Vos, Tom van der Poll, W Joost Wiersinga1	2015	The gut microbiota plays a protective role in the host defence against *Pneumococcal pneumonia*	Experimental study	This experimental study applied Kruskal–Wallis ANOVA for statistical analysis. The results showed that gut microbiota can strengthen host immunity against pneumococcal pneumonia by enhancing the function of primary alveolar macrophages. These findings highlight the potential of exploring the gut–lung axis as a novel therapeutic approach for bacterial infections
4.	Yuxiu Tang, Liquan Chen, Jin Yang, Suqing Zhang, Jun Jin and Yao Wei	2024	Gut Microbies improve prognosis of Klebsiella pneumonia pulmonary infection through the lung-gut axis	Experimental study	This study employed a two-way ANOVA to analyze the probability of associations between grouping categories and the collected samples. The results demonstrated that administration of probiotics or fecal microbiota transplantation improved the prognosis of sepsis caused by Klebsiella pneumoniae by increasing fatty acids, bile acids, and metabolic levels, as well as restoring the intestinal flora structure. These effects contributed to a reduction in systemic inflammation.
5.	Yonglin Zhu, Guannan Ma, Wei Ren, Zhenyu Hu, Ling Zhou, Xin Zhang, Na Zhao, Mingding Zhang, Lei Yan, Qian Yu	2023	Effect of oral probiotics on clinical efficacy and intestinal flora in elderly severe pneumonia patients	Retrospective Case-control	This study enrolled 88 patients with severe pneumonia who were treated at China Aerospace Center Hospital between April 2021 and June 2022. The findings demonstrated that administration of enteric-coated capsules containing live Bacillus subtilis and Enterococcus faecium helped repair antibiotic-induced damage

No.	Author (s)	Year	Title	Methods	Aspect of Probiotic Administration in Pneumonia
	Xuetong Liu, Jichao Chen				in patients with severe pneumonia. Probiotic supplementation also enhanced immune function and improved intestinal microecology in these patients."
6.	Deborah J. Cook, Jennie Johnstone, John C. Marshall, Francois Lauzier, Lehana Thabane, Sangeeta Mehta, Peter M. Dodek, Lauralyn McIntyre, Joe Pagliarello, William Henderson, Robert W. Taylor, Rodrigo Cartin-Ceba, Eyal Golan, Margaret Herridge, Gordon Wood, Daniel Ovakim, Tim Karachi, Michael G. Surette, Dawn M. E. Bowdish, Daphnee Lamarche, Chris P. Verschoor, Erick H. Duan, Diane Heels-Ansdel, Yaseen Arabi, Maureen Meade	2016	Probiotics: Prevention of Severe Pneumonia and Endotracheal Colonization Trial—PROSPECT: a pilot trial	RCT	This study enrolled 150 patients from 14 ICUs in Canada and the United States, conducted over a 10-month period between October 2013 and August 2014. Probiotic capsules from 10 centers (31 batches) were evaluated, with colony-forming units (CFUs) of Lactobacillus rhamnosus GG monitored for 25 months. Each capsule contained 10^{10} CFUs of L. rhamnosus GG. The results showed that probiotic administration helped prevent ventilator-associated pneumonia (VAP) and other infections in critically ill patients. In addition, probiotics were associated with reduced initiation and duration of antimicrobial therapy, highlighting their potential role in infection prevention and overall clinical benefit in this population.
7	Maria Tsilika Giannoula Thoma Zoi Aidoni Georgia Tsaousi Kyriakos Fotiadis George Stavrou Petra Malliou Angeliki Chorti Helen Massa, Elli Antypa, Georgia Vasiliadou, Kyriaki Pagdatoglou, Antonios Voudouris, Spyridoula Vasiliagou, Giakoumis Mitos, Ntina Kontopoulou, Niki Paraforou, Eleni Antoniadou, Helen Mouloudi,	2022	A four-probiotic preparation for ventilator-associated pneumonia in multi-trauma patients: results of a randomized clinical trial	RCT	This placebo-controlled study included a total of 256 patients. Probiotic administration reduced the incidence of VAP [11.9% vs. 28.3%, hazard ratio (HR) 0.34, 95% confidence interval (CI) 0.13–0.92; P=0.034] and sepsis [6.8% vs. 24.5%, odds ratio 0.22, 95% CI 0.07–0.74; P=0.016]. Probiotic use was also associated with a shorter ICU stay and showed positive effects on both VAP and sepsis. These findings support the evidence that probiotics may serve as a potential alternative for preventing complications in critically ill patients with pneumonia. Moreover, probiotics may not only function as a preventive strategy but also contribute to overall

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	Eleni Gkeka, Vasilis Grosomanidis, Evangelos J. Giamarellos-Bourboulis, Katerina Kotzampassi				patient health due to their anti-inflammatory properties that help reduce systemic inflammation.
8	Soheil Roshanzamiri, Maryam Alemzadeh, Seyyedeh Narjes Ahmadizadeh, Azita Behzad, Seyyedeh Masumeh Hashemi, Jamshid Salamzadeh and Bahador Mirrahimi	2022	Probiotic prophylaxis to prevent ventilator-associated pneumonia in children on mechanical ventilation: A randomized double-blind clinical trial	RCT	This study involved a sample of 72 pediatric patients under the age of 12 who received mechanical ventilation for more than 48 hours at Mofid Children's Hospital. The findings indicated that probiotic administration in the intervention group significantly reduced the incidence of ventilator-associated pneumonia (VAP) in pediatric patients with pneumonia. However, the intervention was not associated with a reduction in the length of stay in the ICU.
9.	Zhiwei Wu, Entezar Mehrabi Nasab, Poonam Arora and Seyyed Shamsadin Athari	2022	Study effect of probiotics and prebiotics on treatment of OVA-LPS-induced of allergic asthma inflammation and pneumonia by regulating the TLR4/NF-kB signaling pathway	Experimental study	This study demonstrates that the effects of probiotics and prebiotics on the increased risk of pneumonia (AHR) were assessed using whole-body plethysmography. Probiotics function in eliminating pathogens, producing vitamins and fatty acids, and modulating the systemic immune response. They may also act as regulators of NF-κB activation.
10.	Qiang Zhang and Xuefeng Song	2025	Effect of probiotics on the incidence of acute kidney injury in patients with severe pneumonia	Retrospective Observational study	This study involved 267 pneumonia patients. These included 190 patients with no history of kidney disease and 77 with a history of kidney disease. The study showed that administering probiotics to patients with severe pneumonia reduced inflammation and the incidence of stage 1 AKI, but not those with stage 2 or advanced AKI.

Discussion

Based on the reviewed literature, several studies have reported that the

administration of probiotics in patients with pneumonia can help lower body temperature and reduce inflammation (4). Inflammation can be alleviated through the administration of probiotics or fecal microbiota, which has been shown to improve the prognosis of sepsis caused by pneumonia-related pathogens. This effect is achieved by increasing the production of fatty acids, bile acids, and metabolic levels, as well as by restoring the intestinal microbial structure (5). Furthermore, some studies have reported that probiotics may promote phagocytosis by interacting with CD44 macrophages. This mechanism is thought to stimulate immune activation and support fibroblast activity in cases of immunocompetent pneumonia (6). In addition, other studies have shown that the gut microbiota can enhance the body's immunity against pneumococcal pneumonia by optimizing the function of alveolar macrophages (7). The administration of probiotics serves multiple functions, including eliminating invading pathogens, producing vitamins and fatty acids, and enhancing the overall immune system. (8).

According to a study conducted by Zhu in 2023, supplementation with probiotics containing *Bacillus subtilis* and *Enterococcus faecium* was shown to repair antibiotic-induced damage in patients with severe pneumonia. The use of these probiotics also contributed to enhancing the patients' pneumonie immune function and improving the intestinal microecology. (9). Evidence from previous studies suggests that probiotics may help lower the incidence of VAP and decrease the likelihood of secondary infections in patients receiving critical care. Moreover, probiotics appear to offer additional advantages, such as limiting the need for initiating antimicrobial therapy and shortening the overall course of treatment (3). Other research supports that probiotic administration can reduce ICU stays and improve overall good immunity. (10). However, other studies have shown that probiotic administration does not affect the length of stay or therapy in the ICU for pneumonia patients. Nevertheless, this study shows that probiotic administration can prevent inflammation and reduce the incidence of VAP in pneumonia patients (11). Giving probiotics to patients with severe pneumonia accompanied by other diseases can reduce inflammation and reduce the incidence of stage 1 AKI, but it has no effect if the patient with severe pneumonia is accompanied by advanced stage AKI. (12).

Conclusions and Recommendation

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Based on the explanation above, the administration of probiotics to pneumonia patients has been proven to have many benefits, one of which is to increase immunity by optimizing macrophages formed in the gut-lung axis mechanism. Furthermore, probiotic supplementation has also been shown to function to reduce inflammation in patients with severe pneumonia and reduce the incidence of VAP in pneumonia patients. Probiotic administration is also associated with reduced duration of hospitalization for pneumonia patients. However, other studies have shown that probiotic administration has no relationship with the duration of hospitalization in the ICU in patients with severe pneumonia. Regular consumption of prebiotics and probiotics provides many benefits, not only by helping to reduce inflammation but also by preventing disease when probiotics are taken at the doctor's recommended dose. Further research is needed to determine the types and doses of probiotics that are effective for both treatment and prevention in reducing the incidence of pneumonia.

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Competing Interest

The authors declare that there are no competing interests related to the study

List Of Abbreviations

PRISMA : Preffered Reporting Items for Systematic Reviews and Meta-Analyses
RCT : Randomized Controlled Trial
VAP : VentilatorAssociated Penumonia
AHR : Adjusted Hazard Ratio
ICU : Intensive Care Unit
CFU : Colony-Forming Unit
CI : Confidence Interval
HR : Hazard Ratio
ANOVA : Analysis of Variance
AKI : Acute Kidney Injury
NF-κB :Nuclear Factor kappa-light-chain-enhancer of activated B cells

Authors' Contribution

Author 1 – developing research proposal, collecting data, data analysis, and publication manuscript..

Author 2 – collecting data, data analysis, and publication manuscript..

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