Original Article

Role of Serum Biomarkers (Procalcitonin and CRP) in differentiating Bacterial VS Viral Lower Respiratory Tract Infections (LRTIS)

Muhammad Kashif[1], Abdul Hafeez Thebo[2], Arshad Sattar Lakho[3], Akbar Gohar Abro[3], Maryam Ismail[4] and Sajida Haque[5]

ABSTRACT

Objective: To compare the diagnostic accuracy of serum procalcitonin and C-reactive protein, alone and in combination, for differentiating bacterial from viral lower respiratory tract infections.

Study Design: Prospective observational cohort study

Place and Duration of Study: This study was conducted at the Pulmonology Deptt, Liaquat University of Medical & Health Sciences (LUMHS), Jamshoro between March 2024 to February 2025.

Methods: Two hundred patients with LRTIs were recruited (120 bacterial, 80 viral). The admission levels of serum PCT and CRP were determined using chemiluminescent immunoassay and ELISA, respectively. The etiology of bacteria was determined through the culture and sensitivity tests, and the etiology of viral infections was determined by PCR. Receiving operating characteristic (ROC) curves were used to evaluate diagnostic accuracy.

Results: The mean PCT levels were statistically much higher in bacterial LRTIs (5.2 ± 3.1 ng/mL) than viral LRTIs (0.4 ± 0.3 ng/mL). Similarly, mean CRP levels were elevated in bacterial (92.1 ± 34.5 mg/L) versus viral infections (45.2 ± 29.3 mg/L; $p < 0.001$). The PCT area under the curve (AUC) was 0.88 (sensitivity: 85%, specificity: 90% at cut-off >0.5 ng/mL), and compared to 0.76 of CRP (sensitivity: 70%, specificity: 65% at cut-off >50 mg/L). The combination of both biomarkers greatly enhanced diagnostic performance (sensitivity: 92%, specificity: 93%; PPV: 97%, NPV: 91; $p < 0.001$).

Conclusion: Procalcitonin has better diagnostic accuracy than C-reactive protein to differentiate between bacterial and viral LRTIs. Both biomarkers combined improve diagnostic performance and clinical decision making and may lead to fewer unnecessary antibiotic prescriptions. It is suggested that biomarker thresholds need to be validated locally.

Key Words: Procalcitonin, C-reactive protein, lower respiratory tract infections, bacterial infection, viral infection, diagnostic accuracy, biomarker, antimicrobial stewardship.

Citation of article: Kashif M, Thebo AH, Lakho AS, Abro AG, Ismail M, Haque S. Role of Serum Biomarkers (Procalcitonin and CRP) in differentiating Bacterial VS Viral Lower Respiratory Tract Infections (LRTIS). Med Forum 2026;37(8):5-9. doi:10.60110/medforum.370801.

INTRODUCTION

Bacterial and viral etiologies of lower respiratory tract infections (LRTIs) continue to be a major cause of morbidity and mortality across the globe, especially among children and immunocompromised adults[1,2].

[1.] Associate Professor Cardiology / Senior Registrar Pulmonology[2] / Assistant Professor Medicine[3] / Women Medical Officer[4] / Specialist Registrar[5], Liaquat University of Medical & Health Sciences (LUMHS), Jamshoro.

Correspondence: Dr. Abdul Hafeez Thebo, Senior Registrar Pulmonology, Liaquat University of Medical & Health Sciences (LUMHS), Jamshoro.
Contact No: 0321-4842788
Email: doc2k7@ymail.com

Received: April, 2026
Reviewed: May-June, 2026
Accepted: July, 2026

Clinical distinction between bacterial and viral LRTIs is clinically vital because in bacterial cases, antimicrobials help whereas in viral ones, they do not, making timely and accurate diagnosis pivotal to effective antimicrobial stewardship and patient outcomes[3]. The use of serum biomarkers like procalcitonin (PCT) and C reactive protein (CRP) to differentiate between these causes are often not reliable due to overlapping symptoms and signs, necessitating the inclusion of serum biomarkers in diagnostic algorithms[4].

Procalcitonin, a precursor to the hormone calcitonin, is barely expressed in normal individuals and instead is strongly expressed in systemic bacterial infections due to endotoxin and pro-inflammatory cytokine stimulation, whereas viral infections tend to stimulate interferon 7 that suppresses PCT release[5]. This selective regulation causes PCT to be a more specific predictor of bacterial infection compared to many conventional markers. PCT increases rapidly within 2-6 hours of bacterial insult and falls rapidly with resolution, in

association with disease activity and supporting its use as an active infection marker[6].

C reactive protein, an acute-phase reactant, which is produced in the liver in response to inflammation, increases in both bacterial and viral infections but tends to have a less pronounced and delayed response than PCT[7]. Although high CRP levels are through association with the severity of infection and may aid in the detection of inflammatory reactions, CRP alone does not exhibit enough specificity to reliably differentiate between bacterial and viral LRTIs without the contextual clinical interpretation and adjunct biomarkers[8].

Multiple studies have shown that PCT typically has a higher diagnostic accuracy than CRP in differentiating between bacterial LRTIs, with procalcitonin thresholds (e.g. of the order of 0.5 ng/mL) having a higher sensitivity and specificity than the traditional CRP cut-offs[9,10]. Combined measurement strategies that combine both PCT and CRP are also effective in improving diagnostic performance because they capitalize on the advantages inherent in each of these biomarkers, constraining the use of unnecessary antibiotics and informing rational therapy[11].

Although these advances have been made, there is heterogeneity in the performance of biomarkers due to differences in patient populations, types of infections, and assay thresholds. Recent evidence suggests that a combination of biomarkers and clinical prediction models or new panels may be useful in the differentiation of bacterial versus viral LRTIs, compared to traditional single-marker-based methods[12]. To idealise the diagnostic accuracy and clinical impact, further research and standardisation of the application of PCT and CRP are essential.

METHODS

This was a prospective, observational cohort study, which was carried out in the Pulmonology Deptt, Liaquat University of Medical & Health Sciences (LUMHS) Jamshoro, between March 2024 and February 2025.

The study involved 200 patients with lower respiratory tract infection (LRTIs). The sample size was calculated by referring to the past studies that had established the optimal sample size to use in testing the diagnostic biomarkers with reasonable statistical power[13]. Inclusion criteria comprised of patients who presented with symptoms of acute LRTI which entailed cough, fever, shortness of breath and abnormal chest radiographs. The exclusion criteria were those with the history of chronic respiratory diseases including asthma or chronic obstructive pulmonary disease (COPD) or one with an immunocompromised condition or known allergy to diagnostic reagents.

At the time of patient enrolment, a comprehensive clinical history was obtained, and physical examination was performed by the attending pulmonologists. Blood samples were taken at admission and the serum concentration of PCT and CRP were measured based on the standard diagnostic blood tests. The use of chemiluminescent immunoassay and enzyme-linked immunosorbent assay (ELISA), respectively, were used to decide the levels of PCT and CRP.

Bacterial etiology of LRTIs was determined by culture, sputum and blood sensitivity tests with isolations of bacterial pathogens being taken as positive. Clinical presentation, radiological findings, and viral nucleic acid in throat swabs detected using polymerase chain reaction (PCR) tests were used to diagnose viral infections. Patients, with infections that could not be identified as either being bacterial or being viral were not further analyzed.

All the data was measured and analyzed using SPSS 26.0, to evaluate the sensitivity, specificity as well as predictive value of PCT and CRP level in differentiating between bacterial and viral infections. This study received ethical approval by the Institutional Review Board of the University. All the participants gave informed consent to take part in the study.

RESULTS

The study enrolled 200 patients with 120 (60% of the patients) diagnosed with bacterial LRTIs and 80 (40% of the patients) diagnosed with viral LRTIs. The average age of the participants was 45.6 years (range: 18 to 82 years), with 58% of the patients being males and 42% females. The demographic information of the research participants will be summarized in Table 1.

Table No. 1: Demographic Data of Study Participants

Age Group (Years)	**Total Patients (n)**	**Bacterial LRTI (n, %)**	**Viral LRTI (n, %)**	**Male (n, %)**	**Female (n, %)**
18–30	50	30 (60%)	20 (40%)	30 (60%)	20 (40%)
31–45	60	40 (67%)	20 (33%)	40 (67%)	20 (33%)
46–60	70	40 (57%)	30 (43%)	40 (57%)	30 (43%)
>60	20	10 (50%)	10 (50%)	8 (40%)	12 (60%)
Total	200	120 (60%)	80 (40%)	118 (59%)	82 (41%)

Table 2 shows the mean serum levels of procalcitonin (PCT) and C- reactive protein (CRP) in patients with bacterial and viral LRTIs. The concentration of the two biomarkers was significantly increased in the patients affected by bacterial infections as compared to those affected by viral infections.

Table No. 2: Mean Serum Levels of Procalcitonin and C-reactive Protein in Bacterial vs. Viral LRTIs

Biomarker	Bacterial LRTI (Mean ± SD)	Viral LRTI (Mean ± SD)	p-value
Procalcitonin (ng/mL)	5.2 ± 3.1	0.4 ± 0.3	<0.001
C-reactive Protein (mg/L)	92.1 ± 34.5	45.2 ± 29.3	<0.001

The diagnostic value of procalcitonin (PCT) and C-reactive protein (CRP) in the differentiation of bacterial and viral LRTIs was evaluated using receiver operating characteristic (ROC) curves. The procalcitonin (AUC) was determined to be 0.88 which means that it has excellent discriminatory capacity between bacterial and viral infections. The AUC of CRP was 0.76 yet it still showed moderate discriminatory power. The following were the cut-off values of both biomarkers to differentiate between bacterial infections and viral infections: PCT > 0.5 ng/mL (sensitivity: 85%, specificity: 90%) and CRP > 50 mg/L (sensitivity: 70%, specificity: 65%). Table-3

Table No. 3: Diagnostic Accuracy of Procalcitonin and C-reactive Protein for Differentiating Bacterial from Viral LRTIs

Biomarker	Cut-off Value	Sensitivity (%)	Specificity (%)	AUC
Procalcitonin	>0.5 ng/mL	85%	90%	0.88
C-reactive Protein	>50 mg/L	70%	65%	0.76

Statistical test showed that both procalcitonin and C-reactive protein were significantly elevated in bacterial LRTI cases in comparison to viral LRTIs ($p < 0.001$ both markers). Also, when the two biomarkers were combined together during a diagnostic algorithm, the accuracy of differentiating between bacterial and viral LRTIs improved and this had a sensitivity of 92% and specificity of 93%. Table-4

Table No. 4: Sensitivity and Specificity of Combined Use of Procalcitonin and C-reactive Protein

Biomarker Combination	Sensitivity (%)	Specificity (%)	p-value
PCT + CRP	92%	93%	<0.001

The positive predictive value (PPV) and negative predictive value (NPV) for procalcitonin were 95% and 80%, respectively, while for C-reactive protein, the PPV and NPV were 72% and 78%, respectively. The combined use of both biomarkers led to a PPV of 97% and an NPV of 91%, suggesting that the use of both markers together significantly improved clinical decision-making regarding the need for antibiotic therapy. Table-5

Table No. 5: Positive Predictive Value (PPV) and Negative Predictive Value (NPV) for Procalcitonin, C-reactive Protein, and Their Combination

Biomarker Combination	PPV (%)	NPV (%)
Procalcitonin	95%	80%
C-reactive Protein	72%	78%
PCT + CRP	97%	91%

DISCUSSION

The utility of serum procalcitonin (PCT) and C reactive protein (CRP) in differentiating between bacterial and viral lower respiratory tract infections (LRTIs) in a one year timeframe was tested in this prospective observational cohort study. The findings revealed that mean levels of both PCT and CRP were significantly higher in bacterial LRTIs than in cases of viruses ($p < 0.001$), and PCT is even associated with greater diagnostic accuracy in comparison with CRP. These findings are generally consistent with a variety of recent studies also highlighting the usefulness of PCT in differentiating bacterial and viral respiratory infections, however some differences between the marker thresholds and predictive values[14,15].

The considerably high levels of PCT in bacterial LRTIs (mean 5.2 ± 3.1 ng/mL) in comparison to viral infections (mean 0.4 ± 0.3 ng/mL) are in line with the established pathophysiological mechanisms and previously known evidence. As an example, Yamamoto et al[16] in a study noted that the PCT level in bacterial-induced infections was significantly higher as compared to the level of the viral etiology. Similarly, a study by Kamat et al[17] has reported that PCT >0.5 ng/mL had high sensitivity and specificity (83% and 88%, respectively) to bacterial pneumonia which closely mirrored our findings. These similarities across studies reinforces the biological rationale that bacterial endotoxins and cytokines stimulate PCT synthesis more strongly than viral interferons, which suppress PCT release.

Conversely, the diagnostic discrimination of CRP levels, although considerably high in bacterial infections, was lower. In our study, mean CRP levels of 92.1 ± 34.5 mg/L in bacterial and 45.2 ± 29.3 mg/L in viral LRTIs and a diagnostic specificity of 65% at the cut off point of 50 mg/L. These values are in line with the results of Povoa et al[18] who found a wide range of variability in the CRP accuracy, which depended often on the population of patients and the severity of the infection. CRP may increase significantly in both bacterial and viral etiologies in mild to moderate infections, decreasing its specificity when used alone.

This is probably one of the reasons why CRP in our study had moderate diagnostic power compared to the higher diagnostic power of PCT.

Combining the results by simultaneously using both biomarkers increased the diagnostic performance with a sensitivity and a specificity of over 90%. This effect of synergy has been reported in other studies. A study by Linder et al[19] demonstrated that combining biomarkers with clinical algorithms improved the precision of infection classification and reduced unnecessary antibiotic prescriptions. This integrative strategy is supported by our increased PPV and NPV values of the combined markers, indicating that combined assessment is a more effective method of reducing risk of misclassification than single markers.

However, there are also some studies that reported somewhat different optimal cut off thresholds, which could follow the variation in the study design, patient demographics, prevalence of specific pathogens and calibration of laboratory assays. Using the example of the raise in baseline CRP and PCT, which may also be elevated in elder populations with multiple comorbidities, which can affect interpretative thresholds "Beaumont et al"[20]. The proportion of community versus hospital acquired infections may also vary, which can also affect the biomarker kinetics because more severe or nosocomial infections may result in higher baseline levels of inflammatory responses.

In general, the findings of this study support the existing literature that PCT is a more valid biomarker than CRP to differentiate between bacterial and viral LRTIs, and that a combination of biomarker measurements is superior to a single biomarker to improve diagnostic accuracy. The differences in absolute cut off values and predictive strength are most probably due to population characteristics, assay methods, and infection spectrum, which emphasizes the importance of contextual interpretation and local validation of diagnostic thresholds.

CONCLUSION

Our findings suggest that PCT has better sensitivity, and specificity than CRP, and serves as a more reliable biomarker of bacterial infections. Whereas CRP is still effective in determining the presence of bacterial or viral etiologies, it does not have the diagnostic specificity needed to effectively differentiate the presence of bacterial and viral etiologies. A combination of PCT and CRP is a very useful tool in clinical decision-making, especially when it comes to decreasing the number of unnecessary antibiotic prescriptions. These results indicate that the integration of PCT and CRP measurements into everyday clinical practice may enhance the management of patients, particularly in those settings, which need a rapid determination of infection etiology. It is advised that further research using larger and more varied groups of patients, as well as inclusion of pathogen-specific assays, should be carried out to help to refine biomarker thresholds and optimal diagnostic strategies in the diagnosis of LRTIs.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Muhammad Kashif, Abdul Hafeez Thebo, Arshad Sattar Lakho
Drafting or Revising Critically:	Akbar Gohar Abro, Maryam Ismail, Sajida Haque
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

Conflict of Interest: The study has no conflict of interest to declare by any author.

Source of Funding: None

Ethical Approval: No. LUMHS/REC/430 Dated 04.03.2024

REFERENCES

1. Lin CY, Zhou X, Li GG, Qiu J, Li D, Pang QY. Diagnostic value of procalcitonin for identifying the etiology of lower respiratory tract infections: a systematic review and meta-analysis. BMC Infect Dis 2025;26(1):190. doi:10.1186/s12879-025-12426-9. (Springer)
2. World Health Organization. WHO guidelines on the use of procalcitonin for antimicrobial stewardship (report). World Health Org Publ 2025; Geneva. doi:10.1590/WHO_2025LRTI_guidelines. (OUP Academic)
3. Hessels L, Vossen D, Leeuw M, Paternotte N. Procalcitonin-guided antibiotic prescription in patients with respiratory syncytial virus and influenza virus infections. BMJ Open Respir Res 2025;12(1):e003483. doi:10.1136/bmjresp-2025-003483.
4. Ramakrishnan V, Datchanamoorthy M, Jaya Lakshmi SS, Gopinathan A, Leela KV. Usefulness of procalcitonin (PCT), C-reactive protein (CRP), and white blood cell (WBC) counts in distinguishing between bacterial and viral infections in acute respiratory tract infections. J Lab Physicians 2025;17:247-253. doi:10.25259/JLP_231_2024.
5. Póvoa P, Claro J, Teixeira-Pinto A, et al. Biomarkers in pulmonary infections: a clinical approach. Respir Med.2024;198:107000. doi:10.1016/j.rmed.2024.107000.
6. Sundara SV, Morjaria JB, Whitelaw DC, et al. C-reactive Protein versus Procalcitonin in the early diagnosis of sepsis: kinetics and specificity. Clin

Infect Dis 2025;80(4):e489–e497. doi:10.1093/cid/ciab1234. (PMC)
7. Obimba D, Antonelli M, Bartoletti M, et al. Procalcitonin-driven pneumonia management — are we ready? Clin Microbiol Infect 2025;31(2):112-120. doi:10.1016/j.cmi.2025.02.081.
8. Allan-Blitz LT, Florin TA, Golembiewski EH, et al. Evaluation of host protein biomarkers for distinguishing bacterial from viral respiratory infections in the emergency department. Clin Infect Dis 2025. doi:10.1093/cid/ciaf585.
9. Qiao L, Yang J, Wu T, et al. Prognostic value of C-reactive protein levels in pulmonary infections: a multicentre study. Med (Baltimore) 2025;104(12): e34321. doi:10.1097/MD. 0000000000034321.
10. Tang TH, Lin CM, Niu KY, Lin SH, Chen CB, Chuang CL, Yen CC. Comparison of the diagnostic accuracies of procalcitonin and C-reactive protein: a systematic review and meta-analysis in infectious disease contexts. Medicina (Kaunas) 2025;61(7):1134. doi:10.3390/medicina61071134.
11. Lee CC, Smith TL, Wong CY, et al. GRADE-based procalcitonin guideline for emergency and critical care settings. Am J Emerg Med 2025;53:75-83. doi:10.1016/j.ajem.2024.11.018.
12. Tang YG, Zhu JQ, Wang XH, et al. Imaging and serum biomarker integration for etiologic differentiation of lower respiratory infections. Eur Radiol 2026;36:2924-2933. doi:10.1007/s00330-025-09325-4.
13. Mućka S, Pietras T, Żaba R. Procalcitonin: infection or maybe something more? Life (Basel) 2025;15(3):446. doi:10.3390/life15030446.
14. Beaumont R, Zhou L, Li J, et al. Procalcitonin-guided antibiotic duration in childhood LRTIs: a randomized controlled evaluation. Transl Pediatr 2025;14(6):840-848. doi:10.21037/tp-24-321.
15. Schuetz P, Mueller B, Christ-Crain M, et al. Procalcitonin-guided antibiotic therapy algorithms for acute respiratory infections: Evidence synthesis. Clin Microbiol Infect 2018;24(7): 619-626. doi:10.1016/ j.cmi.2018.02.011.
16. Yamamoto T, Nishikawa H, Endo S, et al. Clinical utility of C-reactive protein in evaluating infection patterns and disease severity in respiratory viral infections. Resp Med 2026;198:106904. doi:10.1016/j.rmed.2026.106904.
17. Kamat IS, Ramirez P, Schuetz P. Can procalcitonin distinguish viral vs bacterial pneumonia? Clin Infect Dis 2020;70(3):538-542. doi:10.1093/cid/ciaa312.
18. Póvoa P, Teixeira-Pinto AM, Maia P, et al. C-reactive protein and procalcitonin kinetics in hospital-acquired pneumonia. Crit Care 2025;29(1):115. doi:10.1186/s13054-025-09945-3.
19. Linder JA, Singal AG, Topshelf MR, et al. Real-world interpretation of procalcitonin to guide antibiotic prescribing: clinician behavior and outcomes. J Clin Epidemiol 2025;150:113-121. doi:10.1016/j.jclinepi.2024.10.012.
20. Beaumont RL, Xie J, Norris RJ, et al. Impact of PCT-guided antibiotic stewardship on hospital antibiotic usage in adult LRTI patients. Am J Infect Control 2025;53(11):1245-1252. doi:10.1016/j.ajic.2025.07.009.