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Elevated Procalcitonin Levels in Pediatric Severe Bacterial Pneumonia Caused by *Klebsiella pneumoniae*

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Background: *Klebsiella pneumoniae* is a major pathogen in pediatric pneumonia. Procalcitonin (PCT) distinguishes between Gram positive and Gram negative infections but lacks data on *K. pneumoniae* infection's relationship with PCT levels in children. Therefore, this study was conducted to investigate the serum PCT levels in children with *K. pneumoniae* infection.

Materials and methods: A cross-sectional study was conducted on 61 pediatric subjects with the age of 2-59 months with severe bacterial pneumonia. Blood and sputum samples were collected and analyzed for PCT and cultured for 24 hours. PCT levels and *K. pneumoniae* infection were statistical analyzed with chi-square and logistic regression. Receiver operating characteristic (ROC) analysis was used to determine the PCT cut-off specific to *K. pneumoniae*.

Results: *K. pneumoniae* was identified in 33%. Median PCT levels were significantly higher in the *K. pneumoniae* group ($p < 0.05$). A PCT cut-off of 0.725 ng/mL yielded 70% sensitivity, 70.7% specificity, negative predictive value (NPV) of 82.9%, and area under the receiver operating characteristic curve (AUROC) of 0.74. Elevated PCT was significantly associated with *K. pneumoniae* infection with Odds ratio (OR) of 12.08, 95% Confidence Interval (CI): 2.54-57.36; $p = 0.002$.

Conclusion: Along with *K. pneumoniae* infection, serum PCT levels was elevated, supporting its potential as a biomarker for early diagnosis.

Keywords: *K. pneumoniae*, procalcitonin, bacterial pneumonia, pediatric

Introduction

Pneumonia is a leading cause of morbidity and mortality among children under five worldwide, contributing to over 800,000 deaths annually. In Indonesia, it remains one of five causes of death in this age group.^{1,2} Accurate identification of the causative pathogen is critical for guiding effective antibiotic therapy, yet microbiological cultures are often delayed or unavailable.^{3,4}

Pneumonia is an acute infection of the lung tissue, affecting the alveoli and interstitial spaces. In Indonesia, childhood pneumonia is commonly caused by non-typeable *Haemophilus influenzae*, respiratory syncytial virus (RSV), *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, and influenza virus. In contrast, *Staphylococcus aureus* and *K. pneumoniae* are the most common bacterial causes of childhood pneumonia in Saudi.⁴

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Early diagnosis and prompt initiation of antibiotic therapy significantly influence clinical outcomes. However, diagnosing bacterial pneumonia in children remains challenging. Clinical symptoms, physical examinations, and supportive tests, such as chest X-rays and laboratory investigations often yield non-specific results regarding the etiology of pneumonia. Identifying the causative agent is crucial for optimizing antibiotic therapy and monitoring local resistance patterns. Although bacterial cultures remain the gold standard for diagnosis, require several days and are not always accessible. This limitation underscores the need for alternative to predict bacterial etiology. One such biomarker under investigation is procalcitonin (PCT).^{3,4}

K. pneumoniae is a Gram negative, encapsulated bacterium recognized for its antibiotic resistance and high virulence. Infections caused by *K. pneumoniae* are increasingly reported in both community-acquired and hospital-acquired pediatric pneumonia.^{2,5,7} Procalcitonin, a precursor of calcitonin, has emerged as a promising biomarker for distinguishing between Gram-positive and Gram-negative bacterial infections. Some studies suggest that Gram-negative infections, including *K. pneumoniae*, may induce higher PCT levels than Gram-positive bacteria. For instance, PCT levels are significantly elevated in *Escherichia coli* and *K. pneumoniae* infections compared to *Staphylococcus epidermidis*. However, conflicting evidence indicates that PCT levels can also be higher in *Streptococcus pneumoniae* (a Gram-positive bacterium) than in certain Gram-negative infections. The mechanisms underlying these differences in PCT response remain poorly understood.^{7,10} Therefore, this study was conducted to determine the serum PCT levels in children with *K. pneumoniae*.

Materials and methods

Study Design and Research Subject

A cross-sectional study was conducted from June to December 2024 on 61 pediatrics subjects aged 2-59 months with severe bacterial pneumonia based on World Health Organization (WHO) criteria and positive cultures results. Subjects who had major surgery, burns, autoimmune disorders, or cirrhosis were excluded from the study.

The subject characteristics including were gestational age, sex, birth weight, age, exclusive breastfeeding, immunization status, nutritional status, exposure to indoor air pollution, and previous antibiotic therapy, were

recorded. Prior to the study, subject's parents have agreed and signed the written informed consent for participating in the study willingly, including the blood sample and sputum collection. The study protocol was approved by The Ethical Committee of Dr. Moewardi Hospital, Surakarta, Jawa Tengah, Indonesia with the (Ethical Clearance Number: 1.371/V/HREC/2024).

Sputum Sample Preparation and *K. pneumoniae* Identification

Samples were collected within the first 24 hours of hospitalization. If sputum could not be obtained through spontaneous coughing, induction of sputum was performed. The recommended sputum was mucoid purulent with a volume of 3-5 mL. The sputum sample should be sent to the microbiology laboratory within less than 2 hours at room temperature. In cases of delayed processing, the sample was stored at 2-8 C for a maximum of 24 hours. Sputum was examined with a microscope and Vitek-2 compactsystem (Vitek-2 compact, bioMerieux Asean Enseval Building, Jakarta, Indonesia). The Vitek-2 system uses a panel of 47 biochemical reactions, including 19 enzymatic tests, interpreted kinetically.

Measurement of PCT

Three mL venous blood samples from each subject within the first 24 hours of hospitalization were placed in tubes without anticoagulant. After 15 minutes of centrifuging the blood sample at 4000 rpm, the serum was extracted and analyzed. PCT levels were measured using the VIDAS® system (bioMerieux, ASEAN Enseval Building, Jakarta, Indonesia) with the enzyme-linked fluorescent assay (ELFA) method. The specific enzyme used is alkaline phosphatase, which is conjugated to anti-procalcitonin antibodies. During the assay, this enzyme catalyzes the hydrolysis of the substrate 4-methylumbelliferyl phosphate to the fluorescent product 4-metmethylumbelliferyl, which is then measured at 450 nm. The fluorescence intensity is proportional to the concentration of procalcitonin in the sample. According to published clinical performance data, the VIDAS® B-R-A-H-M-S PCT assay demonstrates a sensitivity of 95.0% and a specificity of 97.3% for diagnosing sepsis at a cut-off of 0.3 ng/mL. The VIDAS® PCT assay has been validated for use in pediatric settings, including studies at Texas Children's Hospital, which demonstrated good precision (%CV <5% intra-assay), linearity, and correlation with clinical outcomes in children suspected of sepsis.

Statistical Analysis

Data were analyzed with SPSS version 26.00 (IBM Corporation, Armonk, NY, USA) using the bivariate analysis with Fisher's test and Chi-square to produce crude Odd Ratio (OR) values. The Mann-Whitney U test compared median PCT levels between groups. The cut-off of PCT based on the bacterial species *K. pneumoniae* was established using receiver operating characteristic (ROC) curve analysis. Sensitivity, specificity, positive and negative predictive values, and likelihood ratios were calculated. Adjusted ORs were obtained with logistic regression. A 95% confidence interval (CI) with a significance level of $p < 0.05$ was employed.

Results

Subject Characteristics

A total of 61 eligible subjects were enrolled in the current study. The subjects were predominantly of male infants under one year of age. Most subjects had low or very low birth weight, were born preterm (<37 weeks' gestation), had a history of non-exclusive breastfeeding, and had incomplete immunization status. The majority of subjects were classified as having poor nutritional status or malnutrition. A significant proportion of subjects were exposed to indoor air pollution, primarily from cigarette smoke.

Among all subjects, 20 cases (32.8%) were confirmed to have *K. pneumoniae* infection. Comparative analysis between the *K. pneumoniae*-positive and negative groups revealed that congenital heart disease (CHD) was the only characteristic showing a statistically significant association (15 subjects, $p < 0.05$) (Table 1).

K. pneumoniae Infection Elevated Procalcitonin Levels in Pediatric Pneumonia Patients

Subjects with *K. pneumoniae* infection demonstrated significantly had higher PCT levels compared to those without *K. pneumoniae* infection ($p = 0.003$), indicating a distinct biomarker profile associated with this pathogen (Table 2). The delta value in subject with *K. pneumoniae* infection was 0.155 ng/mL and subject without *K. pneumoniae* infection was 0.815 ng/mL. The range of PCT levels in subject with *K. pneumoniae* was 2.54 ng/ml and subject without *K. pneumoniae* was 1.95 ng/mL.

Table 1. Demographic and clinical characteristics of pediatric subjects with severe bacterial pneumonia, stratified by *K. pneumoniae* infection.

Parameter	n (%)	<i>K. pneumoniae</i> n (%)	Non- <i>K. pneumoniae</i> n (%)	p-value
Sex				
Male	32 (52.5)	11 (55.0%)	21 (51.2%)	0.781
Female	29 (47.5)	9 (45.0%)	20 (48.8%)	
Age				
<1 year	38 (62.3)	14 (70.0%)	24 (58.5%)	0.386
≥1 year	23 (37.7)	6 (30.0%)	17 (41.5%)	
Birth weight				
Normal	17 (27.9)	6 (30.0%)	11 (26.8%)	0.795
Low	44 (72.1)	14 (70.0%)	30 (73.2%)	
Exclusive breastfeeding				
No	38 (62.3)	14 (70.0%)	24 (58.5%)	0.386
Yes	23 (37.7)	6 (30.0%)	17 (41.5%)	
Immunization status				
Incomplete	35 (57.4)	15 (75.0%)	20 (48.8%)	0.052
Complete	26 (42.6)	5 (25.0%)	21 (51.2%)	
Nutritional status				
Wasted	32 (52.5)	12 (60.0%)	20 (48.8%)	0.041
Normal	29 (47.5)	8 (40.0%)	21 (51.2%)	
Gestational age				
≥37 weeks	16 (26.2)	5 (25.0%)	11 (26.8%)	0.879
<37 weeks	45 (73.8)	15 (75.0%)	30 (73.2%)	
Exposure to indoor air pollution				
Yes	50 (82.0)	15 (75.0%)	35 (85.4%)	0.479
No	11 (18.0)	5 (25.0%)	6 (14.6%)	
Previous antibiotic therapy				
Yes	15 (24.6)	3 (15.0%)	12 (29.3%)	0.344
No	46 (75.4)	17 (85.0%)	29 (70.7%)	
Congenital heart disease				
Yes	28 (45.9)	15 (75.0%)	13 (31.7%)	0.001*
No	33 (54.1)	5 (25.0%)	28 (68.3%)	
Mechanical ventilator				
Yes	25 (41.0)	8 (40.0%)	17 (41.5%)	0.913
No	36 (59.0)	12 (60.0%)	24 (58.5%)	

*Significant (Chi square/fisher exact test, $p < 0.05$).

Table 2. Comparison of PCT levels between subjects with and without *K. pneumoniae* infection.

<i>K. pneumoniae</i> infection	PCT levels		
	Min-Max	Median	p-value
Yes	0.39-2.93	0.88	0.003*
No	0.35-2.30	0.54	
Total	0.35-2.93	0.63	

*Significant (Mann-Whitney test, $p < 0.05$).**PCT Level Cut-Off of 0.725 ng/mL Predicted *K. pneumoniae* Infection in Pediatric Pneumonia**

ROC curve analysis was used to determine the optimal PCT cut-off level for identifying *K. pneumoniae* infection, yielding an area under the curve (AUC) of 0.740 (95% CI: 0.598-0.881). The optimal PCT threshold was established at 0.725 ng/mL, demonstrating a sensitivity of 70.0% (95% CI: 58.5-81.5) and specificity of 70.7% (95% CI: 59.3-82.1). The test showed a positive predictive value of 53.8% (95% CI: 41.3-66.4), negative predictive value (NPV) of 82.9% (95% CI: 73.4-92.3), positive likelihood ratio of 2.392 (95% CI: 1.321-3.462), negative likelihood ratio of 0.424 (95% CI: 0.300-0.548), and overall accuracy of 70.5% (95% CI: 59.0-81.9) (Figure 1).

***K. pneumoniae* Infection and Good Nutritional Status Independently Elevated PCT Levels in Pediatric Severe Bacterial Pneumonia**

Bivariate analysis of factors influencing PCT levels revealed that sex, birth weight, exclusive breastfeeding status, immunization history, gestational age, indoor air

pollution exposure, prior antibiotic therapy, and mechanical ventilation use showed no significant association with PCT elevation ($p > 0.05$; Table 3). However, three variables demonstrated statistically significant relationships with PCT levels: age < 1 year (OR 3.15; 95% CI 1.02-9.72), *K. pneumoniae* infection (OR 5.64; 95% CI 1.75-18.16), and good nutritional status (OR 0.28; 95% CI 0.09-0.80). Notably, subjects with *K. pneumoniae*-positive sputum cultures were 5.64 times more likely to exhibit PCT levels ≥ 0.725 ng/mL compared to culture-negative cases. Conversely, well-nourished subjects showed significantly lower odds (72% reduction) of elevated PCT compared to malnourished subjects, suggesting a complex interplay between nutritional status and biomarker response in severe bacterial pneumonia.

Following bivariate screening ($p < 0.25$), multivariate logistic regression analysis identified *K. pneumoniae* infection and nutritional status as independent predictors of elevated PCT levels (≥ 0.725 ng/mL) in pediatric severe bacterial pneumonia (Table 4). The analysis revealed that subjects with *K. pneumoniae* infection had 12.08 times higher odds of elevated PCT levels compared to those without infection. (OR=12.08; 95%CI 2.54-57.36; $p = 0.002$) Contrary to expectations, good nutritional status was independently associated with increased PCT levels. These findings demonstrate that while *K. pneumoniae* infection (OR=6.94; 95% CI 1.57-30.61; $p = 0.011$) strongly predicts PCT elevation, the relationship between nutritional status and PCT levels requires further investigation as it contradicts conventional understanding of biomarker behavior in malnutrition.

Discussion

This study examined severe bacterial pneumonia in a pediatric population, with 62.3% of cases in infants under 1 year and 52.5% in males. These findings align with a study reporting a median age of 9 months and 54.7% male predominance in pediatric pneumonia cases.^{11,12} Increased susceptibility in males may be due to developmental immunological differences, as females typically demonstrate stronger innate and adaptive immune responses.¹³⁻¹⁵ This biological advantage in females results in more effective infection clearance but also predisposes them to heightened inflammatory reactions and autoimmune conditions.

Notably, 73.8% of our subjects were premature infants, consistent with established evidence that prematurity

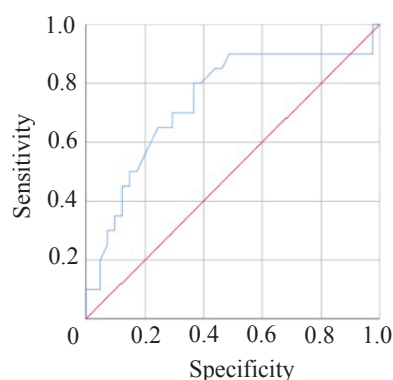
**Figure 1. ROC curve of serum PCT levels for predicting *K. pneumoniae* infection.**

Table 3. Bivariate analysis of factors associated with elevated serum PCT levels (≥ 0.725 ng/mL).

Parameter	PCT		OR	95%CI	p-value
	≥ 0.725 n(%)	< 0.725 n(%)			
Sex					
Male	15 (57.7)	17 (48.6)	0	0.52-4.01	0.481
Female	11 (42.3)	18 (51.4)			
Age					
<1 year	20 (76.9)	18 (51.4)	3.15	1.02-9.72	0.042*
≥ 1 year	6 (23.1)	17 (48.6)			
Birth weight					
Normal	6 (23.1)	11 (31.4)	0.65	0.21-2.08	0.472
Low	20 (76.9)	24 (68.6)			
Exclusive breastfeeding					
No	17 (65.4)	21 (60.0)	1.26	0.44-3.61	0.668
Yes	9 (34.6)	14 (40.0)			
Immunization status					
Incomplete	17 (65.4)	18 (51.4)	1.78	0.63-5.07	0.276
Complete	9 (34.6)	17 (48.6)			
Nutritional status					
Wasted	9 (34.6)	23 (65.7)	0.28	0.09-0.80	0.016
Normal	17 (65.4)	12 (34.3)			
Gestational age					
≥ 37 weeks	4 (15.4)	12 (34.3)	0.35	0.10-1.25	0.097
<37 weeks	22 (84.6)	23 (65.7)			
Exposure to indoor air pollution					
Yes	21 (80.8)	29 (82.9)	0.87	0.23-3.23	1.000
No	5 (19.2)	6 (17.1)			
Previous antibiotic therapy					
Yes	6 (23.1)	9 (25.7)	0.87	0.26-2.84	0.813
No	20 (76.9)	26 (74.3)			
Congenital heart disease					
Yes	14 (53.8)	14 (40.0)	1.75	0.63-4.88	0.283
No	12 (46.2)	21 (60.0)			
Mechanical ventilator					
Yes	13 (50.0)	12 (34.3)	1.92	0.68-5.41	0.217
No	13 (50.0)	23 (65.7)			
<i>K. pneumoniae</i> infection					
Yes	14 (53.8)	6 (17.1)	5.64	1.75-18.16	0.003*
No	12 (46.2)	29 (82.9)			

OR: Odds Ratio; CI: Confidence Interval; *Significant (Chi square/fisher's exact test, $p < 0.05$).

constitutes a significant risk factor for pneumonia due to incomplete transplacental antibody transfer during the final gestational weeks.¹⁶ In this study, demonstrated substantial comorbidities: 45.9% with congenital heart disease (CHD), 72.1% with low/very low birth weight, and 52.5% with malnutrition. These findings corroborate previous studies reporting CHD in 26.1% and malnutrition in 18.6% of pediatric pneumonia cases.^{11,17} The immunological compromise associated with malnutrition likely contributes to this increased susceptibility through impaired leukocyte phagocytic activity.

K. pneumoniae emerged as the predominant pathogen (32.9%) in our study, consistent with Asian epidemiological data showing its significant role in community-acquired pneumonia.¹⁸ The strong association between CHD and *K. pneumoniae* infection ($p < 0.05$) mirrors previous reports of 12-25% *K. pneumoniae* prevalence in CHD patients.¹⁹⁻²¹ This relationship may be explained by three key factors: (1) frequent healthcare exposures increasing acquisition risk, (2) invasive procedures facilitating pathogen entry, and (3) underlying cardiac compromise impairing host defenses. The particular virulence of *K. pneumoniae*, including biofilm formation and antimicrobial resistance patterns, further exacerbates infection risk in this vulnerable population.²²

The biomarker analysis revealed significantly elevated PCT levels in *K. pneumoniae* infections (median=0.88 ng/mL), supporting existing evidence of higher PCT in Gram-negative versus Gram-positive infections.²³⁻²⁵ ROC curve analysis established an optimal PCT cutoff of 0.725 ng/mL with 70.0% sensitivity, 70.7% specificity, and 70.5% overall accuracy. The strong negative predictive value

Table 4. Multivariate logistic regression analysis of independent factors associated with elevated PCT levels.

Parameter	OR	95%CI	p-value
Age (<1 year)	1.46	0.34-6.23	0.611
Nutritional status (normal)	6.94	1.57-30.61	0.011*
Gestational age (≥ 37 weeks)	0.48	0.09-2.58	0.395
Mechanical ventilator	2.65	0.67-10.52	0.165
<i>K. pneumoniae</i> infection	12.08	2.54-57.36	0.002*

OR: Odds Ratio; CI: Confidence Interval; *Significant (Chi square/fisher's exact test, $p < 0.05$)

(82.9%) suggests clinical utility in ruling out *K. pneumoniae* infection when PCT levels fall below this threshold.

Multivariate analysis identified two independent predictors of PCT elevation: *K. pneumoniae* infection (OR=12.08, $p=0.002$) and good nutritional status (OR=6.94, $p=0.011$). The paradoxical association with adequate nutrition may reflect malnutrition-induced immunosuppression blunting PCT response, as malnutrition is known to impair proinflammatory cytokine production.^{26,27} This finding underscores the importance of considering nutritional status when interpreting PCT levels for clinical decision-making.

While this study provides valuable insights into PCT as a biomarker for *K. pneumoniae* pneumonia, several methodological considerations should be noted. PCT sampling timing was not standardized relative to disease onset, and potential variations across different infection stages were not analyzed. These factors may introduce variability in the observed biomarker levels, as patients were enrolled at different phases of disease progression. Future investigations would benefit from protocol defined PCT measurements timed according to carefully documented symptom onset, which would enable more precise characterization of PCT kinetics in pediatric pneumonia.

Conclusion

K. pneumoniae infection elevates serum PCT levels in pediatric severe bacterial pneumonia, with median PCT levels significantly higher in infected subjects (0.88 ng/mL vs 0.54 ng/mL, $p=0.003$). The identified PCT cut-off of 0.725 ng/mL demonstrates clinically meaningful predictive value, correctly classifying 70.5% of cases. These findings support PCT's role as an early diagnostic biomarker for *K. pneumoniae* pneumonia, particularly valuable in settings where culture confirmation is delayed. The 12.08-fold greater likelihood of elevated PCT in infected children reinforces PCT's potential to guide timely antibiotic initiation while awaiting microbiological results.

Authors' Contributions

TK, DA, YH, and IA were involved in conceptualizing and planning the research. TK performed data acquisition and collection, and calculated the experimental data. TK also designed the figures. TK, DA, YH, and IA analyzed the data, drafted the manuscript, interpreted the results, and contributed to the critical revision of the manuscript.

Conflict of Interest

The authors declare that they have no conflicts of interest or competing interests related to the content of this manuscript.

References

1. World Health Organization [Internet]. Pneumonia in children. Geneva: WHO; ©2022 [cited 2023 Mar 4]. Available from: <https://www.who.int/news-room/fact-sheets/detail/pneumonia>.
2. Marangu D, Zar HJ. Childhood pneumonia in low-and-middle-income countries. *Paediatr Respir Rev*. 2019; 32(1): 3-9.
3. Torres A, Cilloniz C, Niederman MS, Menendez R, Chalmers JD, Wunderink RG, *et al*. Pneumonia. *Nat Rev Dis Primers*. 2021; 7(1): 1-25.
4. Wongo D, Wahjudi M. The construction of a multi-epitope vaccine against *K. pneumoniae* using in silico approach. *Mol Cell Biomed Sci*. 2023; 7(2): 90-7.
5. Verani JR, Blau DM, Gurley ES, Akelo V, Assefa N, Baillie V, *et al*. Child deaths caused by *K. pneumoniae* in sub-Saharan Africa and South Asia: a secondary analysis of Child Health and Mortality Prevention Surveillance (CHAMPS) data. *Lancet Microbe*. 2024; 5(2): 131-41.
6. Puspitasari D, Rusli EA, Husada D, Kartina L, Wongo D, Wahjudi M. *Escherichia coli* and *Klebsiella pneumoniae* as the most common bacteria causing catheter-associated urinary tract infection. *Mol Cell Biomed Sci*. 2021; 5(3): 121-6.
7. Akagi T, Nagata N, Miyaza H, Harada T, Takeda S, Yoshida Y, *et al*. Procalcitonin is not an independent predictor of 30-day mortality, albeit predicts pneumonia severity in patients with pneumonia acquired outside the hospital. *BMC Infect Dis*. 2019; 19(3): 1-10.
8. Fernandes CD, Arriaga MB, Costa MC, Costa MH, Vinhaes CL, Mattos PS, *et al*. Host inflammatory biomarkers of disease severity in pediatric community-acquired pneumonia: a systematic review and meta-analysis. *Open Forum Infect Dis*. 2019; 6(12): 1-13.
9. Stockmann C, Ampofo K, Killpack J, Williams D, Edwards KM, Grijalva CG, *et al*. Procalcitonin accurately identifies hospitalized children with low risk of bacterial community-acquired pneumonia. *J Pediatric Infect Dis Soc*. 2018; 7(1): 46-53.
10. Ekaputri DS, Sidiartha IGL, Pratiwi IGAP. Low total lymphocyte count as the risk of hospital-acquired malnutrition in children. *Mol Cell Biomed Sci*. 2021; 5(2): 68-73.
11. Lokida D, Farida H, Triasih R, Mardian Y, Kosasih H, Naysilla AM, *et al*. Epidemiology of community-acquired pneumonia among hospitalised children in Indonesia: a multicentre, prospective study. *BMJ Open*. 2022; 12(6): 1-13.
12. Zaki A, Abdelwahab S, Awad M. Bacterial pathogens in sputum of children with community-acquired pneumonia, unexpected results: a single hospital-based study. *Alex J Pediatr*. 2021; 34(2): 183-9.
13. Williams DJ, Zhu Y, Grijalva CG, Self WH, Harrell FE Jr, Reed C, *et al*. Predicting severe pneumonia outcomes in children. *Pediatrics*. 2016; 138(4): 1-11.
14. Yan X, Li F, Wang X, Yan J, Zhu F, Tang S, *et al*. Neutrophil to lymphocyte ratio as prognostic and predictive factor in patients with coronavirus disease 2019: a retrospective cross-sectional study. *J Med Virol*. 2020; 92(11): 2573-81.
15. Klein SL, Flanagan KL. Sex differences in immune responses. *Nat Rev Immunol*. 2016; 16(10): 626-38.
16. Zar HJ, MacGinty R, Workman L, Burd T, Smith G, Myer L, *et al*.

- K. pneumoniae lower respiratory tract infection in a South African birth cohort: a longitudinal study. *Int J Infect Dis.* 2022; 121(1): 31-8.
17. Elvionita C, Sari IP, Nuryastuti T. Evaluation of the rationality of clinical outcomes of antibiotic use and patterns of bacterial resistance to antibiotics in children with pneumonia. *Farmaseutik.* 2023; 19(1): 131-9.
 18. Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, *et al.* Diagnosis and treatment of adults with community-acquired pneumonia: an official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med.* 2019; 200(7): 45-67.
 19. Yakimishen OO, Boyko SM, Malysheva TA, Goidra AP, Truba IP. Analysis of cases of multidrug-resistant K. pneumoniae infection in children with congenital heart defects. *Ukr J Cardiovasc Surg.* 2022; 30(1): 21-6.
 20. Esmail O, Hassan BA, Sarhan D, Saad A, El-Hindawy E. Pneumonia in children with congenital heart disease: bacterial spectrum and risk of bacteremia. *Zagazig Univ Med J.* 2024; 30(5): 1709-17.
 21. Sadeeva Z, Novikova IE, Lazareva AV, Alyabyeva NM, Karaseva OV, Yanushkina OG, *et al.* Pediatric bacteremia and CNS infections associated with K. pneumoniae: molecular genetic characteristics and clinical features. *Russ J Infect Immun.* 2023; 13(6): 1117-28.
 22. Yakimishen OO, Boyko SM, Malysheva TA, Goidra AP, Truba IP. Analysis of cases of multidrug-resistant K. pneumoniae infection in children with congenital heart defects. *Ukr J Cardiovasc Surg.* 2022; 30(1): 1-6.
 23. StatPearls [Internet]. Typical bacterial pneumonia. Treasure Island (FL): StatPearls Publishing; ©2025 [cited 2023 Apr 24]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK534295/>.
 24. Yadav KK, Awasthi S. Childhood pneumonia: what's unchanged, and what's new? *Indian J Pediatr.* 2023; 90(7): 693-9.
 25. Tujula B, Hamalainen S, Kokki H, Pulkki K, Kokki M. Review of clinical practice guidelines on the use of procalcitonin in infections. *Infect Dis (Lond).* 2020; 52(4): 227-34.
 26. Sturgeon JP, Njunge JM, Bourke CD, Gonzales GB, Robertson RC, Bwakura DM, *et al.* Inflammation: the driver of poor outcomes among children with severe acute malnutrition? *Nutr Rev.* 2023; 81(12): 1636-52.
 27. Phiri TN, Mutasa K, Rukobo S, Govha M, Mushayanembwa P, Mwakamui S, *et al.* Severe acute malnutrition promotes bacterial binding over proinflammatory cytokine secretion by circulating innate immune cells. *Sci Adv.* 2023; 9(44): 1-9.