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**ORIGINAL RESEARCH** **INTENSIVE CARE**

# Combination of interleukin-6 and C-reactive protein levels as predictive biomarkers for early diagnosis of community-acquired pneumonia in ICU patients

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## ABSTRACT

**Background & objective:** Pneumonia is a leading cause of morbidity and mortality globally, accounting for 15.2% of deaths in Malaysia in 2023. Community-acquired pneumonia (CAP) poses diagnostic challenges due to the non-specificity of clinical presentations and inconsistencies in imaging interpretation. This study evaluates the diagnostic utility of biomarker interleukin-6 (IL-6), C-reactive protein (CRP) and procalcitonin (PCT), individually and in combination, to improve the diagnosis of CAP in critically ill patients.

**Methodology:** This prospective cohort study was conducted in an intensive care unit. Adult patients admitted with dyspnea and respiratory failure were recruited, with 33 patients classified as CAP by standardized definition, and 42 as non-CAP. Biomarker levels were assessed in both groups, and diagnostic performance was evaluated with optimum cutoff levels.

**Results:** Individually, IL-6, CRP and PCT showed poor diagnostic accuracy (AUC < 0.7). The IL-6 and CRP combination achieved the highest AUC (0.759, sensitivity 78%, specificity 67%). The IL-6 and PCT combination provided the highest sensitivity (91%) and negative predictive value (85%), aiding in ruling out CAP.

**Conclusion:** Combined biomarker evaluation enhances diagnostic accuracy for community-acquired pneumonia, providing a basis for early treatment. These findings warrant further multicenter validation to confirm their clinical applicability in community-acquired pneumonia diagnosis.

**Abbreviations:** CAP: community-acquired pneumonia, CRP: C-reactive protein, IL-6: interleukin-6, PCT: procalcitonin, ICU: intensive care unit

**Keywords:** Biomarker; Interleukin-6; C-Reactive Protein; Procalcitonin; Community-Acquired Pneumonia; Dyspmea; Respiratory Failure

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# 1. INTRODUCTION

Pneumonia remains a major cause of morbidity and mortality globally. In Malaysia, the principal cause of death in 2023 is pneumonia which account for about 15.2% of death. This aligns closely with the national ICU data that showed 15.6% of ICU admission were due to respiratory failure, with 44% of these cases were community-acquired pneumonia. The diagnosis of community-acquired pneumonia (CAP) has been a challenge due to the non-specificity of the symptoms and signs. The study by Jones et al highlights the diagnostic complexities and treatment ambiguities associated with CAP in the ICU setting.[1] This may result in either underdiagnosis or overdiagnosis of CAP as the clinical presentations alone have limited diagnostic accuracy. There are also no optimal assessment tools or scoring for diagnosing CAP, apart from confirmatory tests that rely on interpretation of changes in the radiological image. Even though the interpretation of the imaging tests is a basic skill for physicians, it is often subject to inconsistencies due to operator skills and the quality of the imaging itself.

The primary etiology of CAP about 70% is bacterial, with common pathogens such as *Streptococcus pneumoniae*, *Hemophilus influenzae*, *Staphylococcus aureus* and other Gram-negative bacilli. Viral infections accounts for approximately 30% of cases, with half of these involving viral/bacterial co-infections. Due to bacterial infections being the major etiology, early initiation of antibiotic therapy is crucial in the management of CAP. Thus, the ability to make an early diagnosis is essential, especially to those who would benefit from the timely antibiotic treatment.

There are many studies on biomarkers to differentiate bacterial CAP from viral CAP and non-infectious respiratory diseases such as malignancies, interstitial lung diseases, pulmonary edema and pulmonary hemorrhage. A review by Ito and Ishida highlighted several inflammatory biomarkers commonly used as diagnostic tools for CAP, including procalcitonin (PCT), soluble triggering receptor expressed in myeloid cells-1 (sTREM-1), pro-adrenomedullin (proADM), and prepepsin[2]. However, each of these biomarkers has limitations: PCT can yield false-positive or false-negative results under certain conditions; sTREM-1 requires invasive bronchoalveolar lavage samples for diagnosis; proADM is not effective in distinguishing bacterial from viral infections; and prepepsin demonstrates low diagnostic accuracy.

Clinical features that have positive likelihood ratios were respiratory rate more than 20 per min, temperature of 38° C or more, heart rate of 100 beats per min and crackles.[3] Whereas laboratory tests that showed the highest pooled positive likelihood ratios were PCT and C-reactive protein (CRP). According to the Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America, the diagnosis of CAP requires the demonstration of opacity on chest imaging in a patient with clinically compatible syndrome (fever, dyspnea, cough and sputum production)[4].

A chest radiograph is relatively inexpensive and is easily available in the primary care setting.[4] However, in the British Thoracic Society guidelines,[5] the chest radiograph is only necessary if the diagnosis by clinical features is doubtful.[6] A few studies also showed the validity of computed tomography in the management of CAP, especially in a situation where a chest radiograph is negative for the presence of pneumonia despite strong clinical suspicion.[7,8] Lung ultrasound has emerged as a valuable tool in detecting pneumonia in adult, where it showed positive findings with sensitivity of 97.4%, specificity of 25% and accuracy of 95% compared to chest radiograph with $p < 0.001$.[9] While in children, the sensitivity is 94%, specificity is 86% and diagnostic odd ratio of 110.77 (95% CI 62.16–197.40).[10]

In a study, bacterial etiology has higher CRP level then viral etiology in acute febrile illness (133 mg/L compared to 23.31 mg/L).[11] Low CRP levels (<10 mg/L) reduce the likelihood of CAP, helping to exclude the diagnosis in doubtful cases.[12] Serial CRP measurements can be used to monitor the effectiveness of antibiotic therapy[13] and patient survival.[14]

Procalcitonin (PCT) is produced by the C-cells in the thyroid and released to the parenchymal tissues such as the liver, kidney, lung, intestine and muscle during bacterial infection. It is released within 2–3 h after bacterial infection, with a peak at 6 hours and a half-life of approximately 22–35 h. This has proven beneficial in neonatal sepsis where early diagnosis can be made by PCT with 84.2% diagnostic accuracy.[15] PCT is significantly lower in COVID-19.[16] In a study on children with CAP, PCT level more than 0.5 ng/mL was significantly associated with radiologically confirmed pneumonia but not in pneumonia based on WHO criteria.[17]

 

Recently IL-6 is developed as a point-of-care test. IL-6 production is initiated by an inflammatory reaction induced by trauma, stress and infection.[18] In COVID-19, IL-6 is used as a predictor of progression of disease and predictor of outcome. IL-6 is shown to correlate with respiratory failure and the level peak was short duration.[19]

This study aimed to investigate the utility of point-of-care biomarkers, such as PCT and interleukin-6 (IL-6), as diagnostic markers for CAP. The study will evaluate these biomarkers individually and in combination to establish potentially early and accurate diagnosis.

# 2. METHODOLOGY

This study was conducted in the ICU of Sultan Ahmad Shah Medical Centre (SASMEC @IIUM), as a prospective cohort study, between March 2024 and December 2024. We included all critically ill adult patients admitted to ICU with symptoms of dyspnea and respiratory failure. Eligible participants were adult patients aged ≥18 y, who were admitted to ICU in less than 48 h of hospital stay. Patients whose pneumonia diagnosis could not be established within 12 h of admission, or who stayed <72 h in ICU were excluded. Patients with immune system dysregulation also were excluded.

All patients admitted to ICU with dyspnea and respiratory failure, who met the standardized diagnostic criteria for CAP – including fever, cough with or without sputum, and radiological features of pneumonia acquired in the community – were classified as the CAP group. The other half that did not fit the criteria were labelled as non-CAP group or the control group. The classification was validated by two independent physicians, with discordances resolved by a third reviewer. Patients' demographic data and baseline clinical parameters were recorded within first hour of admission to ICU, including the studied biomarkers. Within 24 h, the diagnosis of CAP was established according to the above criteria. The treating physicians were blinded to the patients enrolled in this study and the patients were managed according to the ICU standard guidelines and protocols.

A convenience sampling method was used to recruit study participants during the study period. The sample size was calculated based on Song et al. study which resulted in AUC of 0.89 for IL-6 in diagnosing sepsis via Sepsis-3 criteria in the hospital.[20] Approximately 70 samples were required to achieve a power of 90% and an alpha level of 0.05, based on sample size estimation method proposed by Hanley and McNeil.

## 2.1. Statistical analysis

The results were analyzed using IBM SPSS Statistics for Windows, Version 27.0. The patients' demography with continuous variable such as age, NUTRIC score and APACHE III score were not normally distributed; therefore, the Mann-Whitney U test was used. For SOFA score, which is normally distributed, the independent t-test was used to compare the mean. Chi-square test was used for categorical variables, such as gender. A P-value of $< 0.05$ was considered statistically significant.

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of IL-6, CRP and PCT. The areas under the curve (AUCs) were calculated to assess the discriminative ability of each biomarker and their combinations. The optimal cutoff values were determined based on Youden index, which maximized sensitivity and specificity. Sensitivity and specificity values at these cutoffs were calculated and reported. Logistic regression was used to assess the combined biomarker performance, and the resulting probabilities were analyzed using ROC curves to compute AUCs, confidence intervals, and diagnostic metrics.

The central tendencies of IL-6, CRP and PCT based on the cutoff levels were compared between the CAP and Non-CAP groups using the Mann-Whitney U test for non-parametric data. A significant threshold of $P < 0.05$ was applied.

Biomarker levels and their combinations were evaluated for their diagnostic performance in distinguishing CAP from non-CAP patients. Statistical significance of differences in biomarker distributions between CAP and non-CAP groups was assessed using the Chi-square test. The predictive probabilities were used to calculate positive and negative predictive values for each biomarker and combinations.

# 3. RESULTS

Table 1 summarizes the baseline characteristics of patients with CAP and those without CAP. The total of 75 patients were included, with 33 patients in the CAP group and 42 in the non-CAP group. The baseline characteristics, including age, gender, and the scores were comparable between groups.

 

**Table 1: Baseline Characteristics Between CAP and Non-CAP Patients.**

| Variable | CAP (n = 33) | Non-CAP (n = 42) | P-value |
|---|---|---|---|
| Age (y) | 64.00 (55.00–70.00) | 65.00 (54.00–71.00) | 0.919 |
| Gender | | | |
| • Male | 19 (25) | 22 (29) | 0.654 |
| • Female | 14 (19) | 20 (27) | |
| SOFA score | 5.34 ± 3.26 | 4.29 ± 3.01 | 0.706 |
| NUTRIC score | 3.00 (2.00–5.00) | 3.00 (2.00–4.00) | 0.310 |
| APACHE III score | 13.00 (10.25–16.75) | 12.50 (9.75–19.00) | 0.896 |

*Significance based on p < 0.05. CAP: community-acquired pneumonia, SOFA: Sequential Organ Failure Assessment, NUTRIC: Nutrition Risk in Critically Ill, APACHE: Acute Physiologic and Chronic Health Evaluation*

*Data presented as mean (IQR), n (%) or mean ± SD*

For the individual biomarkers, all IL-6, CRP and PCT have poor diagnostic accuracy to diagnose CAP on their own, with AUC of less than 0.7. However, combining the biomarkers generally improved diagnostic accuracy to acceptable diagnostic performance, with improved sensitivity but reduced specificity. The combination of IL-6 and CRP yielded the highest AUC of 0.759 (95% CI: 0.650–0.868). The combination of IL-6 and PCT have the highest sensitivity (91%) but reduced specificity (56%).

**Table 2: Diagnostic performance of IL-6, CRP and PCT and their combinations based on AUC, sensitivity and specificity**

| Variable | AUC | 95% CI | P-value | Cutoff value | Sensitivity | Specificity |
|---|---|---|---|---|---|---|
| IL-6 | 0.670 | 0.543–0.796 | 0.012 | ≥ 155.81 pg/mL | 55% | 79% |
| CRP | 0.698 | 0.579–0.816 | 0.003 | ≥ 2.17 mg/dL | 73% | 60% |
| PCT | 0.618 | 0.489–0.747 | 0.081 | ≥ 6.10 ng/mL | 52% | 74% |
| IL-6 and CRP | 0.759 | 0.650–0.868 | 0.000 | ≥ -0.54 | 78% | 67% |
| IL-6 and PCT | 0.744 | 0.632–0.856 | 0.000 | ≥ -0.46 | 91% | 56% |
| CRP and PCT | 0.710 | 0.593–0.827 | 0.002 | ≥ -0.65 | 81% | 56% |
| IL-6 and PCT and CRP | 0.718 | 0.602–0.834 | 0.001 | ≥ -0.65 | 75% | 64% |

*Significance based on p < 0.05. AUC: area under the curve, CI: confidence interval, IL-6: interleukin-6, CRP: C-reactive protein, PCT: procalcitonin*

 

As shown in Table 3, the IL-6 and CRP levels were significantly higher is patients with CAP compared to those without CAP, suggesting their potential role in distinguishing CAP from non-CAP patients. Although PCT levels were higher in the CAP group, the difference was not statistically significant.

**Table 3: Comparison of IL-6, CRP and PCT between CAP and non-CAP groups.**

| Biomarkers | CAP | Non-CAP | p-value |
|---|---|---|---|
| IL-6 (pg/mL) | 170.95 (26.56–442.33) | 25.30 (9.67–151.04) | 0.012 |
| CRP (mg/dL) | 8.59 (1.60–19.69) | 1.32 (0.50–9.00) | 0.003 |
| PCT (ng/mL) | 6.29 (0.49–24.90) | 1.66 (0.19–7.78) | 0.081 |

*Significance based on $p < 0.05$. CAP: community-acquired pneumonia, IL-6: interleukin-6, CRP: C-reactive protein, PCT: procalcitonin*

In Table 4, the individual biomarkers (IL-6, CRP and PCT) showed moderate diagnostic accuracy based on their PPV and NPV values, with IL-6 providing the highest PPV (67%). Combining biomarkers improved diagnostic performance, with the IL-6 and PCT combination achieving the highest NPV (85%), indicating its utility in ruling out CAP.

**Table 4: Diagnostic performance of IL-6, CRP and PCT and their combinations based on positive and negative predictive value and positive and negative likelihood ratio**

| Biomarkers with Cutoff Value | CAP | Non-CAP | P-value | PPV | NPV | LR+ | LR- |
|---|---|---|---|---|---|---|---|
| **IL-6** | | | | | | | |
| ≥ 155.81 pg/mL | 18 | 9 | 0.003 | 67% | 69% | 2.62 | 0.57 |
| < 155.81 pg/mL | 15 | 33 | | | | | |
| **CRP** | | | | | | | |
| ≥ 2.17 mg/dL | 24 | 17 | 0.005 | 59% | 74% | 1.83 | 0.45 |
| < 2.17 mg/dL | 9 | 25 | | | | | |
| **PCT** | | | | | | | |
| ≥ 6.10 ng/mL | 17 | 11 | 0.024 | 61% | 66% | 2.00 | 0.65 |
| < 6.10 ng/mL | 16 | 31 | | | | | |
| **IL-6 and PCT** | | | | | | | |
| ≥ -0.46 | 28 | 19 | < 0.001 | 60% | 85% | 2.07 | 0.16 |
| < -0.46 | 4 | 23 | | | | | |
| **CRP and PCT** | | | | | | | |
| ≥ -0.65 | 26 | 18 | < 0.001 | 59% | 80% | 1.84 | 0.34 |
| < -0.65 | 6 | 24 | | | | | |
| **IL-6 and PCT and CRP** | | | | | | | |
| ≥ -0.65 | 26 | 18 | < 0.001 | 59% | 80% | 2.08 | 0.39 |
| < -0.65 | 6 | 24 | | | | | |

 

*Significance based on p < 0.05. CAP: community-acquired pneumonia, PPV: positive predictive value, NPV: negative predictive value, LR+: positive likelihood ratio, LR-: negative likelihood ratio, IL-6: interleukin-6, CRP: C-reactive protein, PCT: procalcitonin*

# 4. DISCUSSION

The baseline characteristics of the CAP and non-CAP groups were comparable, which suggest that the observed differences in biomarker levels were likely due to the presence or absence of CAP rather than confounding demographic or clinical variables.

The findings highlight the limited diagnostic utility of IL-6, CRP, and PCT when used individually, with their AUCs falling below the threshold for acceptable diagnostic accuracy (AUC > 0.7). This indicates that they do not reliably differentiate CAP and non-CAP cases. Even though the IL-6 has poor diagnostic accuracy, it provided the highest PPV (67%), making it relatively more effective for identifying CAP. Studies on sepsis have reported IL-6 as a reliable marker with high sensitivity and sensibility, but this may reflect differences in the inflammatory milleu between CAP and sepsis. [21]

The IL-6 cutoff value identified through this study is 155 pg/mL for CAP diagnosis differs significantly from previously reported values in various contexts. For example, studies in adult COVID-19 pneumonia identified a much lower cutoff of 35 pg/mL,[22] while a higher value of 363.23 pg/mL was reported in adult postoperative day 1 pneumonia.[23] In pediatric populations, an IL-6 cutoff of 201.13 pg/mL was identified for severe pneumonia cases in pediatric ICU.[24] These discrepancies underscore the variability in IL-6 expression across different patient populations and clinical settings, emphasizing the need for tailored diagnostic thresholds based on specific disease contexts. In fact, the level of IL-6 taken on five consecutive days after surgery to diagnose postoperative pneumonia showed a wide range of cutoff points from day 1 to 5: 363.23 pg/mL, 94.24 pg/mL, 71.53 pg/mL, 24.32 pg/mL, 20.58 pg/mL respectively.[23]

The diagnostic performance of biomarker combinations was more promising. The combination of IL-6 and CRP achieved the highest AUC (0.759, 95% CI: 0.650–0.868) with a balanced sensitivity (78%) and specificity (67%), indicating acceptable diagnostic accuracy for CAP.

The IL-6 and PCT combination showed the highest sensitivity (91%) at the expense of lower specificity (56%). Importantly, this combination also had the highest NPV at 85%. From a clinical perspective, this means that if IL-6 is less than 155.81 pg/mL and PCT is less than 6.1 ng/mL, there is a 91% chance that the patient does not have CAP. This is finding is particularly valuable in ruling out CAP in patients with low likelihood of the disease thereby minimizing unnecessary antibiotic use and reducing the risk of antimicrobial resistance.

While the combination of all three biomarkers offered a slightly improvement in diagnostic performance, it did not outperform, the IL-6 and CRP combination. A larger study involving adult COVID-19 pneumonia cases, have demonstrated higher diagnostic accuracy with these combinations, albeit with varying cutoff values. For instance, higher CRP (41.8 mg/L), and lower PCT (0.07 ng/mL) and IL-6 (32.1 pg/mL) thresholds were reported, highlighting the influence of disease-specific factors on biomarker profiles.[25]

Our comparative analysis of biomarker levels between CAP and non-CAP patients revealed significant differences for IL-6 and CRP. Median levels of IL-6 and CRP were significantly higher in the CAP group ($p = 0.012$ and $p = 0.003$, respectively), supporting their potential role as markers. However, while PCT levels were also elevated in the CAP group, the difference did not reach statistical significance ($p = 0.081$). This reinforces the notion that PCT may have limited standalone diagnostic value in CAP but retains its utility as part of a biomarker panel for ruling out the disease in low-risk patients.

# 5. LIMITATIONS

This study is limited by its relatively small sample size and single-center design, which limits the generalizability of the findings. Further multicenter studies with larger sample sizes are necessary to validate the diagnostic performance of these biomarkers and their combination in diverse populations.

# 6. CONCLUSIONS

 

IL-6, C-reactive protein and procalcitonin are valuable biomarkers for diagnosing community-acquired pneumonia, with IL-6 and procalcitonin demonstrating the greatest utility when combined. The IL-6 and C-reactive protein combination emerged as the most effective diagnostic tool, offering balanced sensitivity and specificity. Additionally, the IL-6 and procalcitonin combination has high negative predictive value, can aid in ruling out community-acquired pneumonia and guide appropriate clinical management. These findings provide a basis for further exploration of multi-biomarker diagnostic panels in pneumonia diagnosis.

## 7. Data availability

The numerical data generated during this research is available with the authors.

## 8. Conflict of interest

The authors declare no conflict of interest.

## 9. Funding

The study utilized the hospital resources only, and no external or industry funding was involved.

## 10. Authors' contribution

NFR: Concept, conduction of the study work and manuscript writing

LKW: Conduction of the study work

SN, MRAG, IAR: Manuscript editing

# 11. REFERENCES

1. Jones BE, Chapman AB, Ying J, Rutter ED, Nevers MR, Baker A, et al. Diagnostic discordance, uncertainty, and treatment ambiguity in community-acquired pneumonia. Ann Intern Med. 2024;177(9):1179-89. [PubMed] DOI: 10.7326/M23-2505
2. Ito A, Ishida T. Diagnostic markers for community-acquired pneumonia. Ann Transl Med. 2020;8(9):609. [PubMed] DOI: 10.21037/atm.2020.02.182
3. Htun TP, Sun Y, Chua HL, Pang J. Clinical features for diagnosis of pneumonia among adults in primary care setting: a systematic and meta-review. Sci Rep. 2019;9(1):1-10. [PubMed] DOI: 10.1038/s41598-019-44145-y
4. 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):e45-67. [PubMed] DOI: 10.1164/rccm.201908-1581ST
5. Lim WS, Baudouin SV, George RC, Hill AT, Jamieson C, Le Jeune I, et al. BTS guidelines for the management of community-acquired pneumonia in adults: update 2009. Thorax. 2009;64(Suppl 3):iii1-55. [PubMed] DOI: 10.1136/thx.2009.121434
6. Makhnevich A, Sinvani L, Cohen SL, Feldhamer KH, Zhang M, Lesser ML, et al. The clinical utility of chest radiography for identifying pneumonia: accounting for diagnostic uncertainty in radiology reports. Am J Roentgenol. 2019;213(6):1207-12. [PubMed] DOI: 10.2214/AJR.19.21521
7. Loubet P, Tubiana S, Claessens YE, Epelboin L, Ficko C, Le Bel J, et al. Community-acquired pneumonia in the emergency department: an algorithm to facilitate diagnosis and guide chest CT scan indication. Clin Microbiol Infect. 2020;26(3):382.e1-7. [PubMed] DOI: 10.1016/j.cmi.2019.06.026
8. Hunold KM, Mion LC, Gure TR, Schwaderer AL, Exline M, Hebert C, et al. Clinical performance of existing diagnostic criteria for pneumonia in older emergency patients: a prospective cohort study. J Am Geriatr Soc. 2024;72(10):3068-77. [PubMed] DOI: 10.1111/jgs.19113
9. Walaa M, Mansour W, Lakouz KA, Hussein MM. Role of chest ultrasonography in the diagnosis and follow-up of community-acquired pneumonia at Zagazig University Hospitals. Egypt J Bronchol. 2017;11(1):29-35. DOI: 10.4103/1687-8426.198991
10. Shi C, Xu X, Xu Y. Systematic review and meta-analysis of the accuracy of lung ultrasound and chest radiography in diagnosing community-acquired pneumonia in children. Pediatr Pulmonol. 2024;59(9):3130-3147. [PubMed] DOI: 10.1002/ppul.27221
11. Largman-Chalamish M, Wasserman A, Silberman A, Levinson T, Ritter O, Berliner S, et al. Differentiating between bacterial and viral infections by estimated CRP velocity. PLoS One. 2022;17(12):e0277401. [PubMed] DOI: 10.1371/journal.pone.0277401
12. Bruehlman R. CRP for CAP, a new diagnostic approach? Evid Based Pract. 2021;24:4. DOI: 10.1097/EBP.0000000000001209
13. Liu C, Zhang Y, Shang Y, Fang C, He Q, Xie L. Clinical values of common biomarkers for efficacy monitoring of antibiotics in early-onset neonatal sepsis. Transl Pediatr. 2020;9(5):669. [PubMed] DOI: 10.21037/tp-20-326

 

14. Travlos A, Bakakos A, Vlachos KF, Rovina N, Koulouris N, Bakakos P. C-reactive protein as a predictor of survival and length of hospital stay in community-acquired pneumonia. J Pers Med. 2022;12(10):1710. [PubMed] DOI: 10.3390/jpm12101710
15. Habib A, Raza S, Ali U, Zubairi AM, Salim E. Diagnostic accuracy of serum procalcitonin (PCT) as an early biomarker of neonatal sepsis using blood culture as gold standard. J Coll Physicians Surg Pak. 2021;31(4):383-7. [PubMed] DOI: 10.29271/jcpsp.2021.04.383
16. Zhou YZ, Teng XB, Han MF, Shi JF, Li CX, Zhang XH, et al. The value of PCT, IL-6, and CRP in the early diagnosis and evaluation of COVID-19. Eur Rev Med Pharmacol Sci. 2021 Jan;25(2):1097-1100. [PubMed] DOI: 10.26355/eurrev_202101_24680
17. Ratageri VH, Panigatti P, Mukherjee A, Das RR, Goyal JP, Bhat JI, et al. Role of procalcitonin in diagnosis of community-acquired pneumonia in children. BMC Pediatr. 2022;22(1):1-7. [PubMed] DOI: 10.1186/s12887-022-03286-2
18. Henning DJ, Hall MK, Watsjold B, Bhatraju PK, Kosamo S, Shapiro NI, et al. Interleukin-6 improves infection identification when added to physician judgment during evaluation of potentially septic patients. Am J Emerg Med. 2020;38(5):947-52. [PubMed] DOI: 10.1016/j.ajem.2019.158361
19. Santa Cruz A, Mendes-Frias A, Oliveira AI, Dias L, Matos AR, Carvalho A, et al. Interleukin-6 is a biomarker for the development of fatal severe acute respiratory syndrome coronavirus 2 pneumonia. Front Immunol. 2021;12:613422. [PubMed] DOI: 10.3389/fimmu.2021.613422
20. Song J, Park DW, Moon S, Cho HJ, Park JH, Seok H, et al. Diagnostic and prognostic value of interleukin-6, pentraxin 3, and procalcitonin levels among sepsis and septic shock patients: a prospective controlled study according to the Sepsis-3 definitions. BMC Infect Dis. 2019;19(1):968. [PubMed] DOI: 10.1186/s12879-019-4618-7
21. Jerome E, McPhail M, Menon K. Diagnostic accuracy of procalcitonin and interleukin-6 for postoperative infection in major gastrointestinal surgery: a systematic review and meta-analysis. Ann R Coll Surg Engl. 2022;104(8):561-70. [PubMed] DOI: 10.1308/rcsann.2022.0053
22. Guirao JJ, Cabrera CM, Jiménez N, Rincón L, Urra JM. High serum IL-6 values increase the risk of mortality and the severity of pneumonia in patients diagnosed with COVID-19. Mol Immunol. 2020;128:64-8. [PubMed] DOI: 10.1016/j.molimm.2020.10.006
23. Chen W, Zhong K, Guan Y, Zhang HT, Zhang H, Pan T, et al. Evaluation of the significance of interleukin-6 in the diagnosis of postoperative pneumonia: a prospective study. BMC Cardiovasc Disord. 2022;22(1):1-7. [PubMed] DOI: 10.1186/s12872-022-02744-0
24. Khattab AA, El-Mekkawy MS, Shehata AM, Whdan NA. Clinical study of serum interleukin-6 in children with community-acquired pneumonia. Egypt Pediatr Assoc Gaz. 2018;66(2):43-8. DOI: 10.1016/j.epag.2018.03.003
25. Liu F, Li L, Xu M, Wu J, Luo D, Zhu Y, et al. Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19. J Clin Virol. 2020;127:104370. [PubMed] DOI: 10.1016/j.jcv.2020.104370


 