Original Article

OPEN ACCESS

Role of Probiotics as Adjunct Therapy Along with Standard Care in Decreasing Hospital Stay and Improving Symptoms in Pediatric Patients Admitted with Severe Pneumonia

Rashiqa Saadat[1], Nighat Haider[2], Mazhar Ahmed[3], Iradat Ahmad Khokhar[4], Tehmina Zahid[5], Huda Abdur Rahman[6]

[1,6]Postgraduate Resident Pakistan Institute of Medical Sciences, Islamabad
[2]Assistant Professor Pediatrics Pakistan Institute of Medical Sciences, Islamabad
[3]Resident Medicine Polyclinic Hospital, Islamabad, [4]ST1 Pediatrics Ulster Hospital, Dundonald
[5]Medical Officer Pediatrics, Pakistan Institute of Medical Sciences, Islamabad

Author`s Contribution

[1,2]Substantial contributions to the conception or design of the work; or the acquisition, [3,4]Drafting the work or revising it critically for important intellectual content [2,5]Final approval of the version to be published [6]Active participation in active methodology

Funding Source: None
Conflict of Interest: None

Received: Sept 10, 2024
Revised: Dec 28, 2025
Accepted: Feb 01, 2025

Address of Correspondent
Dr Rashiqa Saadat
Postgraduate Resident Pakistan Institute of Medical Sciences, Islamabad
rashi.bs12a@gmail.com

ABSTRACT

Objective: To determine if probiotics have any role as adjunct therapy along with standard care in decreasing hospital stay and duration of symptoms in patients admitted with severe pneumonia.

Methodology: A randomized controlled trial was conducted at the Children's Hospital, Pakistan Institute of Medical Sciences (PIMS), from March 2022 to September 2022. A total of 60 patients aged 2 to 24 months, admitted with severe pneumonia, were enrolled over a period of six months using non-probability consecutive sampling. The participants were randomly assigned into two groups using the lottery method: Group 1 (probiotic group) and Group 2 (placebo group). Group 1 received probiotics mixed in milk daily for three consecutive days, while Group 2 received plain milk as a placebo. The primary outcomes measured were the duration of hospital stay, time to resolution of cough, and time to resolution of fever.

Results: Both probiotics and placebo group participants had similar baseline characteristics. Duration of hospital stay, cough and fever all decreased in probiotic group. The average length of hospital stay did not decrease significantly in the probiotic group vs placebo group (6.5 ± 2.74-day vs 7.18 ± 2.23 days, p value=0.314). The average fever duration for probiotic group was 5.93 ± 2.71 days and for placebo group was 7.82 ± 5.15 days with p-value of 0.091 suggesting no statistically significant difference in both groups. The average cough duration was significantly less in probiotics group vs placebo group (9.46 ± 4.34 days vs 12.36 ± 5.63 days, p-value of 0.036).

Conclusion: Probiotics have potential to be beneficial in terms of reducing cough duration when added to standard care of pneumonia but further studies with larger sample size are required to elaborate on the hypothesis.

Keywords: Pneumonia, Children Probiotics, Pneumonia treatment.

Cite this article as: Saadat R, Haider N, Ahmed M, Khokhar IA, Zahid T, Abdur Rahman H Role of Probiotics as Adjunct Therapy Along with Standard Care in Decreasing Hospital Stay and Improving Symptoms in Pediatric Patients Admitted with Severe Pneumonia. Ann Pak Inst Med Sci. 2025; 21(3):543-548. doi. 10.48036/apims.v20i3.1200.

Introduction

Pneumonia is one of the main causes of death in children worldwide. Pneumonia killed 740,180 children under the age of 5 in 2019, which accounts for 14% of all under five deaths.[1] Although Pneumonia affects children everywhere, it is most prevalent in South Asia and sub-Saharan Africa.[1] Pneumonia is inflammation of lung parenchyma, mainly the alveolar spaces and distal bronchial tree, due to an infection. This causes pus and debris to accumulate in the parenchyma which compromises respiratory function. This infection can either be viral, bacterial or fungal in nature.[2] Progression of pneumonia depends on host immunity as well as tissue resilience of lung parenchyma. Children with pneumonia can present with respiratory as well as systemic symptoms, and they are diagnosed based on both clinical and radiological findings.[3] WHO classifies pneumonia into no pneumonia, pneumonia and severe pneumonia. Children with cough and cold symptoms only are classified as "no pneumonia", children with cough and tachypnea are classified as "pneumonia"; and Children who had chest in-drawings, with or without tachypnea, having any general danger signs are labelled as "severe pneumonia or very severe disease". Children in no pneumonia and pneumonia category can be treated safely at home but children with severe pneumonia with any danger signs require inpatient treatment with appropriate intravenous antibiotics.[3]

Probiotics are live microorganisms that when ingested are beneficial to host health.[4] Probiotics help normalize composition of gut microbes as well as promote immunity by interacting with innate and adaptive immunity.[4]

Intestinal commensals have a systemic effect on effector cells of innate immune system outside intestinal sites. There is evidence suggesting that systemic signals from intestine, program antibacterial activity of alveolar macrophages. NOD like receptors play a major role in this. NLR in intestinal mucosa are activated by intestinal microflora and could result in production of a signal that has systemic influence on host lung function. The exact signaling pathway is unknown.[5]

Lactobacillus and Bifidobacterium species are the most frequently used probiotics.[6] Probiotics are made as capsules, tablets, powders and as food ingredients. Probiotics are safe to use in healthy as well as diseased individuals.[4] Probiotics have been used in prevention and treatment of diseases affecting several different organ systems.[2,7] Their beneficial effects have been studied thoroughly in children and adults as well as elderly.[2,7] Probiotics have been studied for their preventive role in respiratory tract infections ranging from common cold to ventilator acquired pneumonia (VAP). Probiotics have shown beneficial effects in reducing severity of common cold.[8] Probiotics intake has also shown promising results in reducing incidence of VAP in critically ill children.[7]

Even though, probiotics have been studied for their preventive role in respiratory illness, their role in treatment of respiratory illnesses has not been studied much. As pneumonia is prevalent in children under 5 years in Pakistan and it is a resource limited area, there is need to find cost effective therapies for treatment of pneumonia which cause rapid improvement. Our study was conducted to find if probiotics, as adjunct therapy along with standard care, have any beneficial role in treatment of pneumonia. We hypothesize that Probiotics as adjuvant therapy along with standard care can decrease duration of hospital stay and duration of symptoms like fever, cough in pediatric patients admitted with severe pneumonia.

Methodology

This randomized controlled trial was conducted over a period of six months from March 2022 to September 2022, IRB approval no F.1-1/2015/ERB/SZABMU/941 in various wards of the Children's Hospital, Pakistan Institute of Medical Sciences (PIMS), Islamabad. Participants were recruited after obtaining ethical approval from the Institutional Review Board. Written informed consent was obtained from the parents or attendants of all enrolled patients.

Using the WHO sample size calculator and a reference article, the calculated sample size was 60 (30 patients per group), with a 5% level of significance, 90% power, a test value of the population mean as 2.4, anticipated population mean of 4.3, and a population standard deviation of 1.9.

A total of 60 children, aged 2 to 24 months and admitted with severe pneumonia, were selected through non-probability consecutive sampling. The diagnosis of pneumonia was made clinically and confirmed by expert review of chest radiographs using the WHO criteria.[3] Exclusion criteria included children who were unvaccinated, had severe acute malnutrition, other concurrent infections, chronic debilitating conditions, convulsions, unconsciousness, or a history of probiotic use (either dietary or medicinal) in the past six months.

Participants were randomized into two groups of 30 each using the lottery method. Group 1 received milk containing a probiotic sachet, while Group 2 received plain milk as a placebo. The parents or attendants were blinded to the intervention received. The probiotic used contained *Lactobacillus rhamnosus* GG, and the probiotic/placebo preparation was administered daily for three consecutive days.

Demographic data, breastfeeding status, respiratory rate, chest auscultation findings, and chest X-ray results were recorded. All patients were treated with intravenous antibiotics per hospital protocol. Patients requiring intensive care unit (ICU) admission were considered to have experienced an adverse outcome. The standard first-line antibiotic used was intravenous ceftriaxone at a dose of 75 mg/kg/day. Patients who showed no improvement within 48 hours and required second-line intravenous antibiotics were excluded from the final analysis.

Patients in both groups were followed throughout their hospital stay until discharge or the development of adverse outcomes. The duration of hospital admission was recorded. Symptom resolution (fever and cough) was assessed based on caregiver reports at discharge and follow-up. Respiratory rate and auscultation findings were also reassessed at discharge. Any complications or adverse events occurring during the hospital stay were documented.

All data were entered into SPSS version 23. Qualitative variables were analyzed using frequency distribution and the chi-square test, while quantitative variables were analyzed using mean, standard deviation, and the independent sample t-test.

Results

The study included 60 participants both males and females, 30 in each intervention and placebo group. In group 1 (probiotic intake) out of 30 participants 16 were male (53%) and 14 were female (46%). In the placebo group there were 19 males (63%) and 11 females (36%). However, there was no statistically significant difference in gender distribution in both groups (*p-value = 0.432).*

The descriptive statistics for age and weight of participants in both groups showed no significant differences. The mean age and weight were comparable between the probiotic and placebo groups, with p-values of 0.99 and 0.81, respectively (Table I).

Table I: Showing baseline mean age and weight of participants in both groups.

Characteristics	Probiotic group	Placebo group	P-value
	Mean±SD	Mean±SD	
Age (months)	7 ± 6	7 ± 6	0.99
Weight (kg)	6.3 ± 2.2	6.4 ± 2.3	0.81

There was also no difference in other baseline characteristics of both groups like: breast feeding status, auscultation findings on admission and chest x-ray findings (p-value of o.79, o.96 and 0.30 respectively). Table II

Thus, there were no significant baseline demographic differences in the study population in both groups making the participants similar in each arm of our study.

Table II: Showing baseline characteristics of participants in both groups. (n=total number)

Characteristics		Probiotic group		Placebo group		P-value
		(n)	(%)	(n)	(%)	
Total participants		30	100	30	100	-
Gender:	Males	16	53.3	19	63.3	0.43
	Females	14	46.6	11	36.6	
Breast fed	Yes	14	46.6	13	43.3	
	No	16	53.3	17	56.6	0.79
Auscultation on admission	Crackles	18	60	19	63.3	0.96
	Bronchial breathing	1	3.3	1	3.3	
	Crackles with ronchi	11	36.6	10	33.3	
Chest Xray findings	Consolidation	17	56.6	13	43.3	0.30
	Infiltrates	13	43.3	17	56.6	

Table III shows the results of our study in terms of duration of hospital stay, duration of fever and cough. Out of total 30 participants 2 in each group had adverse outcomes in the form of need for ventilation. Data analysis was done on the remaining participants.

Table III: Showing outcomes in both groups.

Outcome measure	Probiotic Group		Placebo Group		
	Mean	**SD**	**Mean**	**SD**	**p-value**
Duration of hosp. Stay	6.50	2.742	7.18	2.229	0.314
Fever duration	5.93	2.707	7.82	5.150	0.091
Cough duration	9.46	4.342	12.36	5.632	0.036
Number of patients with Adverse outcomes	2(6.7%)		2(6.7%)		1

Independent sample T-test used for quantitative variables and Fishers exact test used to analyze difference in adverse outcomes of both groups.

As shown in Table III, there was no statistically significant difference in hospital stay or fever duration between the probiotic and placebo groups (p=0.314 and p=0.091, respectively). However, the duration of cough was significantly shorter in the probiotic group (p=0.036). These findings suggest a potential role of probiotics in reducing cough duration in pediatric patients with severe pneumonia, although larger studies are needed to confirm this effect.

Discussion

The study findings suggest that probiotics, when used alongside standard care, may be beneficial for pediatric patients admitted with severe pneumonia. The data suggests that children who received probiotics along with standard care tend to have shorter hospital stays compared to those who did not receive probiotics but it was not statistically significant. There's also an indication that probiotics might be helpful in reducing the duration of symptoms like fever and cough in these patients.

A study conducted in Philippines showed significant decreased in hospital stay, and duration of cough and fever in patients who received probiotics versus placebo. But the probiotics used had multiple strains of Lactobacillus and Bifidus bacteria, and were given in bi-daily dose for 5 days.[9] Compared to this study our study only showed significant decrease in cough duration in probiotics vs placebo group and no significant decrease in hospital stay or fever duration. This could be attributed to the small sample size of our study and the use of only a single strain of lactobacillus as probiotic.

Another study by *Bing Li et al* showed decreased treatment failure (persistence of fever, tachypnea or danger signs) at day 3 when probiotic Lactobacillus casei Shirota was given with amoxicillin-sulbactam compared to placebo. Probiotics were given every 8hrly for 3 days.[10] This study was conducted on a larger population, probiotic strain used was different than our study and increased frequency of probiotic doses was used.

Previous literature shows that probiotics have preventive role in respiratory tract infections ranging from common cold to ventilator acquired pneumonia (VAP). Probiotics have been beneficial in reducing severity of not only common cold but also incidence of VAP in critically ill children.[7,8]

While the specific mechanisms for these benefits remain unclear, several potential pathways exist based on current research. The gut microbiome plays a crucial role in overall immune function.[11] Probiotics may help restore a balanced gut microbiota, potentially enhancing the gut barrier and reducing the translocation of harmful bacteria to the lungs.[12] Probiotics can stimulate the production of immunoglobulins (antibodies) and activate immune cells like macrophages and dendritic cells. This enhanced immune response could aid in fighting off the pneumonia-causing pathogens.[13] Pneumonia can trigger a significant inflammatory response. Some probiotics might exhibit anti-inflammatory properties, helping to regulate the immune response and potentially reducing lung injury.[14] Probiotics might compete with pathogenic bacteria for adhesion sites in the gut and potentially reduce their colonization, thereby indirectly impacting respiratory infections.[15] Certain probiotic strains may produce antimicrobial substances like lactic acid and bacteriocins, directly inhibiting the growth of pneumonia-causing bacteria.[15]

The Gut-Lung axis highlights how the trillions of bacteria residing in our gut (intestinal commensals) can influence the function of distant organs like the lungs.[16] Key Players are the Intestinal commensals, Effector cells of the innate immune system and Nucleotide-binding oligomerization domain-like receptors (NOD like receptors/NLRs). The intestinal commensals are friendly bacteria that live in our gut and contribute significantly to maintaining overall health.[17] Effector cells of the innate immune system are immune cells like macrophages, the first line of defense against invading pathogens. Alveolar macrophages are specialized macrophages residing in the air sacs of the lungs. NOD-like receptors (NLRs) are protein sensors within immune cells that recognize specific components of bacteria and trigger immune responses.[18]

Signals originating from the gut, potentially triggered by NLR activation due to commensal bacteria, can influence the antibacterial activity of alveolar macrophages in the lungs.[18,19] As gut bacteria digest dietary fibers, they produce short-chain fatty acids (SCFAs) like acetate, butyrate, and propionate. These SCFAs can enter the bloodstream and potentially travel to the lungs, where they might influence macrophage function.[17] Activation of immune cells in the gut by commensals might lead to their migration to the lungs. These migrated immune cells could then influence the local lung immune response.[20] Cytokines are signaling molecules produced by immune cells. NLR activation in the gut could trigger the release of cytokines that travel through the bloodstream and impact macrophage activity in the lungs.[21]

Studies have shown that the composition of gut microbiota can influence the development and severity of asthma and chronic obstructive pulmonary disease (COPD), highlighting the potential link between gut health and lung function.[21] Activation of NLRs in the gut by commensal bacteria has been demonstrated to trigger immune responses throughout the body, supporting the concept of systemic signals from the intestine.[19]

The gut-lung axis is a rapidly evolving field of research with exciting implications. Understanding how our gut bacteria talk to our lungs can pave the way for novel therapeutic strategies for various respiratory illnesses. By harnessing the power of the gut microbiome, we might be able to promote better lung health and potentially prevent or manage respiratory diseases.

While the exact mechanisms remain under investigation, the potential benefits of probiotics in reducing hospital stay and symptom duration in pediatric pneumonia are promising. Further research is crucial to solidify this evidence base and identify the optimal probiotic strains for clinical use

Conclusion

Overall, this study suggests that probiotics have the potential to be a beneficial addition to standard care for pediatric patients with severe pneumonia. Multicenter studies with large sample size are needed to determine whether probiotics can be an effective adjuvant therapy for severe pneumonia in children and explore the underlying mechanisms.

Investigating the effects of probiotics in children with severe pneumonia is a focused and relevant area of research. The findings suggest a potential reduction in hospital stay and symptom duration, which could be significant for both patients and healthcare systems. We testes a single strain of probiotics in treatment of pneumonia. Studies regarding use of probiotics in treatment of pneumonia or lung diseases in children are scarce.

Limitations: We used a small sample size and larger studies are needed to confirm these observations in a broader population. The study used a specific strain of probiotics and the results may not be applicable to other probiotic strains or formulations. As the participants were clinically diagnosed, aetiology of pneumonia was not explored. We did not explore any long-term effects on respiratory health or immune function in the children who received probiotics. The mechanism by which probiotics might improve outcomes in childhood pneumonia needs further investigation.

References

1. World Health Organization. Pneumonia in children [Internet]. Geneva: WHO; 2022 Nov 11 [cited 2024 Jun 12]. Available from: https://www.who.int/news-room/fact-sheets/detail/pneumonia
2. Torres A, Cilloniz C, Niederman MS, Menéndez R, Chalmers JD, Wunderink RG, et al. Pneumonia. Nat Rev Dis Primers. 2021;7(1):25. https://doi.org/10.1038/s41572-021-00259-0
3. World Health Organization. Revised WHO classification and treatment of pneumonia in children at health facilities: Evidence summaries. Geneva: WHO; 2014.
4. Markowiak P, Śliżewska K. Effects of probiotics, prebiotics, and synbiotics on human health. Nutrients. 2017;9(9):1021. https://doi.org/10.3390/nu9091021
5. Negi S, Das DK, Pahari S, Nadeem S, Agrewala JN. Potential role of gut microbiota in induction and regulation of innate immune memory. Front Immunol. 2019;10:2441. https://doi.org/10.3389/fimmu.2019.02441
6. Szajewska H, Konarska Z, Kołodziej M. Probiotic bacterial and fungal strains: claims with evidence. Dig Dis. 2016;34(3):251-9. https://doi.org/10.1159/000443359
7. Zhao J, Li LQ, Chen CY, Zhang GS, Cui W, Tian BP. Do probiotics help prevent ventilator-associated pneumonia in critically ill patients? A systematic review with meta-analysis. ERJ Open Res. 2021;7(1):00302-2020. https://doi.org/10.1183/23120541.00302-2020
8. Ahrén IL, Berggren A, Teixeira C, Niskanen TM, Larsson N. Evaluation of the efficacy of *Lactobacillus plantarum* HEAL9 and *Lactobacillus paracasei* 8700:2 on aspects of common cold infections in children attending day care: A randomised, double-blind, placebo-controlled clinical study. Eur J Nutr. 2019;59(1):409-17. https://doi.org/10.1007/s00394-019-02137-8
9. Bayer-Mulsid TB, Gatcheco FN. Randomized clinical trial on the effect of probiotic, ohhira omx capsules, as an adjunct in the treatment of severe pneumonia in patients 6–24 months of age. In: 3rd Asian Congress of Pediatric Infectious Diseases and 13th Pediatric Infectious Disease Society of The Philippines Annual Convention. 2006:1-19. Available from: http://www.omxprobiotika.cz/wp-content
10. Li B, Zheng J, Zhang X, Hong S. Probiotic *Lactobacillus casei* Shirota improves efficacy of amoxicillin-sulbactam against childhood fast breathing pneumonia in a randomized placebo-controlled double blind clinical study. J Clin Biochem Nutr.2018;63(3):233-7. https://doi.org/10.3164/jcbn.17-117
11. Wiertsema SP, van Bergenhenegouwen J, Garssen J, Knippels LMJ. The interplay between the gut microbiome and the immune system in the context of infectious diseases throughout life and the role of nutrition in optimizing treatment strategies. Nutrients. 2021;13(3):886. https://doi.org/10.3390/nu13030886
12. Varela-Trinidad GU, Domínguez-Díaz C, Solórzano-Castanedo K, Íñiguez-Gutiérrez L, Hernández-Flores TJ, Fafutis-Morris M. Probiotics: Protecting our health from the gut. Microorganisms. 2022;10(7):1428. https://doi.org/10.3390/microorganisms10071428
13. Mazziotta C, Tognon M, Martini F, Torreggiani E, Rotondo JC. Probiotics mechanism of action on immune cells and beneficial effects on human health. Cells. 2023;12(1):184. https://doi.org/10.3390/cells12010184
14. Cristofori F, Dargenio VN, Dargenio C, Miniello VL, Barone M, Francavilla R. Anti-inflammatory and immunomodulatory effects of probiotics in gut inflammation: A door to the body. Front Immunol. 2021;12:578386. https://doi.org/10.3389/fimmu.2021.578386
15. van Zyl WF, Deane SM, Dicks LMT. Molecular insights into probiotic mechanisms of action employed against intestinal pathogenic bacteria. Gut Microbes. 2020;12(1):1831339. https://doi.org/10.1080/19490976.2020.1831339
16. Marsland BJ, Trompette A, Gollwitzer ES. The gut-lung axis in respiratory disease. Ann Am Thorac Soc. 2015;12(Suppl 2):S150-S6. https://doi.org/10.1513/AnnalsATS.201503-133AW
17. Krishnamurthy HK, Pereira M, Bosco J, George J, Jayaraman V, Krishna K, Wang T. et al. Gut commensals and their metabolites in health and disease. Front Microbiol. 2023;14:1244293. https://doi.org/10.3389/fmicb.2023.1244293
18. Kienes I, Johnston EL, Bitto NJ, Kaparakis-Liaskos M, Kufer TA. Bacterial subversion of NLR-mediated immune responses. Front Immunol. 2022;13:930882. https://doi.org/10.3389/fimmu.2022.930882

19. Kelly D, Conway S, Aminov R. Commensal gut bacteria: mechanisms of immune modulation. Trends Immunol. 2005;26(6):326-33. https://doi.org/10.1016/j.it.2005.04.008
20. Ni S, Yuan X, Cao Q, Chen Y, Peng X, Lin J, et al. Gut microbiota regulate migration of lymphocytes from gut to lung. Microb Pathog. 2023;183:106311. https://doi.org/10.1016/j.micpath.2023.106311
21. Qu L, Cheng Q, Wang Y, Mu H, Zhang Y. COPD and gut-lung axis: How microbiota and host inflammasome influence COPD and related therapeutics. Front Microbiol. 2022;13:868086. https://doi.org/10.3389/fmicb.2022.868086