Archives of Pediatric Infectious Diseases
Volume 14 · Issue 1 · e157948

OPEN PEER REVIEW

Secondary Bacterial Pneumonia in Pediatrics with Influenza and COVID-19

Ehsan Shokraei, Alireza Fahimzad, Seyed Ahmad Tabatabaii, Mitra Khalili, Hassan Pourmoshtagh

SUBMITTED	REVISED	ACCEPTED	DOI
25 Nov 2024	7 Jul 2025	21 Jul 2025	10.5812/apid-157948

About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

More about open peer review: brieflands.com/knowledgebase/opr

Contents

1 **Original submission** Zahra Pourmoghaddas, Referee 1, Referee 2, Associate Editor 2
2 **Revision 1** Referee 2, Referee 1, Associate Editor 4
Authors' reply to reviewers 5
Reviewer and editor comments 24
3 **Revision 2** Referee 3, Referee 4, Referee 1, Associate Editor, Editor-in-Chief 25
Authors' reply to reviewers 26
Reviewer and editor comments 29
4 **Revision 3** Associate Editor, Editor-in-Chief 30
Authors' reply to reviewers 31
Reviewer and editor comments 33

1 Original submission

4 comments · 6 Dec 2024 – 3 Jan 2025

Zahra Pourmoghaddas Reviewer

MAJOR REVISION 6 Dec 2024

Thank you for your valuable research, but there are some points:
1. In the introduction: this part is too long. Why do you need to speak about BSI or similar topics? Please specify the goal of the study.
2. In the methods section: how many of the criteria must a child meet to be considered to have pneumonia? For example, does a child with fever, chills, and leukocytosis have pneumonia?
3. The results section: for BMI in children, you must use the Z score. A BMI of 15 in adults has a different meaning than in children.
Please define the abbreviations you use in the table, for example, CP.
Your title is about secondary bacterial pneumonia in COVID-19 and influenza.
Why is it necessary to speak about antibiotics when you did not identify any organisms and all of the antibiotics were empirical? It is better to evaluate which factors, such as age, weight, and sex, correlated with developing bacterial pneumonia in the 32 patients with pneumonia.
4- The discussion section: in this part, you speak about a study that did not use the same methods. Because the results section needs to be rewritten, the discussion section also needs to be rewritten.
Thanks

Referee 1 Reviewer

MAJOR REVISION 7 Dec 2024

Dear Author :
Thank you for your submission.
There are some notes.
Introduction :
1- Please explain the risk factors for bacterial pneumonia in cases with influenza and COVID19 pneumonia.
2- Please give the results of studies in Iran on this issue.
Material and Method:
1- Please give the exact criteria for the diagnosis and severity of pneumonia, with a strong and more up-to-date reference.
Results :
1- Diagram 1 is confusing. Each column may show one variable. This diagram shows a number of variables in one column. Please check with a statistical advisor.
2- The imaging findings would be better presented in text rather than in diagram 2. This diagram can be omitted.
3- Please do not use information in the title of table 2 or examination in the title of table 3.
Discussion :
1- Please check that all findings reported in the results and the review of the corresponding literature findings are included in the discussion.
2- Please give the results of Iranian studies.
3- What are the advantages and disadvantages of your study?
4- Please check the articles "https://doi.org/10.5812/apid-147482" and "https://doi.org/10.5812/pedinfect.104598" and use them in your references if possible.
Conclusion:

1- The conclusion section does not state the findings. This section gives the important points of the article and recommendations on further results.
Best Regards

Referee 2 Reviewer

MAJOR REVISION 21 Dec 2024

Dear Editor
The kind authors should consider the following comments:
1. The abstract should provide balanced information on methods, including approaches to describing and analyzing data.
2. In the conclusion, the authors repeated the findings. The clinical implications of the findings could be the focus.
3. The study design is a case series based on hospital data.
4. Instead of reporting the P-values, it could be better to calculate the odds ratio and 95% confidence interval around the point estimate to gain better insight.
5. Percentages in the tables should add up to 100 percent. Please check the decimal places and round them up correctly.
6. Replace "diagram" with "Figure" for all figures.
7. It is better to redraw the bar charts horizontally to make them easier to understand.
8. Discuss the generalizability of the study findings and potential biases.
9. There are no headings in Table 1.

Associate Editor

MAJOR REVISION 3 Jan 2025

Editor's comments
Your manuscript [ID Number 157948] has passed the review stage and is ready for revision.

To ensure the Editor and Reviewers can recommend that your revised manuscript be accepted, please pay careful attention to each comment posted underneath this email. This way we can avoid future clarifications and revisions, moving swiftly to a decision.

Technical points:
1. Please provide a point-by-point response to the Editor's and reviewers' comments.
2. Please highlight all the amendments in your manuscript in yellow.
3. Improve the English language of the manuscript.

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Response to reviewers

Dear editor and reviewers, I would like to thank you for your kind consideration of this article. The research team did their best to satisfy you. I hope that you will inform us if any further corrections are needed so that we can act on your suggestions. Also, the paper was edited by native person.

Thank you a lot

Reviewers' Comments:

Reviewer 1:

Dear Editor

The kind authors should consider the following comments:

1. The abstract should provide balanced information on methods including approaches to describe and analyze data.

Done: **Methods:** This cross-sectional study involved pediatric patients admitted due to influenza and COVID-19to Mofid Hospital from October to March 2023, focusing on the occurrence of secondary bacterial pneumonia and its contributing factors. We examined the clinical, laboratory, and admission data of the patients. The data were analyzed through SPSS version 22 using chi-square or Fisher's exact tests. A significance level of less than 0.05 was established.

2. In conclusion, the authors repeated the findings. The clinical implications of the findings could be focused on.

Done: **Conclusion:** The occurrence of secondary bacterial pneumonia in pediatric patients following COVID-19 and influenza was prevalent in which its severity can be affected by PICU admissions and the occurrence of pneumonia-related complications.

3. The study design is a case series based on hospital data.

Done in the abstract and body text: This descriptive case-series study based on the hospital data was carried out.....

4. Instead of reporting the P-values, it could be better to calculate the odds ratio and 95 % confidence interval around the point estimate to gain better insight.

Reply of the statistical software is as follows: Risk Estimate statistics cannot be computed. They are only computed for a 2*2 table without empty cells.

5. Percentages of the Tables should be equaled to 100 percent. Please check the decimal places and round it up correctly.

Done as follows:

Table 1. Clinical records of patients with secondary bacterial pneumonia

Variable		N	%
Prior hospital admission	No	26	81.3
	Yes	6	18.7
Past medical history	No	29	90.7
	Cerebral palsy	1	3.1
	Immunity deficiency	1	3.1
	Kartagener syndrome	1	3.1
Recent antibiotic intake	No	19	59.4
	Yes	13	40.6

Table 2. Complications of secondary bacterial pneumonia, mechanical ventilation and admission to PICU

Variable		N	%
Complication of pneumonia	None	20	62.5
	Pneumothorax	3	9.3
	Empyema	2	6.3
	Plural effusion	1	3.1
	Chest tube	3	9.4
	Pneumothorax, Empyema	2	6.3
	Plural effusion, Chest tube	1	3.1
PICU admission	No	25	78.1
	Yes	7	21.9
Mechanical ventilation	No	30	93.8
	Yes	2	6.2

Table 3. Relationship between secondary bacterial pneumonia severity and complications, hospitalization in PICU, and the need for mechanical ventilation.

Variable	Severity of pneumonia			P value*
	Mild (N=3)	Moderate (N=18)	Severe (N=11)	
Complication of pneumonia	-	2 (11.1%)	10 (90.9%)	0.02
PICU admission	-	1 (14.29%)	6 (85.71%)	<0.001
Need to mechanical ventilation	-	-	2 (100%)	0.13

6. Replace the "diagram" with "Figure" for all figures.

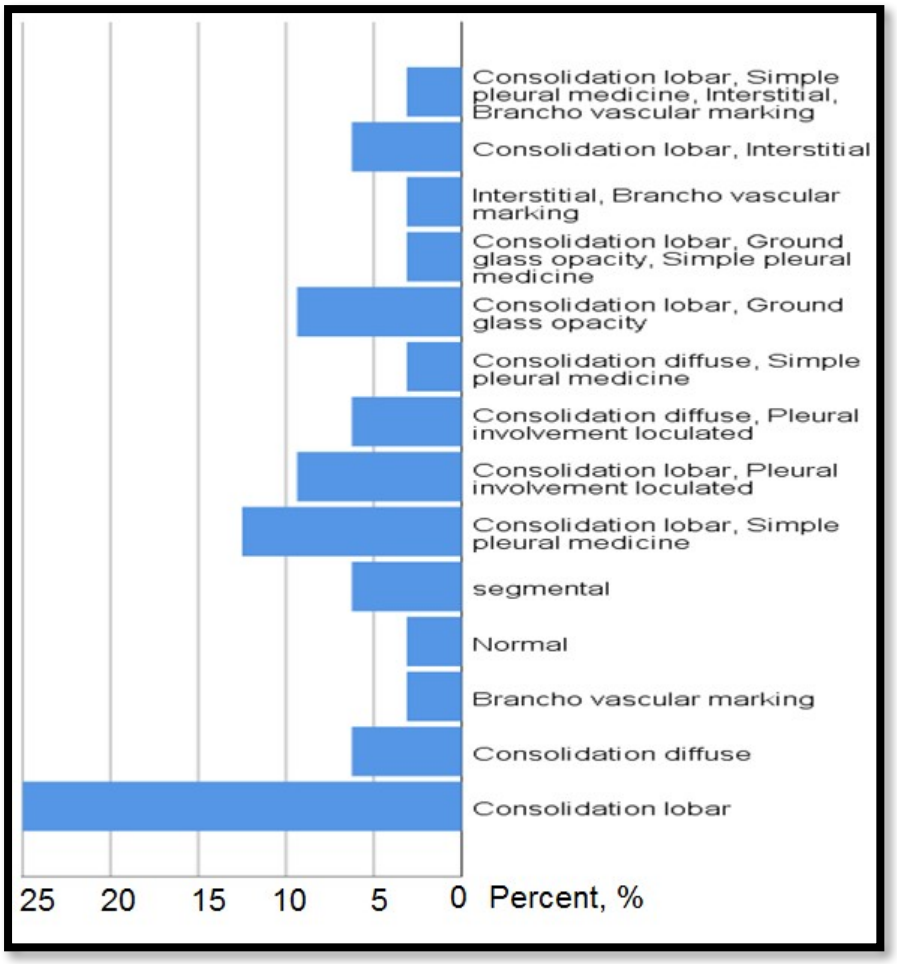
Done:

Figure 1. Clinical symptoms of patients with secondary bacterial pneumonia

Figure 2. Imaging findings of lung involvement following bacterial pneumonia

7. It is better to redraw the bar charts horizontally to better understand.

Done:



8. discuss the generalizability of study findings and potential biases.

Done in discussion section, last paragraph as follows:

Given that only 32 patients had secondary bacterial pneumonia and this sample size cannot be generalized to the entire population, the results should not be interpreted as a general rule because the sample selected was only hospital patients and in the community, healthier people naturally become infected with influenza or COVID-19, and therefore, only referrals are not the decision-making criteria, and the written interpretations should be used with caution, or a more generalizable conclusion may be presented after the publication of related meta-analyses in this field.

9. There are no headings in Table 1.

Done. It was added:

Table 1. Clinical records of patients with secondary bacterial pneumonia

Reviewer 2:

Dear authors, please consider below comments:

Comment 1: Choose a more appropriate title for Diagram 1and Diagram 2.

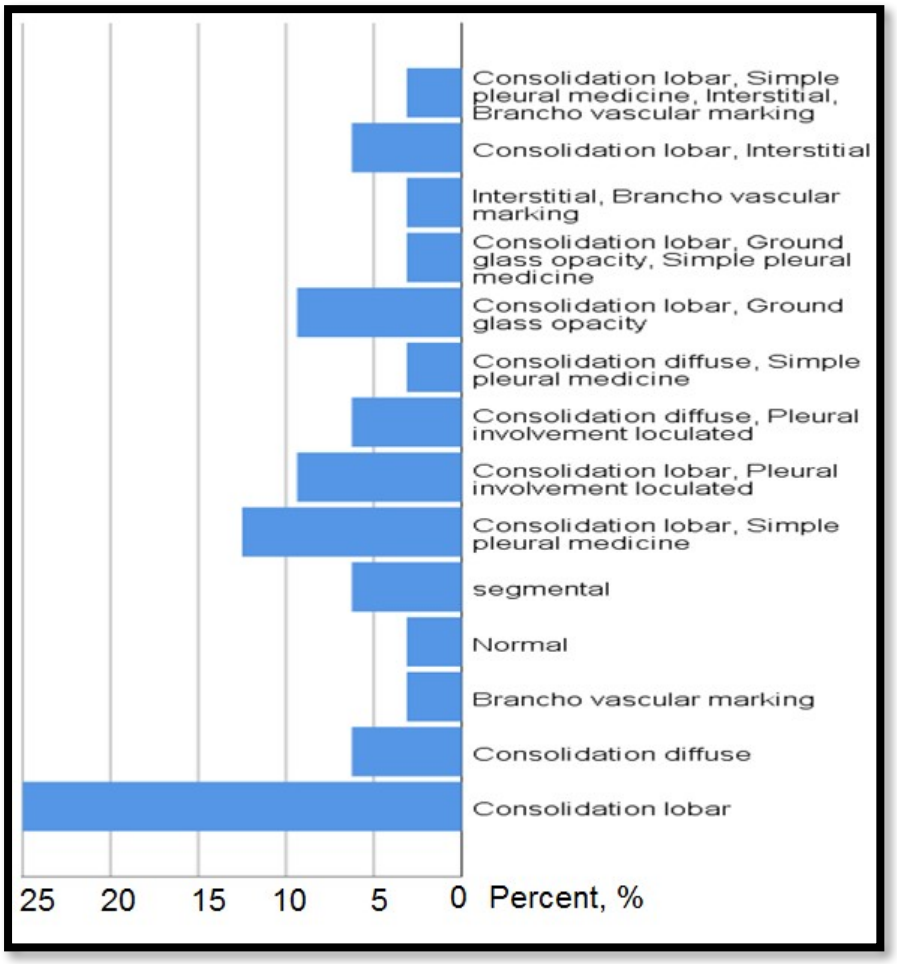
Done:

Figure 1. Clinical symptoms of patients with secondary bacterial pneumonia

Figure 2. Imaging findings of lung involvement following bacterial pneumonia

Comment 2: It is better to plot diagram 1 in such a way that overall what percentage of patients showed each symptom, in this case the more common symptoms are more easily identified.

It was changed to transfer visually the findings as follows:



Comment 3: In Table 1, the column headings should be indicated. The first row does not need to be written in bold format.

All is correct now as you recommended.

Comment 4: In Table 1, the sum of the percentages of variables "prior hospital admission" and "past medical history" does not add up to 100. Please check it.

All is correct now as you recommended.

Variable		N	%
Prior hospital admission	No	26	81.3
	Yes	6	18.7
Past medical history	No	29	90.7
	Cerebral palsy	1	3.1
	Immunity deficiency	1	3.1
	Kartagener syndrome	1	3.1
Recent antibiotic intake	No	19	59.4
	Yes	13	40.6

Comment 5: In Table 2, the sum of the percentages of variables " Complication of pneumonia" and "mechanical ventilation" does not add up to 100. Please check it.

All is correct now as you recommended.

Variable		N	%
Complication of pneumonia	None	20	62.5
	Pneumothorax	3	9.3
	Empyema	2	6.3
	Plural effusion	1	3.1
	Chest tube	3	9.4
	Pneumothorax, Empyema	2	6.3
	Plural effusion, Chest tube	1	3.1
PICU admission	No	25	78.1
	Yes	7	21.9
Mechanical ventilation	No	30	93.8
	Yes	2	6.2

Comment 6: Why didn't you compare quantitative variables across the three disease severity groups?

It was the clinical data that we guess they can be effective factors.

Comment 7: Please make Table 3 more complete and understandable. Also include the number of people at other levels of the variables under consideration in the table.

Now it is clearer:

Variable	Severity of pneumonia			P value*
	Mild (N=3)	Moderate (N=18)	Severe (N=11)	
Complication of pneumonia	-	2 (11.1%)	10 (90.9%)	0.02
PICU admission	-	1 (14.29%)	6 (85.71%)	<0.001
Need to mechanical ventilation	-	-	2 (100%)	0.13

Comment 8: Mark significant variables with a mark in the table.

It was done in red color.

Comment 9: you should use statistical models to control confounding variables effect.

Dear editor, we had not enough data/samples with secondary infection to run advanced statistical test like logistic regression to adjust confounders so we did not report it as our methodologist did not accept to run regression. If you have another suggestion or emphasize to do it, we will finally perform it.

Reviewer 3:

Dear Author :

Thank you for submission

Thank you for precise comments

There are some notes

Introduction :

1- Pls give explanation on risk factors of bacterial pneumonia in cases with influenza and COVID19 pneumonia .

It was added: The risk factors associated with co-bacterial infections in patients diagnosed with COVID-19 and influ encompass several elements, including age, the classification of pneumonia, pre-existing medical conditions, admission to the intensive care unit, the occurrence of invasive surgical procedures, duration of hospitalization, and the administration of hormone therapy (9).

Gan Y, Zhang G, Sun H, Lyu X. Clinical characteristics and risk factors for bacterial co-infections in COVID-19 patients: A retrospective study. J Glob Antimicrob Resist. 2024 Sep;38:6-11. doi: 10.1016/j.jgar.2024.04.007.

2- Pls give the result of studies in IRAN on this issue

There was no the same study but there was a study as follows in meta-analysis design not original study:

Koupaei M, Asadi A, Mahdizade Ari M, Seyyedi ZS, Mohammadi F, Afifi Rad R, Ghanavati R, Rezaei Khozani N, Darbandi A, Masjedian Jazi F. Secondary Klebsiella pneumoniae infection in patients with COVID-19: A systematic review. Diagn Microbiol Infect Dis. 2024 Feb;108(2):116105. doi: 10.1016/j.diagmicrobio.2023.116105.

Except the following that was added in discussion:

In a cohort of nineteen COVID-19 patients, by Sharifipour et al. (23), the mean duration of stay in the intensive care unit was around 15 days. All patients tested positive for bacterial infections, with 17 strains of Acinetobacter baumannii (90%) and 2 strains of Staphylococcus aureus (10%) identified. No variations in bacterial species were observed across different sampling points. All 17 strains of Acinetobacter baumannii exhibited resistance to the antibiotics tested. Notably, no strains of Acinetobacter baumannii producing metallo-beta-lactamases were detected. Among the Staphylococcus aureus isolates, one was identified as methicillin-resistant and was obtained from the patient who passed away, whereas another strain was found to be methicillin-sensitive and susceptible to the antibiotics tested. This study highlights the significant risk of superinfection in COVID-19 patients associated with Acinetobacter baumannii and Staphylococcus aureus, underscoring the necessity of monitoring bacterial co-infections in critically ill COVID-19 patients.

Material and Method:

1- Pls give the exact criteria for diagnosis and severity of pneumonia with a strong and more update reference

Done as follows:

Eligibility criteria

The inclusion criteria were a confirmed diagnosis of COVID-19 through a polymerase chain reaction (PCR) test or influenza based on a PCR test from a nasopharyngeal swab sample, with patients referred to Mofid Children

Hospital between October and March 2023. The sole exclusion criterion was the absence of consent to participate in the study.

Bacterial pneumonia was described as an inflammation of the lung parenchyma based on the 6 following findings (Nelson guidelines for treatment for community-acquired pneumonia in children)(18):

1. Clinical symptoms consistent with pneumonia (fever and chills, chest pain, dyspnea, etc.)

2. Imaging findings in chest X-ray or CT scan of the lung (lobar, or segmental, pleural effusion, empyema in favor of bacterial pneumonia, and interstitial or alveolar involvement in favor of viral pneumonia)

3. Initial laboratory findings including the number of peripheral blood leukocytes and neutrophil percentage, CRP, ESR, and blood culture (the presence of lymphopenia, low CRP, and low ESR in favor of viral infection, peripheral blood leukocytosis, increased CRP and ESR are in favor of bacterial pneumonia)

4. Lung auscultation manifestation (rales, fine crackles, or decreased sound in a part of the lungs)

5. Epidemiological findings (epidemic of specific viral infections at specific times, such as the epidemic of COVID-19 or influenza at a certain point in time)

6. Positive culture of the organism from the blood or pleural fluid sample or both (pneumococcus, staphylococcus, gram-negative bacteria, etc.)

Determining the severity of pneumonia (19):

Mild: Tachypnea is defined by age-specific respiratory rates. In newborns under one month, a respiratory rate exceeding 60 breaths per minute is noted. For infants aged one month to one year, the threshold is more than 50 breaths per minute. In children aged 1 to 5 years, tachypnea is indicated by a rate above 40 breaths per minute, while in individuals older than 5 years, a rate exceeding 20 breaths per minute is classified as

tachypnea. In cases of mild pneumonia, tachypnea is present, but other symptoms such as cyanosis and intercostal muscle retraction are absent.

Moderate: In moderate cases, tachypnea is observed alongside retraction of the intercostal, suprasternal, or subcostal muscles, depending on the child's age.

Severe: Severe cases are characterized by tachypnea accompanied by retraction, as well as episodes of apnea or cyanosis.

Results :

1- Diagram 1 is confusing. each column may show one variable. This diagram is showing a number of variables in one column. Pls check with statistical advisor

Its legend was modified as follows:

Figure 1. Clinical symptoms of patients with secondary bacterial pneumonia

So it is obvious that the figure is taking about the symptoms found in the studied patients.

2- Results of imaging findings is better to be shown by text rather than diagram 2 . This Diagram can be omitted.

As the other reviewers asked to changed its direction so we cannot perform the comment politely.

3- Pls don't use the information in title in table 2 and examination in title of table 3

All were done:

Table 2. Complications of secondary bacterial pneumonia, mechanical ventilation and admission to PICU

Table 3. Relationship between secondary bacterial pneumonia severity and complications, hospitalization in PICU, and the need for mechanical ventilation

Discussion :

1- Pls check for all reported findings in results and its review of literature findings in discussion

Done

2- Pls give the results of Iranian studies

In a cohort of nineteen COVID-19 patients, by Sharifipour et al. (23), the mean duration of stay in the intensive care unit was around 15 days. All patients tested positive for bacterial infections, with 17 strains of Acinetobacter baumannii (90%) and 2 strains of Staphylococcus aureus (10%) identified. No variations in bacterial species were observed across different sampling points. All 17 strains of Acinetobacter baumannii exhibited resistance to the antibiotics tested. Notably, no strains of Acinetobacter baumannii producing metallo-beta-lactamases were detected. Among the Staphylococcus aureus isolates, one was identified as methicillin-resistant and was obtained from the patient who passed away, whereas another strain was found to be methicillin-sensitive and susceptible to the antibiotics tested. This study highlights the significant risk of superinfection in COVID-19 patients associated with Acinetobacter baumannii and Staphylococcus aureus, underscoring the necessity of monitoring bacterial co-infections in critically ill COVID-19 patients.

3- what are advantages and disadvantages of your study

Reporting of the secondary infection following pandemics is an alarm for medical systems and authorities when it is prevalent (more than 20%). Also, it needs further studies with large sample size.

4-pls check for for" https://doi.org/10.5812/apid-147482" and "https://doi.org/10.5812/pedinfect.104598"articles and use them in your references if possible

Soheila R, Arezoo B, Galavani H, Saber R. Comments on" Genetic characterization and phylogenetic analysis of Fasciola species based on ITS2 gene sequence, with first molecular evidence of intermediate Fasciola from water buffaloes in Aswan, Egypt". Annals of parasitology. 2021;67(2).

and

Abdolkarimi B, Hatami Mazinani N, Amanati A. Differentiation Syndrome Mimicking COVID-19 Pneumonia. Arch Pediatr Infect Dis. 2020;8(3):e104598. https://doi.org/10.5812/pedinfect.104598.

were cited in refs 31 and 32.

Conclusion:

1-The conclusion part in not declaring the result findings . this part gives the important notes of article and recommendations on further results .

It was changed to:

The analysis revealed a significant prevalence of secondary bacterial pneumonia infections in pediatric patients recovering from COVID-19 and influenza at a tertiary care facility. The severity of pneumonia was associated with admissions to the pediatric intensive care unit and subsequent complications. Common clinical manifestations in patients with secondary bacterial infections included fever, cough, and difficulty breathing. The majority of patients responded positively to first-line antibiotic treatment. Notably, there were no reported fatalities among those who developed secondary bacterial pneumonia.

Best Regards

Reviewer 4:

Thanks for your valuable research but there are some points

1. In the introduction: this part is too long, why do you need speak about BSI or so on please specify the goal of the study

It was shortened and edited

2. In the method part: by how many of the criteria do you consider the child suffering from pneumonia, for example a child with fever and chill and leukocytosis have pneumonia?

Dear, we had determined criteria as follows:

Eligibility criteria

The inclusion criteria were a confirmed diagnosis of COVID-19 through a polymerase chain reaction (PCR) test or influenza based on a PCR test from a nasopharyngeal swab sample, with patients referred to Mofid Children Hospital between October and March 2023. The sole exclusion criterion was the absence of consent to participate in the study.

Data collection

Data collected included patient demographics such as age, gender, and weight, as well as clinical symptoms, pneumonia severity, recent attendance at kindergarten or school, history of prior hospitalization for pneumonia, any underlying health conditions, use of oral antibiotics in the preceding month, imaging results indicating lung involvement, organisms cultured from blood, pleural fluid, and tracheal tube secretions, peripheral blood leukocytosis, erythrocyte sedimentation rate (ESR), C-reactive

protein (CRP) levels, complications arising from pneumonia during treatment, the necessity for admission to pediatric intensive care units (PICU), mechanical ventilation requirements, characteristics of aspirated pleural fluid, treatment with first-line antibiotics for pneumonia, treatment response after 48 hours of antibiotic initiation, duration of antibiotic therapy, length of hospital stay, and the sensitivity and resistance of organisms to antibiotics as determined by antibiogram. Subsequently, the study examined the prevalence of bacterial pneumonia among patients with influenza and COVID-19 infections.

Bacterial pneumonia was described as an inflammation of the lung parenchyma based on the 6 following findings (Nelson guidelines for treatment for community-acquired pneumonia in children)(18):

1. Clinical symptoms consistent with pneumonia (fever and chills, chest pain, dyspnea, etc.)

2. Imaging findings in chest X-ray or CT scan of the lung (lobar, or segmental, pleural effusion, empyema in favor of bacterial pneumonia, and interstitial or alveolar involvement in favor of viral pneumonia)

3. Initial laboratory findings including the number of peripheral blood leukocytes and neutrophil percentage, CRP, ESR, and blood culture (the presence of lymphopenia, low CRP, and low ESR in favor of viral infection, peripheral blood leukocytosis, increased CRP and ESR are in favor of bacterial pneumonia)

4. Lung auscultation manifestation (rales, fine crackles, or decreased sound in a part of the lungs)

5. Epidemiological findings (epidemic of specific viral infections at specific times, such as the epidemic of COVID-19 or influenza at a certain point in time)

6. Positive culture of the organism from the blood or pleural fluid sample or both (pneumococcus, staphylococcus, gram-negative bacteria, etc.)

Determining the severity of pneumonia (19):

Mild: Tachypnea is defined by age-specific respiratory rates. In newborns under one month, a respiratory rate exceeding 60 breaths per minute is noted. For infants aged one month to one year, the threshold is more than 50 breaths per minute. In children aged 1 to 5 years, tachypnea is indicated by a rate above 40 breaths per minute, while in individuals older than 5 years, a rate exceeding 20 breaths per minute is classified as tachypnea. In cases of mild pneumonia, tachypnea is present, but other symptoms such as cyanosis and intercostal muscle retraction are absent.

Moderate: In moderate cases, tachypnea is observed alongside retraction of the intercostal, suprasternal, or subcostal muscles, depending on the child's age.

Severe: Severe cases are characterized by tachypnea accompanied by retraction, as well as episodes of apnea or cyanosis.

3. The result part: for BMI in children you must use the Z score, BMI 15 in adult meaning is different from children

It was reported as z-score:

The body mass index (BMI) z-score was normal (-1.88 to 0.54 for boys and -1.88 to 0.66 for girls).

Please identify the abbreviation you use in table for example CP.

Variable		N	%
Prior hospital admission	No	26	81.3
	Yes	6	18.7
Past medical history	No	29	90.7
	Cerebral palsy	1	3.1
	Immunity deficiency	1	3.1
	Kartagener syndrome	1	3.1
Recent antibiotic intake	No	19	59.4
	Yes	13	40.6

It seems the result part is copy paste of thesis result, but your title is about the secondary bacterial pneumonia in COVUD-19 and influenza

Dear reviewer, to have a weighted paper we reported all the available data related to the co-infections so in the table we focused on the title.

Why is need to speak about antibiotics when you did not have organisms and all od them were empiric. It is better to evaluate which factor in 32 patients with pneumonia corelated with getting bacterial pneumonia, such as age, weight, sex.

Dear reviewer, that is why our sample size was not enough to predict the affective factors and risk factor.

4- The discussion part:in this part you speak about the study which did not use the same methods. Because the result parts need to be rewritten so the discussion part also needs to re-write

We rewrite this section and added an Iranian study as well.

Thanks

Peer Review Using STROBE Cross-Sectional Checklist

Title and Abstract

Question: Indicate the study’s design with a commonly used term in the title or the abstract.

Review: The abstract clearly indicates that the study is a cross-sectional study.

Dear editor, as you know, the reviewer#1 asked us to write case-series based on hospital data and in our opinion both is correct, if you agree

Abstract

Question: Provide in the abstract an informative and balanced summary of what was done and what was found.

Review: The abstract provides a summary of the study's aim, methods, results, and conclusion, indicating the frequency of secondary bacterial pneumonia in pediatric patients with influenza and COVID-19【4:5†source】.

Thanks for your kind consideration

Introduction

Question: Explain the scientific background and rationale for the investigation being reported.

Review: The introduction provides a background on the difficulty of differentiating between influenza, COVID-19, and bacterial infections, and the concern of antibiotic overuse【4:5†source】.

Thanks for your kind consideration

Objectives

Question: State specific objectives including any prespecified hypotheses.

Review: The objective is clearly stated as assessing the frequency of secondary bacterial pneumonia in children with influenza and COVID-19【4:5†source】.

Thanks for your kind consideration

Methods

Question: Present key elements of study design early in the paper.

Review: The methods section states that it is a cross-sectional study conducted on pediatric patients admitted to a specific hospital【4:5†source】.

Dear editor, as you know, the reviewer#1 asked us to write case-series based on hospital data and in our opinion both is correct, if you agree

Setting

Question: Describe the setting, locations, and relevant dates including periods of recruitment, exposure, follow-up, and data collection.

Review: The study was conducted at Mofid Hospital from October 2023 to May 2024【4:5†source】.

Thanks for your kind consideration

Eligibility Criteria

Question: Give the eligibility criteria and the sources and methods of selection of participants.

Review: The abstract does not specify the eligibility criteria or the methods of participant selection【4:5†source】.

It was specified as follows:

Eligibility criteria

The inclusion criteria were a confirmed diagnosis of COVID-19 through a polymerase chain reaction (PCR) test or influenza based on a PCR test from a nasopharyngeal swab sample, with patients referred to Mofid Children Hospital between October and March 2023. The sole exclusion criterion was the absence of consent to participate in the study.

Variables

Question: Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria if applicable.

Review: The abstract mentions clinical, laboratory, and admission data but does not detail specific variables or diagnostic criteria【4:5†source】.

Thanks for your kind consideration

Data Sources/Measurement

Question: For each variable of interest, give sources of data and details of methods of assessment (measurement).

Review: The abstract does not provide detailed methods of data assessment【4:5†source】.

It was added: Nelson guidelines for treatment for community-acquired pneumonia in children was used to assess the occurrence of outcome.

Bias

Question: Describe any efforts to address potential sources of bias.

Review: The abstract does not mention any efforts to address bias【4:5†source】.

Dear editor, we had not enough data/samples with secondary infection to run advanced statistical test like logistic regression to adjust confounders so we did not report it as our methodologist did not accept to run regression.

Study Size

Question: Explain how the study size was arrived at.

Review: The abstract does not explain how the study size was determined【4:5†source】.

It was added: consensus sampling method

Statistical Methods

Question: Describe all statistical methods including those used to control for confounding.

Review: The abstract mentions a significance level of less than 0.05 but does not detail the statistical methods used【4:5†source】.

It was added: The data were analyzed through SPSS version 22 using chi-square or Fisher’s exact tests. A significance level of less than 0.05 was established.

Results

Question: Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed.

Review: The abstract reports the number of hospitalized patients and those with secondary bacterial infections【4:5†source】.

Thanks for your kind consideration

Descriptive Data

Question: Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders.

Review: The abstract provides limited information on participant characteristics, mentioning fever as a common clinical manifestation 【4:5†source】.

Dear editor, we reported all available data.

Outcome Data

Question: Report numbers of outcome events or summary measures.

Review: The abstract reports the frequency of secondary bacterial pneumonia and treatment responses【4:5†source】.

Thanks for your kind consideration

Discussion

Question: Summarize key results with reference to study objectives.

Review: The conclusion summarizes the key findings related to the frequency and severity of secondary bacterial pneumonia【4:5†source】.

Thanks for your kind consideration

Limitations

Question: Discuss limitations of the study taking into account sources of potential bias or imprecision.

Review: The abstract does not discuss the limitations of the study 【4:5†source】.

We hinted small sample size in the conclusion.

Interpretation

Question: Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.

Review: The conclusion provides an interpretation of the results but does not discuss limitations or compare with other studies【4:5†source】.

It was changed

Conclusion: The occurrence of secondary bacterial pneumonia in pediatric patients following COVID-19 and influenza was prevalent in which its severity can be affected by PICU admissions and the occurrence of pneumonia-related complications. Further studies with large sample size are required to generalize the findings.

Generalisability

Question: Discuss the generalisability (external validity) of the study results.

Review: The abstract does not discuss the generalisability of the findings【4:5†source】.

It was added: Further studies with large sample size are required to generalize the findings.

Best regards

2 Revision 1

3 comments · 20 Feb 2025 – 15 Mar 2025

Referee 2 Reviewer

ACCEPT 20 Feb 2025

Dear Editor
The comments raised were considered by the kind authors.
Reviewer,

Referee 1 Reviewer

MINOR REVISION 3 Mar 2025

dear author
Thank you for the correction.
Overall: A point of particular note in this study is secondary bacterial pneumonia. One important question is why the author chose COVID19 and influenza cases, why the number of positive cases in each group is not reported, and why there is no statistical comparison between the two groups in terms of severity and type of organisms. Please check this issue.
Method:
- Please check for methods to address bias.
- The study size determination and participant flow are not adequately explained.
- Result:
- More comprehensive descriptive data on participants should be provided.
- Conclusion:
- This part may present the main findings and recommend further studies on the resulting points and other aspects relevant to the study.
Please add this article "https://doi.org/10.5812/apid-145434" if it is appropriate.
Best Regards

Associate Editor

MAJOR REVISION 15 Mar 2025

Dear authors,
We are pleased to inform you that your manuscript has successfully passed the review stage and is ready for revision. Although the overall presentation of the manuscript has improved following amendments, it still requires further revision.
Yours sincerely,

3

Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Manuscript No. 157948

Greetings and Regards

Dear Editor

Please find attached a revised version of our manuscript “Secondary bacterial pneumonia in pediatrics with influenza and COVID-19”. Your comments and those of the reviewers were highly insightful and enabled us to greatly improve the quality of our manuscript. In the following pages are our point-by-point responses to each of the comments of the reviewers. We hope that the revisions in the manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication in Archives of Pediatric Infectious Diseases.

Looking forward to hearing from you at your earliest convenience,

Sincerely yours,

Reviewers' Comments:

Reviewer 1:
Dear Editor
The raised comments were considered by the kind authors.

- **Author response**: *Thank you for your positive feedback.*

Reviewer 2:

Dear authors, thanks for applying my comments, please also consider below comments: Comment 1: in table 3, in last row, you just have 2 patients in one cell, how did you report p-value? What test did you use?

- **Author response**: *Thank you for your observation. We agree that the sample size, in the subgroup of patients who need mechanical ventilation (n=2), is limited. We utilized Fisher's exact test in this case, which is appropriate for small sample sizes and categorical data. Given this small number, the statistical power is inherently low, and the resulting p-value (0.13) should be interpreted with caution. However, we acknowledge that despite its appropriateness, the results are limited in generalizability due to the small sample size. We have added a note in the discussion section to reflect this limitation. (lines 259-261)*

Comment 2: It is better to write percentages on the bars in the diagram.

- **Author response**: *Thank you for your observation. Added as suggested. (figures1-2)*

Comment 3: you stated that “A total of one hundred fifty-five pediatric patients were admitted to the hospital due to complications arising from COVID-19 and influenza. Among these, 32 patients, representing 20.64%, developed secondary bacterial pneumonia.”, so you had case and control groups, why you did not compare these two groups in your study by using advanced statistical models such as logistic regression or firth logistic regression?

• ***Author response****: Thank you for this valuable suggestion. We acknowledge that logistic or firth regression could have provided a more comprehensive analysis of the factors associated with the development of secondary bacterial pneumonia. However, the primary objective of our study was to describe the Secondary bacterial pneumonia in pediatrics with influenza and COVID-19, rather than to explore predictive risk factors. Additionally, given the relatively small number of cases (n=32), applying multivariable logistic models could lead to overfitting and unreliable estimates. Nevertheless, we agree that a case-control comparison using advanced statistical modelling is an important direction for future research, particularly in larger datasets. We have now noted this limitation and the potential for future analysis in the discussion section. (lines 317-322)*

Comment 4: It seems better to look at this study as a case-control study and come to better results through comparison.

• ***Author response****: Thank you for this insightful comment. We agree that the structure of our data, with a group of patients who developed secondary bacterial pneumonia and a group who did not, could be viewed as a case-control design. A comparative analysis using this framework could indeed yield additional insights. However, our primary aim was descriptive in nature. Additionally, due to the relatively small number of cases, conducting a case-control analysis using advanced statistical methods (e.g., logistic or Firth regression) would risk overfitting and reduce the reliability of the results. We have now acknowledged this point in the discussion and recommended it as a direction for future research.*

Reviewer 3:
Thanks for your consideration
1 in method part, the question how did your diagnosis the bacterial pneumonia did not answer
I did not understand according to Nelson criteria (having one. Two, or all 6…. criteria is needed to diagnosis the bacterial pneumonia? Please clarify this

• ***Author response****: Thank you for pointing this out. We apologize for the lack of clarity regarding the diagnostic criteria for secondary bacterial pneumonia. In our study, the diagnosis was based on the Nelson Textbook of Pediatrics criteria, which consider a combination of clinical, radiological, and laboratory findings.*

A diagnosis was made when at least two or more of the following six criteria were present: persistent or recurrent fever, worsening respiratory symptoms, elevated inflammatory markers (e.g., CRP, procalcitonin), new or progressive infiltrates on chest imaging, purulent respiratory secretions, and positive bacterial cultures when available A diagnosis was considered when two or more criteria were present. We have now clarified this point in the Methods section. (lines 91-92)

2. You check CRP and ESR level, we did not see the mean level of these two markers in results please consider this and mention is there any differences in bacterial and non-bacterial pneumonia?

• ***Author response****: The descriptives statistics of CRP and ESR Added as suggested. (table 4). Our study did not include a non-bacterial pneumonia group for comparison. Future studies suggest to better establish the diagnostic utility of these markers in distinguishing bacterial from non-bacterial pneumonia, future studies should include both bacterial and non-bacterial cases for direct comparison.*

3.Did you have any positive culture? According to criteria it was needed to get culture

- ***Author response****: In our study, no positive cultures were obtained. In our setting, the diagnosis of bacterial pneumonia was made based on clinical, radiological, and laboratory findings consistent with bacterial infection. Future studies with more comprehensive microbiological workup, including timely culture collection, would be beneficial for confirming etiology and improving diagnostic accuracy.*

4.please use the CRP, ESR level for bacterial pneumonia diagnosis in discussion part

- ***Author response**: Added as suggested. (lines 289-293)*

Reviewer 4:
dear author
thank you for correction
Totally : Special note in this study is secondary bacterial pneumonia. one important question is why the author choose COVID19 and Influenza cases and why there is no report about the number of positive cases in each group and why there is no statistical comparison between two groups on severity and type of organisms.Pls check this issue.

- ***Author response**: Thank you for your comment. Specifically, the study was conducted during a peak in influenza activity, while the number of COVID-19 PCR-positive cases was relatively low. As a result, the majority of included patients were influenza-associated cases, which limited the ability to perform a meaningful statistical comparison between the two groups in terms of severity and bacterial pathogens. Additionally, due to the small number of confirmed COVID-19 cases, reporting subgroup statistics or conducting comparative analysis between COVID-19 and influenza cases would not have yielded statistically reliable results.*

Method:
- Please check for methods to address bias.

- ***Author response**: Thank you for your comment regarding bias. We recognize the importance of minimizing bias to ensure the reliability of our findings. To address this, we employed [e.g., clear inclusion/exclusion criteria and standardized data collection methods. (lines 106-107)*

-The study size determination and participant flow are not adequately explained.

- ***Author response**: Thank you for your comment. The samples were selected prospectively based on predefined clinical and laboratory criteria documented in medical records. While no formal sample size calculation was performed, the selection aimed to ensure relevance and consistency with the study objectives. We edited to improve clarity. (lines 107-108)*

- Result:
-More comprehensive descriptive data on participants should be provided.

- ***Author response**: Thank you for your comment. The more details were presented in text at lines 139-144.*

- Conclusion:
- This part may give the main part of findings and it may recommend further studies on the resulted points and other facts that should be in concern of study

- ***Author response**: Revised as your valuable suggestion. (lines 331-334)*

Pls add this article "https://doi.org/10.5812/apid-145434" if it is appropriate

- ***Author response**: Added as suggested. (lines 250-251)*

3 Revision 2

5 comments · 18 May 2025 – 9 Jun 2025

Referee 3 Reviewer

ACCEPT 18 May 2025

Dear Associate Editor,
In my opinion, this article is suitable for publication.

Referee 4 Reviewer

MINOR REVISION 23 May 2025

Dear Authors,
Thank you for the authors' responses.
It seems that the type of study was not chosen correctly; please take this point into consideration.
Thanks,

Referee 1 Reviewer

MINOR REVISION 27 May 2025

Dear Author
Thank you for the corrections.
There are still a few notes:
1- What is the study type: case series or descriptive cross-sectional?
2- How did you calculate the sample size?
3- Table number 4 is not necessary.
4- The conclusion is very long. Please give the main concept and recommendations for other studies.
Best wishes

Associate Editor

MINOR REVISION 30 May 2025

Dear Authors,
The invited reviewers posted new comments. So, the manuscript requires a round of revision. Please provide a point-by-point response to the reviewers' comments and highlight all the changes in your manuscript in yellow.
Yours,

Editor-in-Chief

MINOR REVISION 9 Jun 2025

Dear authors,
Expert reviewers in the field have evaluated your manuscript, "title: Secondary bacterial pneumonia in pediatrics with influenza and COVID-19".
According to the reviewer's comments, this manuscript needs minor revision. The authors have to submit the revised manuscript along with a point-by-point response to the reviewer comments.

4

Revision 3

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Manuscript No. 157948

Greetings and Regards

Dear Editor

Please find attached a revised version of our manuscript “Secondary bacterial pneumonia in pediatrics with influenza and COVID-19”. Your comments and those of the reviewers were highly insightful and enabled us to greatly improve the quality of our manuscript. In the following pages are our point-by-point responses to each of the comments of the reviewers. We hope that the revisions in the manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication in Archives of Pediatric Infectious Diseases.

Looking forward to hearing from you at your earliest convenience,

Sincerely yours,

Reviewers' Comments:

Reviewer 1:

Dear Associate Editor,

In my opinion, this article is suitable for publication.

- **Author response**: *Thank you for your positive feedback.*

Reviewer 2:

Dear Author

Thank you for correction

There are still a few notes

1- What is the study type case series or descriptive cross sectional?

- ***Author response****: Thank you for your comment. We agree it is a cross sectional study.*

2- How did you calculate the sample size

- **Author response**: The sample size reflects the entire accessible population.

3- Table number 4 is not necessary

- **Author response**: *Thank you for your observation. Removed as suggested.*

4- Conclusion is very long . Please give the main concept and give reomendation for other studies

- ***Author response****: Thank you for pointing this out. Edited as suggested.*

Reviewer 3:

Dear Authors,

Thank you for the author’s responses.

It seems that the type of study was not chosen correctly; please take this point into consideration.

Thanks,

- ***Author response****: Revised as your valuable suggestion.*

4 Revision 3

2 comments · 12 Jul 2025 – 21 Jul 2025

Associate Editor

ACCEPT 12 Jul 2025

Editor comments
The authors have effectively utilized all available resources and data to revise the manuscript in a manner that is more scientifically sound than previously. In my opinion and based on the respected reviewers' comments, the manuscript could be published in its current form.
Yours,

Editor-in-Chief

ACCEPT 21 Jul 2025

My decision about this manuscript is "accept".