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Effectiveness of probiotic supplementation in pneumonia treatment in Vietnamese children

Submission date
16/12/2025

Recruitment status
Not yet recruiting

Registration date
17/12/2025

Overall study status
Ongoing

Last Edited
17/12/2025

Condition category
Respiratory

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims

Pneumonia remains a leading cause of morbidity and hospitalization among young children, particularly in low- and middle-income countries. Despite improvements in vaccination coverage and clinical care, pneumonia continues to place a substantial burden on healthcare systems and families. Antibiotic therapy is the cornerstone of treatment for bacterial pneumonia and severe pneumonia in children. However, antibiotic use is associated with several challenges, including gastrointestinal side effects, disruption of the gut microbiota, prolonged recovery, and increased risk of recurrent respiratory infections.

Probiotics are live microorganisms that, when administered in adequate amounts, confer health benefits to the host. Current evidence suggests that probiotics may modulate immune responses, enhance mucosal barrier function, and influence both gut and respiratory tract immunity through the gut–lung axis. These mechanisms provide a biological rationale for using probiotics as an adjunctive therapy in respiratory tract infections, including pneumonia.

Several randomized controlled trials and systematic reviews have evaluated the role of probiotics in respiratory tract infections in children. Systematic reviews have consistently shown that probiotics may reduce the incidence, duration, and severity of upper and lower respiratory tract infections, particularly in community and daycare settings. These effects are thought to be mediated by improved innate and adaptive immune responses, reduced inflammatory burden, and decreased pathogen colonization.

Evidence specific to pneumonia and hospitalized children is more limited but increasingly supportive. A previous randomized controlled trial conducted in Indonesia, demonstrated that probiotics used as an adjunct to standard antibiotic therapy significantly improved clinical outcomes in children under five years of age with severe pneumonia, including faster clinical recovery. Similar findings have been reported in studies evaluating probiotic supplementation alongside antibiotics in hospitalized patients with pneumonia, showing improvements in symptom resolution and overall clinical course.

More recent trials have highlighted the benefits of multi-strain probiotics in reducing disease severity, shortening hospital stay, and decreasing antibiotic use in children with acute respiratory tract infections. A double-blind, placebo-controlled trial in hospitalized young children showed that probiotic supplementation reduced the duration of illness, antibiotic exposure, and length of hospital stay. Importantly, these studies reported good safety profiles, with probiotics being well tolerated and associated mainly with mild gastrointestinal symptoms,

such as transient diarrhea.
In Viet Nam, probiotics are widely available and commonly prescribed in pediatric practice, including for children receiving antibiotics. However, their use in hospitalized children with pneumonia is largely empirical, and standardized, evidence-based recommendations are lacking. Most available studies were conducted in different healthcare settings, involved heterogeneous patient populations, or focused primarily on prevention rather than treatment. Data from well-designed randomized controlled trials in hospitalized Vietnamese children with pneumonia are scarce.
In addition, few studies have examined both short-term inpatient outcomes and post-discharge outcomes, such as recurrent respiratory infections and subsequent antibiotic use. Laboratory markers of inflammation and nutrition, including C-reactive protein, ferritin, hemoglobin, albumin, and total protein, may provide objective insights into disease resolution and recovery but have not been consistently assessed in previous trials.
Therefore, there is a clear need for a randomized controlled trial to evaluate the effectiveness and safety of oral probiotics as an adjunct to standard antibiotic therapy in children hospitalized with pneumonia in Viet Nam. Such evidence is essential to inform clinical practice, optimize antibiotic use, and potentially improve recovery and longer-term respiratory health in children.

Study aims
The primary aim of this study is to determine whether adding oral probiotics to standard antibiotic treatment reduces the length of hospital stay in children hospitalized with pneumonia.
The secondary aims are to:
Evaluate the effect of probiotics on clinical recovery, including resolution of fever and fast breathing.
Assess antibiotic use during hospitalization, including total duration and number of antibiotics prescribed.
Assess the need for respiratory support during hospitalization.
Evaluate the safety of oral probiotics, including the occurrence of diarrhea and other adverse events.
Compare inflammatory and nutritional laboratory markers (CRP, ferritin, hemoglobin, albumin, and total serum protein) 3–5 days after admission and at discharge.
Assess respiratory infections, antibiotic use, and healthcare utilization during the 3-month follow-up after discharge.

Who can participate?
Children can take part in this study if they:
-Are admitted to hospital with a diagnosis of pneumonia
-Are treated as inpatients at one of the participating hospitals
-Have an indication for antibiotic treatment based on clinical assessment and CRP blood tests
-Have a parent or legal guardian who understands the study and provides written informed consent
Children cannot take part if they:
-Have allergy or intolerance to probiotics
-Have severe immune deficiency or serious underlying diseases requiring special treatment
-Have taken probiotics shortly before hospital admission
-Are unable to complete follow-up during hospital stay
-Refuse blood tests or other required clinical procedures

What does the study involve?
Children who take part will be randomly assigned to one of two groups.
One group will receive standard antibiotic treatment plus oral probiotics containing Lactobacillus and Bifidobacterium.

The other group will receive standard antibiotic treatment without probiotics.
The assignment is done by chance using a computer-generated list.
The child, parents, doctors, and data analysts will not know which group the child is in.
All children will receive routine hospital care for pneumonia.
Doctors will record symptoms, treatments, laboratory test results, and recovery during the hospital stay.
Blood tests may be taken at hospital discharge and again 3–5 days after discharge.
After discharge, parents or caregivers will be contacted by phone and asked about the child's health over the next 3 months, including respiratory infections and antibiotic use.

What are the possible benefits and risks of participating?
Possible benefits:
-The child may recover faster from pneumonia.
-Probiotics may reduce side effects of antibiotics, such as diarrhea.
-Information from this study may help improve treatment for other children in the future.
Possible risks:
-Probiotics may cause mild side effects, such as bloating or diarrhea.
-Blood sampling may cause brief discomfort or bruising.
-All children will receive standard medical treatment whether or not they benefit directly from the study.

Where is the study run from?
The study is conducted at two provincial pediatric hospitals in Viet Nam: Thai Binh Pediatric Hospital and Hung Yen Obstetrics and Pediatrics Hospital
Follow-up after discharge is coordinated by the study team through phone interviews with caregivers.

When is the study starting and how long is it expected to run for?
The hospital-based part of the study is expected to start in September 2026 and finish in April 2027.
Each child will be followed during the hospital stay and for 3 months after discharge.
The post-discharge follow-up is expected to continue until September 2027.

Who is funding the study?
The study is funded by Hung Yen Provincial People's Committee and Hung Yen Provincial Department of Science and Technology.
There is no commercial or pharmaceutical company involved in the design, conduct, or analysis of the study.

Who is the main contact?
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Study information

Scientific Title
The effectiveness of probiotic as adjuvant therapy of pneumonia in children in Vietnam: a randomized clinical trial

Acronym
ProbiPneu

Study objectives
Primary outcome:
To evaluate whether adding oral probiotics to standard antibiotic treatment reduces the length of hospital stay in children hospitalized with pneumonia, compared with standard antibiotic treatment alone.

Secondary objectives:
1. To compare the time to clinical recovery between the two groups, including resolution of fever and fast breathing.
2. To compare antibiotic use, including total duration and number of antibiotics used.
3. To assess the need for respiratory support during hospitalization.
4. To evaluate the safety of oral probiotics, including the occurrence of diarrhea and other adverse events.

5. To compare inflammatory and nutritional laboratory markers between the two groups, including C-reactive protein (CRP), ferritin, hemoglobin, albumin, and total serum protein, measured at 3–5 days after admission and at discharge.
6. To assess respiratory infections and antibiotic use during the 3-month follow-up after discharge.

Ethics approval required
Ethics approval required

Ethics approval(s)
submitted 15/12/2025, Thai Binh University of Medicine and Pharmacy (373 Ly Bon Street, Tran Lam Wrad, Hung Yen, 410000, Viet Nam; +84 (0)2273838545; hoidongdaoduc@tbump.edu.vn), ref: IRB-VN01.009

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Active

Assignment
Single

Purpose
Treatment

Study type(s)

Health condition(s) or problem(s) studied
Pediatric patients with pneumonia

Interventions
Children will be randomly assigned to one of two groups in a 1:1 ratio. The intervention group will receive standard antibiotic treatment plus oral probiotics. The control group will receive standard antibiotic treatment without probiotics. To ensure fair comparison, both children, doctors, and data analysts will not know which treatment group each child belongs to (triple-blind design). The study will be carried out under routine clinical care conditions.

Intervention group:
Participants will receive standard antibiotic treatment according to hospital and national guidelines, plus oral probiotics containing Lactobacillus and Bifidobacterium. Probiotics will be administered daily during hospitalization. If the child is discharged before completing 14 days, probiotics will be continued at home to complete a total of 14 days.

Control group:
Participants will receive standard antibiotic treatment according to the same guidelines. They will not receive probiotics. To maintain blinding, children in the control group will receive boiled and cooled water prepared in the same manner as the probiotic solution.

Both groups will receive identical clinical care apart from the use of probiotics.

Randomization
Participants will be randomized in a 1:1 ratio to either standard antibiotic treatment plus oral probiotics or standard antibiotic treatment without probiotics.
Randomization will be conducted separately within each participating hospital because the expected number of eligible patients differs between sites. Approximately 200 children will be enrolled at Thai Binh Pediatric Hospital (TBPH) and 100 children at Hung Yen Obstetrics and Pediatrics Hospital (HYOPH), based on annual admission volume for pediatric pneumonia.
Within each hospital (TBPH and HYOPH), randomization will be stratified by age group (2-<12 months, 12-<36 months, 36-59 months, and ≥60 months) and by pneumonia severity (pneumonia, severe pneumonia, and very severe pneumonia) at admission to ensure comparability between the two treatment groups.
Within each hospital, randomization will be stratified by age group and by pneumonia severity at admission to ensure comparability between groups. For each “hospital x age x severity” stratum, a computer-generated randomization list will be prepared in advance using permuted block randomization with randomly varying block sizes of 4 and 6. The allocation order within each block will be randomly permuted. This approach maintains group balance while reducing the predictability of assignments.
The randomization lists will be generated by a study coordinator who is not involved in clinical care, outcome assessment, or data analysis. Allocation concealment will be maintained by restricting access to the randomization lists to designated study nurses responsible for preparing the intervention or control treatment.
When an eligible child is admitted and written informed consent has been obtained, the child will be assigned to the next available allocation in sequence from the appropriate stratum-specific randomization list. Randomization occurs immediately after enrolment, allowing probiotics to be started as soon as possible after hospital admission.
Participants are enrolled and randomized individually as they are admitted and do not need to be enrolled in pairs or at the same time. Treating clinicians, caregivers, outcome assessors, and data analysts will remain blinded to treatment allocation until completion of the primary analysis.

Intervention Type
Supplement

Primary outcome(s)
1. Length of hospital stay (number of days from hospital admission to discharge) measured using hospital medical records at during index hospitalization

Key secondary outcome(s))
1. Time to fever resolution (number of days from admission to the first day without fever [temperature <38°C for ≥24 hours]) measured using clinical charts at during hospitalization

2. Time to resolution of fast breathing, measured using number of days from admission to normalization of respiratory rate according to age-specific standards, at during hospitalization

3. Total duration of antibiotic use, measured using total number of days antibiotics are administered during hospitalization, at during hospitalization

4. C-reactive protein (CRP) level (mg/L) measured using routine hospital laboratory assay; comparison of absolute values and change from admission to discharge, at 3–5 days after admission and at discharge

5. Serum ferritin concentration (ng/mL) measured using routine laboratory assay; comparison of absolute values and change from admission to discharge, at 3–5 days after admission and at discharge

6. Hemoglobin (Hb) level measured using complete blood count (CBC); comparison of absolute values and change from admission to discharge, at 3–5 days after admission and at discharge

7. Serum albumin level (g/L) measured using routine biochemistry assay; comparison of absolute values and change from admission to discharge, at 3–5 days after admission and at discharge

8. Total serum protein level (g/L) measured using routine biochemistry assay; comparison of absolute values and change from admission to discharge, at 3–5 days after admission and at discharge

9. Need for respiratory support (proportion of children requiring respiratory support [yes/no], type of support [oxygen via nasal cannula/mask, non-invasive ventilation, invasive ventilation], and total duration [days]) measured using medical records at during hospitalization

10. Diarrhea (occurrence of diarrhea [yes/no], defined as ≥3 loose stools per day_ measured using clinical staff and caregiver report at during hospitalization

11. Post-discharge respiratory infections (occurrence of ≥1 respiratory infection episode after discharge) measured using caregiver phone interview using a standardized questionnaire at within 3 months after discharge

12. Antibiotic use for respiratory tract infections after discharge (any antibiotic use after discharge [yes/no], number of courses and total days) measured using caregiver phone interview at within 3 months after discharge

Completion date
31/12/2027

Eligibility

Key inclusion criteria
1. A confirmed diagnosis of pneumonia at any severity level.
2. CRP testing performed to determine the indication for antibiotic therapy according to the study protocol. Only children with CRP ≥30 mg/dL were eligible for inclusion.
3. Written informed consent obtained from the family after full explanation of the study objectives, potential benefits, risks, and participants' rights; consent signed by a parent or legal caregiver.

Healthy volunteers allowed
No

Age group
Child

Lower age limit
2 months

Upper age limit
16 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Contraindications to probiotics, including allergy or hypersensitivity to any component of the probiotic preparation.
2. Severe immunodeficiency or congenital immunological disorders.
3. Use of probiotics, probiotic supplements, or products with similar components prior to hospital admission, which may confound the assessment of the intervention’s effectiveness.
4. Presence of severe underlying conditions or the need for special treatment regimens, such as: cancer receiving chemotherapy or radiotherapy, hepatic failure, advanced renal failure, severe cyanotic congenital heart disease requiring surgery, or other life-threatening conditions requiring intensive care.
5. Inability to ensure complete in-hospital follow-up, for example: likelihood of early referral, transfer to another facility, or discharge within 48 hours of admission.
6. Lack of cooperation with necessary procedures for treatment evaluation, such as blood sampling for laboratory tests.

Date of first enrolment
01/09/2026

Date of final enrolment
01/07/2027

Locations

Countries of recruitment
Viet Nam

Sponsor information

Organisation
Hung Yen Provincial People’s Committee

Organisation
Hung Yen Provincial Department of Science and Technology

Organisation
Thai Binh Pediatrics Hospital

Funder(s)

Funder type

Funder Name
Hung Yen Provincial People’s Committee

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available