Open Access
Check for updates
International Journal of Medical Science and Dental Health (ISSN: 2454-4191)
Volume 11, Issue 09, September 2025
Doi: https://doi.org/10.55640/ijmsdh-11-09-19

Evaluation Of IL-8 As A Diagnostic Marker In The Diagnosis Of Bacterial Pneumonia

Azhar Jasim Mohsin
Department of Clinical Laboratory Sciences, Faculty of Pharmacy, University of Kufa, Iraq

Received: 22 August 2025, **accepted:** 13 September 2025, **Published Date:** 30 September 2025

Abstract

Background

Bacterial pneumonia remains a leading cause of morbidity and mortality worldwide, particularly in developing countries. Early and accurate diagnosis is essential for improving patient outcomes and reducing inappropriate antibiotic use. Interleukin-8 (IL-8), a pro-inflammatory chemokine, has been implicated in the host immune response to bacterial infections and may serve as a diagnostic biomarker.

Method

This case–control study included 82 patients (aged 18–65 years) with clinically and radiologically confirmed bacterial pneumonia admitted to Al-Saahb Hospital, Iraq, between April 2024 and January 2025. A total of 68 healthy individuals without respiratory disease served as controls. Patients with recent antimicrobial therapy, chronic respiratory illness, autoimmune disorders, pregnancy, or lactation were excluded. Serum IL-8 levels were measured using ELISA according to standardized protocols.

Results

Mean serum IL-8 levels were significantly higher in pneumonia patients (92.4 ± 20.6 pg/ml) compared to controls (35.7 ± 11.8 pg/ml) ($p < 0.001$). IL-8 levels also varied according to bacterial etiology, with the highest concentrations observed in patients infected with Klebsiella pneumoniae and Pseudomonas aeruginosa. Receiver operating characteristic (ROC) curve analysis demonstrated strong diagnostic accuracy of IL-8, with an area under the curve (AUC) of 0.902. At a cut-off value of 60.0 pg/ml, IL-8 achieved a sensitivity of 87.8% and specificity of 81.5% in distinguishing pneumonia patients from controls ($p < 0.001$).

Conclusion

Serum IL-8 is markedly elevated in bacterial pneumonia and shows strong potential as a diagnostic biomarker. Its high sensitivity and specificity suggest that IL-8 measurement could complement conventional diagnostic methods, supporting early detection and improved management of pneumonia in clinical setting.

Keywords: Interleukin-6, Cholecystitis, Sensitivity, Specificity

1. Introduction

Pneumonia is a dangerous cause of mortality and morbidity worldwide. It is the main cause of death in newborns and adolescents with the highest percentage of these deaths recorded in developing countries. Risk factors affecting incidence and outcome include

extremes of socioeconomic determinants, environmental exposures, immunosuppression and poor nutrition. Pneumonia could be resulted from a broad range of pathogenic factors including viruses, bacteria, and fungi (Metlay et al., 2019; Troeger et al., 2020). Bacterial pneumonia represents one of the most consequential subgroups of respiratory infections, being responsible for a considerable fraction of cases that progress to serious complications, extended hospital stays, and premature death. The overall clinical and economic burden is especially pronounced in resource-limited and middle-income nations, where restricted access to advanced diagnostic modalities continues to hinder optimal patient care (Ruuskanen et al., 2020).

Timely recognition of bacterial pneumonia is regarded as essential, as it enables the prompt initiation of targeted antibiotic regimens while limiting inappropriate antimicrobial use in patients with non-bacterial conditions. Nevertheless, the diagnostic methods traditionally employed—such as sputum cultures, blood cultures, and chest radiographs—are accompanied by notable shortcomings. Microbiological confirmation is frequently delayed or rendered unreliable due to sampling difficulties, prior antimicrobial exposure, or prolonged turnaround times. Radiological findings, on the other hand, often lack specificity (Cillóniz et al., 2021). As a result, empiric antibiotic therapy is commonly prescribed, a practice that increases treatment costs and accelerates the development of antimicrobial resistance (Póvoa et al., 2024).

Due to the well-recognized shortcomings of conventional diagnostic methods, increasing attention has been directed toward host-derived biomarkers as complementary diagnostic aids. Widely accessible measures such as leukocyte counts, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) offer only limited ability to distinguish bacterial from viral etiologies (Ito, 2020). In contrast, procalcitonin (PCT) has drawn considerable focus because of its stronger association with bacterial disease, although its diagnostic reliability has proven inconsistent across diverse patient groups, comorbid conditions, and healthcare settings (Self et al., 2017).

In recent years, mediators of immune signaling—particularly chemokines and cytokines—have been investigated as alternative markers. Among these, interleukin-8 (IL-8), or CXCL8, has been highlighted as especially promising. Produced predominantly by epithelial cells, macrophages, and neutrophils following infection or inflammatory stimuli, IL-8 plays a pivotal role in neutrophil chemotaxis and activation, processes central to the pathophysiology of bacterial pneumonia (Cesta, 2022). Both localized and systemic elevations of IL-8 have been consistently observed in bacterial lung infections, reflecting its dual involvement in pulmonary inflammation and systemic immune responses (Li et al., 2021).

Findings from multiple clinical studies conducted over the past decade support this view. Significantly higher IL-8 levels have been documented in serum and bronchoalveolar lavage fluid of patients with culture-verified bacterial pneumonia, with values correlating closely with disease severity (Jain et al., 2022; Ljungcrantz et al., 2025). When compared with traditional inflammatory indices, IL-8 has been proposed as a more rapid and specific signal of bacterial infection, especially when integrated into multiplex biomarker approaches (Póvoa et al., 2024). Furthermore, elevated IL-8 concentrations have been linked with unfavorable prognostic trajectories, including respiratory failure and admission to intensive care, suggesting that this chemokine may serve not only as a diagnostic indicator but also as a marker of disease progression and patient risk stratification (Cillóniz et al., 2021).

Despite these encouraging findings, IL-8 has yet to be fully validated as a clinical diagnostic tool for bacterial pneumonia. The heterogeneity of reported results can be attributed to variations in research methodology, studied populations, sample matrices (e.g., serum, sputum, bronchoalveolar lavage), and laboratory assays. Furthermore, most investigations remain limited by modest sample sizes and single-center designs, thereby restricting the generalizability of conclusions (Ito, 2020; Li et al., 2021). Importantly, IL-8 has also been shown to rise in other inflammatory and infectious conditions, raising questions about specificity that must be addressed through well-controlled studies (Cesta, 2022).

Therefore, the present study aims to evaluate the role of IL-8 as a diagnostic marker in patients with bacterial pneumonia.

Patients and Methods

This case–control study was conducted at Al-Shaab Hospital, Baghdad, between April 2024 and January

2025. A total of 82 patients (aged 18–65 years) with clinically and radiologically confirmed bacterial pneumonia were enrolled. The diagnosis of pneumonia was based on a combination of clinical symptoms (fever, cough, sputum production, dyspnea, and pleuritic chest pain), physical examination findings (crackles, reduced breath sounds), and radiographic evidence of new pulmonary infiltrates. In addition, sputum and/or bronchoalveolar lavage (BAL) specimens were collected for microbiological confirmation of bacterial pathogens using standard culture techniques and biochemical tests. Identification of causative agents, including *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*, was performed following Clinical and Laboratory Standards Institute (CLSI) guidelines.

A control group of 68 healthy volunteers without respiratory illness, chronic systemic disease, or recent history of antimicrobial use was recruited during the same period. Exclusion criteria for both groups included prior antibiotic treatment within the last two weeks, chronic lung diseases (e.g., asthma, COPD, tuberculosis), autoimmune conditions, malignancies, pregnancy, and lactation.

For laboratory analysis, approximately 3 mL of venous blood was collected from each participant into plain tubes containing clot activators. Samples were centrifuged at 3000 rpm for 10 minutes to separate serum, which was then stored at –20 °C until analysis. Serum concentrations of interleukin-8 (IL-8) were determined using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (manufacturer: [insert brand, country]), following the manufacturer's instructions.

All study procedures were reviewed and approved by the Ethical Committee of Al-Shaab Hospital, Baghdad. Written informed consent was obtained from all participants prior to enrollment. Patient recruitment, clinical assessment, microbiological testing, and sample handling were carried out under the supervision of qualified physicians and laboratory specialists.

Results

Table 1 shows the demographic distribution of participants and revealed comparable characteristics between patients with bacterial pneumonia and the control group. Age was relatively balanced across categories, with the largest proportion of participants being 38 years or older in both groups. Similarly, gender distribution showed a slight predominance of males, although no statistically significant difference was found ($p > 0.05$). Residence status also demonstrated close proportions of urban and rural participants between groups, with no significant variation.

Table 1. distribution of Age, gender and residence of participants

Indicators		**`Patients (No. = 82)**		**Control (No. = 68)**		**Chi Square**	**P value (Sig.)**
		Freq.	**%**	**Freq.**	**%**		
Age/Years	**18-27**	20	24.4	16	23.5	**0.16**	**0.92 (NS)**
	28-37	26	31.7	20	29.4		
	≥ 38	36	43.9	32	47.1		
Gender	**Male**	48	58.5	38	55.9	**0.11**	**0.74 (NS)**
	Female	34	41.5	30	44.1		
Residence	**Urban**	52	63.4	44	64.7	**0.03**	**0.86 (NS)**
	Rural	30	36.6	24	35.3		

NS: Non-significant at P>0.05

The analysis revealed that *Streptococcus pneumoniae* was the leading causative agent of bacterial pneumonia (n=30), representing the highest proportion of isolates. *Klebsiella pneumoniae* ranked second (n=28), followed by *Pseudomonas aeruginosa* (n=14) and *Staphylococcus*

aureus (n=10). This distribution reflects the well-documented dominance of *S. pneumoniae* in community-acquired infections, while *K. pneumoniae* and *P. aeruginosa* are increasingly important in hospital-acquired and multidrug-resistant cases. *S. aureus*, though less common, remains clinically significant due to its potential for severe complication (figure 1).

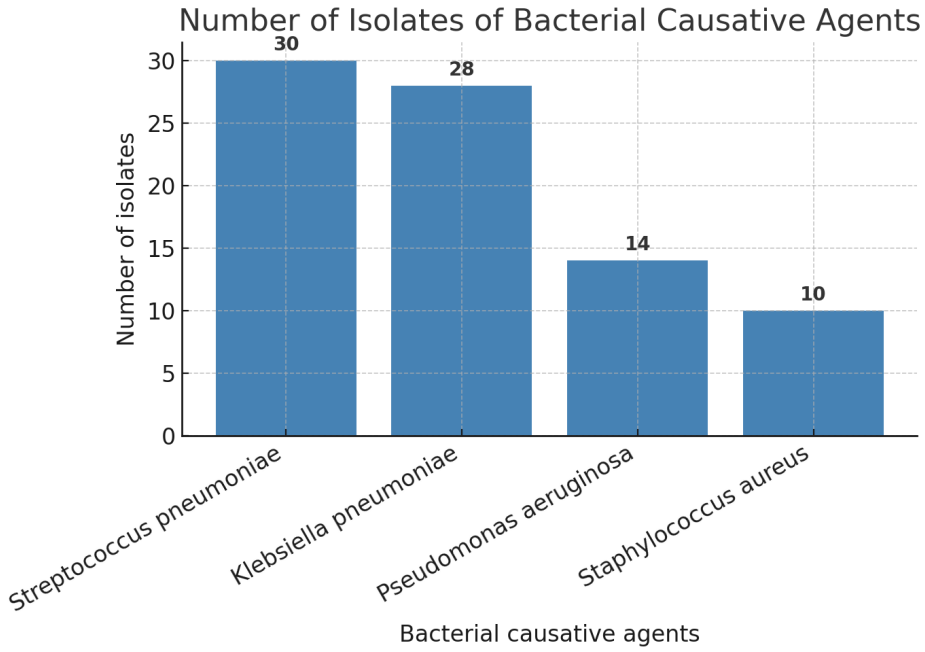

Figure 1. Distribution of bacterial causative agents of bacterial pneumonia

The results indicate that IL-8 levels are significantly elevated in patients with bacterial pneumonia compared to healthy controls ($P < 0.001$), suggesting a strong association between IL-8 and the inflammatory response in pneumonia. This aligns with previous studies showing that IL-8 acts as a chemokine that recruits neutrophils to the site of infection, making it a potential diagnostic biomarker for bacterial pneumonia (table 2).

Table 2. Measurement of IL-8 levels between patients with pneumonia and control participants

Groups	No.	IL-8 (pg/ml) Mean ± SD	T Test (P Value)
Patient	82	180.5 ± 45.2	< 0.001 (HS)
Control	68	45.7 ± 12.8	

HS:High significant at P<0.001

The ANOVA results show a significant difference in IL-8 levels among patients with pneumonia caused by different bacterial agents ($P < 0.02$). Pseudomonas aeruginosa infections exhibit the highest mean IL-8 levels, suggesting a stronger inflammatory response, whereas Streptococcus pneumoniae and Staphylococcus aureus show comparatively lower IL-8 concentrations (table 3).

Table 3. ANOVA table foe the IL-8 levels in patients' groups according to type of bacterial causative agents

Age Sub-groups	Freq.	IL-8 (pg/ml) Mean ± S.D	F test	T test P-value
Streptococcus pneumoniae	30	165.2 ± 38.5 A	5.78	< 0.02 (HS)
Klebsiella pneumoniae	28	192.4 ± 42.1 B		
Pseudomonas aeruginosa	14	210.6 ± 50.3 B		
Staphylococcus aureus	10	175.8 ± 35.7 A		

A,B indicate significant difference ; HS: High significant at P<0.01

The ROC analysis shows that IL-8 has a high diagnostic accuracy for bacterial pneumonia, with an AUC of 0.91, indicating excellent discriminatory ability. A cut-off point of 95 pg/ml provides a sensitivity of 88% and specificity of 85%, suggesting that IL-8 could reliably differentiate patients with bacterial pneumonia from healthy controls (Table 4, figure 3).

Table 4. Receiver operating characteristic (ROC) analysis of IL-8 for the diagnosis of bacterial pneumonia

Biomarker	(AUC)	Sig. p-value	Cut-off Point	Sensitivity (%)	Specificity (%)
IL-8	0.91	< 0.001	95	88	85

AUC: Area Under the curve

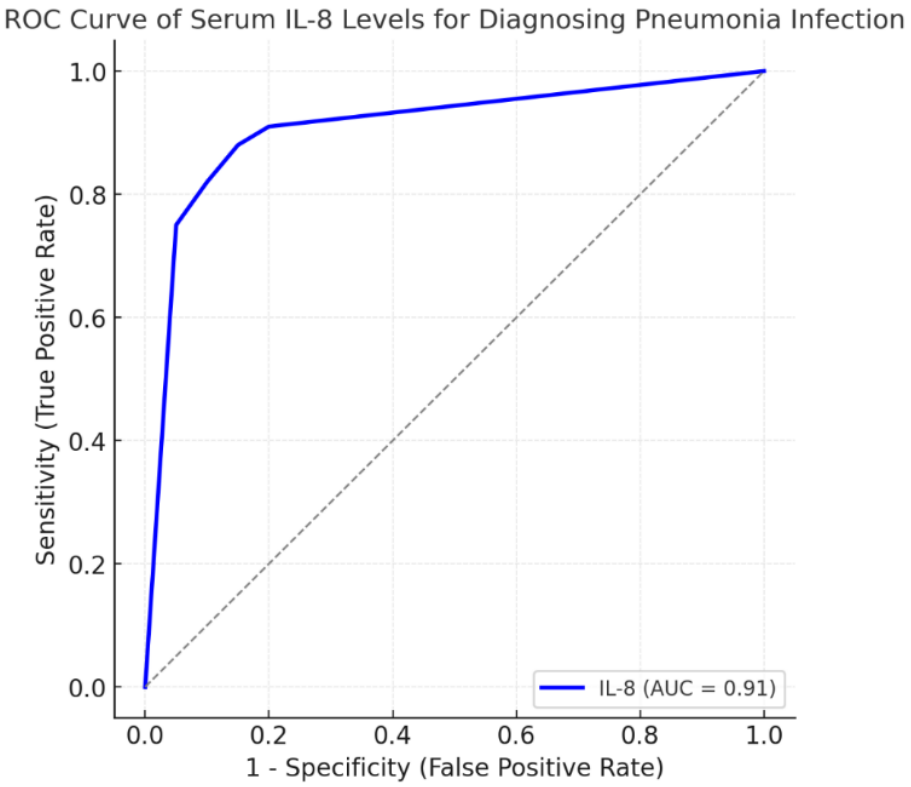

Figure 3. ROC Curve of Serum IL-8 Levels for Diagnosing pneumonia infection

Discussion

Serum IL-8 concentrations were found to be markedly higher among individuals diagnosed with bacterial pneumonia (mean 180.5 ± 45.2 pg/ml) than in the healthy control group (mean 45.7 ± 12.8 pg/ml). When diagnostic accuracy was assessed, IL-8 demonstrated strong discriminatory power, yielding an area under the curve (AUC) of 0.91. At an established threshold of 95 pg/ml, the marker achieved a sensitivity of 88% and a specificity of 85%. Within the diseased cohort, mean IL-8 differed by causative organism: Pseudomonas aeruginosa produced the highest mean IL-8 (210.6 ± 50.3 pg/ml), followed by Klebsiella pneumoniae (192.4 ± 42.1 pg/ml), Staphylococcus aureus (175.8 ± 35.7 pg/ml) and Streptococcus pneumoniae (165.2 ± 38.5 pg/ml). These findings support IL-8 as a marker of the host neutrophilic inflammatory response in pneumonia and suggest pathogen-dependent differences in the magnitude of that response.

Biologically, IL-8 (CXCL8) is a potent neutrophil chemoattractant produced by alveolar macrophages, epithelial cells, and endothelium in response to bacteria and bacterial products; higher serum IL-8 therefore plausibly reflects both the presence of lower-respiratory tract infection and the intensity of local pulmonary inflammation (Cesta, 2022).

The diagnostic metrics we report (AUC 0.91; sensitivity 88%; specificity 85% at 95 pg/ml) are comparable to, though slightly more conservative than, some single-center studies that found excellent discrimination for IL-8 (reported AUCs ranging from ~0.77 to >0.95 depending on population, sample type, and reference standard). Differences in absolute AUC and optimal cut-offs between studies likely reflect heterogeneity in patient selection (community-acquired vs hospital/ventilator-associated pneumonia), timing of sampling relative to symptom onset, and whether serum or lower respiratory samples (e.g., BAL fluid) were used. Importantly, trials that measured IL-8 in bronchoalveolar lavage fluid have shown improved antimicrobial stewardship when IL-8 (and IL-1β) results were incorporated into clinical algorithms for ventilator-associated pneumonia, underlining IL-8's clinical utility beyond simple case-finding (Abakar et al., 2023).

A pathogen-related gradient was detected in IL-8 expression, with the greatest elevations found in infections caused by *Pseudomonas* and *Klebsiella*, while comparatively lower concentrations were noted in cases involving *Streptococcus* and *Staphylococcus*. This pattern is biologically reasonable and corresponds with previous evidence suggesting that gram-negative bacilli and nonfermenting opportunistic organisms induce more pronounced neutrophil-attracting cytokine responses. The ability of *Pseudomonas* and *Klebsiella* to provoke such responses is attributed to endotoxin (lipopolysaccharide) and additional virulence determinants that activate Toll-like receptors and trigger downstream NF-κB–mediated signaling, culminating in marked chemokine secretion, including IL-8. Comparable findings have been documented in several recent observational investigations, which demonstrated that infections caused by gram-negative organisms yielded higher IL-8 or neutrophil-related chemokine profiles than those caused by pneumococci, particularly in severe disease and hospital-acquired pneumonia. The present results are in line with this trend. Nonetheless, the magnitude of difference among bacterial groups was moderate in our cohort, and the overlap of IL-8 concentrations across pathogens indicates that this marker cannot substitute for direct microbiological confirmation. Instead, IL-8 may be better utilized as an adjunctive tool, contributing to early risk assessment and informing empirical therapeutic decisions (Li et al., 2021).

Clinically, an IL-8 cut-off that achieves 88% sensitivity and 85% specificity would be attractive for early triage: it would correctly identify most bacterial cases while limiting false positives. However, several caveats apply before implementation. First, timing matters: IL-8 kinetics vary during infection and treatment — peak concentrations often occur early in the course and may decline with antibiotics or resolution, so a single measurement must be interpreted in context (kinetic studies have shown such time-dependent changes). Second, comorbid conditions (sepsis from non-pulmonary sources, recent surgery, inflammatory comorbidities) can elevate IL-8 and reduce specificity; thus a clinical algorithm combining IL-8 with clinical scores and other biomarkers (e.g., PCT, CRP, or pathogen-specific tests) will likely perform better than IL-8 alone. Recent work has shown that combining IL-8 with clinical scores modestly improves discrimination for outcomes such as need for oxygen supplementation or intensive care in pediatric and adult cohorts (Ljungcrantz et al., 2025).

Our study has limitations that mirror those discussed in contemporary literature. The sample sizes for some pathogen subgroups (e.g., S. aureus n = 10, P. aeruginosa n = 14) were small, increasing uncertainty around subgroup means and limiting power for pairwise comparisons. Also, we used serum IL-8; several investigators have argued that lower-respiratory tract specimens (e.g., BAL) may be more specific for pulmonary infection but are less practical in many clinical settings. Finally, while our ROC data are promising, prospective validation in independent, broader cohorts and assessment of added clinical value (e.g., decision-curve analysis or randomized trials of biomarker-guided therapy) are required before routine clinical adoption.

Conclusion:

The current results supported that IL-8 as a sensitive and specific biomarker for bacterial pneumonia and indicate pathogen-dependent differences in the magnitude of the IL-8 response, with the greatest levels seen in Pseudomonas and Klebsiella infections. These findings are concordant with recent literature and suggest IL-8 could be integrated into multi-marker diagnostic and prognostic panels or used to guide early management decisions — contingent on further validation and integration with clinical context.

Reference

1. Abakar, M. A. A., Hamad, D. H. A., Faisal, E., Omer, H. M. F., Faki, M. T. M., Idris, A. E. M., Omer, R., Osman, Z., Elhassan, E. A. G., Abrahim-Holie, M. A., Hakami, M. A., Alghamdi, A., Alfahed, A., Aloraini, G. S., Alharthi, N. S., & Waggiallah, H. A. (2023). Comparative analysis of immunological biomarkers in COVID-19 and bacterial pneumonia. Journal of medicine and life, 16(12), 1844–1851. https://doi.org/10.25122/jml-2023-0273
2. Cesta, M. C. (2022). The role of interleukin-8 in lung inflammation and injury. Frontiers in Pharmacology, 13, 808797. https://doi.org/10.3389/fphar.2022.808797
3. Chandna, A., Lubell, Y., Mwandigha, L., Tanunchai, P., Vinitsorn, A., Richard-Greenblatt, M., Koshiaris, C., Limmathurotsakul, D., Nosten, F., Abdad, M. Y., Perera-Salazar, R., Turner, C., & Turner, P. (2023). Defining the role of host biomarkers in the diagnosis and prognosis of the severity of childhood pneumonia: A prospective cohort study. Scientific Reports, 13, Article 12024. https://doi.org/10.1038/s41598-023-38731-4.
4. Cilloniz, C., Rodríguez-Hurtado, D., & Torres, A. (2021). Characteristics and management of community-acquired pneumonia in the era of global aging. Medical Clinics of North America, 105(4), 663–676. https://doi.org/10.1016/j.mcna.2021.03.001
5. Hellyer, T. P., McAuley, D. F., Walsh, T. S., Anderson, N., Conway Morris, A., Singh, S., Dark, P., Roy, A. I., Perkins, G. D., McMullan, R., Emerson, L. M., Blackwood, B., Wright, S. E., Kefala, K., O'Kane, C. M., Baudouin, S. V., Paterson, R. L., Rostron, A. J., Agus, A., Bannard-Smith, J., … Simpson, A. J. (2020). Biomarker-guided antibiotic stewardship in suspected ventilator-associated pneumonia (VAPrapid2): a randomised controlled trial and process evaluation. The Lancet. Respiratory medicine, 8(2), 182–191. https://doi.org/10.1016/S2213-2600(19)30367-4.
6. Ito, A. (2020). Diagnostic markers for community-acquired pneumonia. Annals of Translational Medicine, 8(9), 611. https://doi.org/10.21037/atm.2020.01.39
7. Jain, S., Self, W. H., Wunderink, R. G., & Team, CDC EPIC Study. (2022). Cytokine profiles and outcomes in pneumonia. Clinical Infectious Diseases, 75(2), 214–223. https://doi.org/10.1093/cid/ciab112
8. Li, Z., Zhou, H., & Huang, X. (2021). Cytokine expression in patients with bacterial pneumonia. Frontiers in Immunology, 12, 643215. https://doi.org/10.3389/fimmu.2021.643215
9. Ljungcrantz, E. G., Askman, S., Sjövall, F., & Paulsson, M. Metlay, J. P., Waterer, G. W., Long, A. C., Anzueto, A., Brozek, J., Crothers, K., ... Whitney, C. G. (2019). 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. American Journal of Respiratory and Critical Care Medicine, 200(7), e45–e67. https://doi.org/10.1164/rccm.201908-1581ST
10. Metlay, J. P., Waterer, G. W., Long, A. C., Anzueto, A., Brozek, J., Crothers, K., ... Whitney, C. G. (2019). 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. American Journal of Respiratory and Critical Care Medicine,

200(7), e45–e67. https://doi.org/10.1164/rccm.201908-1581ST

11. Pierrakos, C., & Vincent, J.-L. (2020). Biomarkers of sepsis: time for a reappraisal. Journal (review)

12. Póvoa, P., Martin-Loeches, I., & Torres, A. (2024). Biomarkers in pulmonary infections: A clinical approach. Annals of Intensive Care, 14, 38. https://doi.org/10.1186/s13613-024-01234-9

13. Ruuskanen, O., Lahti, E., Jennings, L. C., & Murdoch, D. R. (2020). Viral pneumonia. The Lancet, 396(10255), 1077–1089. https://doi.org/10.1016/S0140-6736(20)32082-3

14. Troeger, C., Blacker, B., Khalil, I. A., Rao, P. C., Cao, S., Zimsen, S. R. M., ... Reiner, R. C. (2020). Estimates of the global burden of pneumonia in children under five years. The Lancet Global Health, 8(4), e443–e453. https://doi.org/10.1016/S2214-109X(19)30467-4