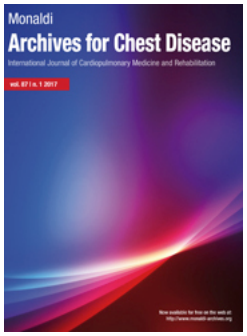

Monaldi Archives for Chest Disease

eISSN 2532-5264 https://www.monaldi-archives.org/

Monaldi Arch Chest Dis 2025 [Online ahead of print]

To cite this Article:
Garg I, Chauhan NK, Vardhan H, et al. **Pentraxin-3 as a novel biomarker in predicting outcomes of nosocomial pneumonia: a prospective observational study.** *Monaldi Arch Chest Dis* doi: 10.4081/monaldi.2025.3225

Pentraxin-3 as a novel biomarker in predicting outcomes of nosocomial pneumonia: a prospective observational study

Isha Garg,[1] Nishant Kumar Chauhan,[1] Harsh Vardhan,[1]
Shrimanjunath Sankanagoudar,[2] Naveen Dutt,[1] Gopal Durgeshwar,[1]
Hariharan Iyer,[1] Nikhil Kothari,[3] Ravisekhar Gadepalli,[4] Deepak Kumar[5]

[1]Department of Pulmonary Medicine, All India Institute of Medical Sciences, Jodhpur; [2]Department of Biochemistry, All India Institute of Medical Sciences, Jodhpur; [3]Department of Anaesthesiology and Critical Care, All India Institute of Medical Sciences, Jodhpur; [4]Department of Microbiology, All India Institute of Medical Sciences, Jodhpur; [5]Department of General Medicine, All India Institute of Medical Sciences, Jodhpur, India

Correspondence: Nishant Kumar Chauhan, Room-3026, Department of Pulmonary Medicine, All India Institute of Medical Sciences, Jodhpur, Rajasthan – 342005, India.
Tel.: +918003996884. E-mail: nishant97@gmail.com

Contributions: IG, study design, data collection, manuscript writing; NKC, concept and study design, manuscript editing; HV, manuscript editing; SS, data collection, sample handling; ND, manuscript editing, expert consultation; GD, HI, expert consultation; NK, manuscript editing; RG, statistical analysis; DK, manuscript review. All the authors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest: the authors declare that they have no competing interests, and all authors confirm accuracy.

Ethics approval and consent to participate: the study protocol was approved by the Institutional Ethics Committee of All India Institute of Medical Sciences, Jodhpur, Rajasthan (AIIMS/IEC/2022/3940).

Informed consent: written informed consent was obtained from all participating individuals or their authorized representatives for information to be used in an anonymized manner and for scientific publication.

Patient consent for publication: the consent for publication of patient's data was obtained.

Availability of data and materials: the datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Funding: none.

Abstract

Pneumonia, among all nosocomial infections, is known for its dismal prognosis, imposing substantial morbidity and mortality. While the diagnostic performance of various blood biomarkers has undergone scrutiny, their prognostic implications remain relatively unexplored. This study aimed to evaluate the prognostic significance of clinical factors, microbial etiology, and blood biomarkers, including procalcitonin, C-reactive protein (CRP), and pentraxin-3, in determining the outcome of nosocomial pneumonia. We enrolled 72 patients with microbiologically confirmed hospital-acquired pneumonia (HAP) or ventilator-associated pneumonia (VAP). Patient data comprising demographics, comorbidities, duration of hospitalization, isolated pathogen, and laboratory parameters, including CRP, procalcitonin, and pentraxin-3 levels, were compiled to assess their correlation with 28-day survival outcomes. The study included 58 VAP and 14 HAP patients. The mean age was 52.78±16.98 years, and the majority were males (68.06%). Out of 72, 30 (41.67%) died. Carbapenem-resistant *Acinetobacter baumannii* (44.44%) and Carbapenem-resistant *Enterobacteriaceae* (25%) were the most common isolated pathogens. On univariate analysis, male gender, smoking, opium addiction, underlying neurological condition as comorbidity, presence of septic shock, elevated blood urea, and serum pentraxin-3 levels were significantly associated with 28-day mortality. However, multivariate analysis of subgroup data revealed serum pentraxin-3 levels to be an independent risk factor for mortality in VAP patients. Serum pentraxin-3 levels may be a potential and superior prognostic marker compared to CRP and procalcitonin in predicting mortality in VAP patients.

Key words: C-reactive protein, nosocomial pneumonia, pentraxin-3, procalcitonin.

Introduction

Nosocomial pneumonia are among the most prevalent hospital-acquired infection (HAI), comprising 22% of all cases. These infections worsen patient outcomes, extending hospital stay by 1-2 weeks thereby incurring higher costs. Ventilator associated pneumonia (VAP) lengthens duration of mechanical ventilation by 7.6 to 11.5 days and hospitalization by 11 to 13.1 days [1]. The overall mortality associated with VAP has been reported between 20% and 50%. However, a meta-analysis of randomized studies on VAP prevention estimated the attributable mortality to be around 13% [2]. While hospital acquired pneumonia (HAP) is generally considered less severe than VAP, about 50% of HAP patients experience serious complications such as respiratory failure, septic shock, pleural effusions, renal failure and empyema [3]. Both VAP and HAP caused by high-risk pathogens such as *Pseudomonas aeruginosa, Acinetobacter spp., Stenotrophomonas maltophilia* significantly elevates morbidity and mortality [4].

Given the high mortality associated with nosocomial pneumonia, early prognostic blood biomarkers can offer a promising alternative to traditional complex scoring systems. Various inflammatory markers and their kinetics, particularly procalcitonin (PCT) and C-reactive protein (CRP) have been studied to predict treatment outcomes in sepsis and VAP with additional potential in indicating sepsis severity, antimicrobial efficacy and in-hospital mortality [5-9]. Both markers can be influenced by non-infectious inflammation, organ dysfunction and prior antibiotic use, leading to potential misinterpretation [10]. Furthermore, PCT levels vary by infection site, peaking in those with positive blood cultures and lowest with pulmonary infections, limiting its prognostic value in pneumonia [7,11]. Although serial trends in PCT and CRP levels may provide some moderate prognostic information, relying solely on their absolute values at a single point of time is insufficient for assessing outcomes in HAP and VAP cases [10].

Pentraxin-3 (PTX3), an emerging biomarker, is an acute-phase protein with low blood levels in normal conditions (< 2 ng/mL in humans). It rises earlier than conventional markers, in response to inflammation and infections. Many studies have been conducted depicting its significant association with disease severity and mortality in sepsis and septic shock [12-17]. Elevated PTX3 levels strongly correlates with the severity of lung infection, warranting further research to ascertain their prognostic value in nosocomial pneumonia [18]. Given the paucity of literature on prognostic biomarkers of hospital acquired pneumonia, this study seeks to

determine the value of various blood biomarkers such as procalcitonin, CRP and pentraxin-3, in anticipating outcomes of nosocomial pneumonia.

Materials and Methods

This prospective observational study was conducted at tertiary care centre in western India from March 2022 to December 2023. After obtaining informed consent, patients aged 18 years and above with microbiologically confirmed HAP or VAP were recruited and followed-up for 28 days. Culture proven HAP and VAP was defined as "isolation of known nosocomial microbes with new lung infiltrate plus clinical evidence that infiltrate is of infectious origin, which included new onset fever, purulent sputum/secretions, leucocytosis, and decline in oxygenation" after 48 hours of admission and mechanical ventilation respectively [3]. Only the first VAP/HAP episode was included. Patients with community acquired pneumonia; other concurrent hospital acquired infections like urinary tract infection or bloodstream infection, history of malignancy, neutropenic patients, those who received chemotherapy or radiotherapy within 4 weeks, patients with HIV/AIDS and pregnant females were excluded from the study. Institute ethics committee approval was taken prior to the commencement of the study (AIIMS/IEC/2022/3940).

Data and sample collection

Data was collected according to a predesigned structured proforma. Admitted patients were being daily evaluated for clinical diagnostic criteria of HAP or VAP. Microbiological culture results of respiratory samples like sputum or endotracheal aspirate (ETA) or bronchoalveolar aspirate (BAL), collected under sterile precautions were recorded. Basic demographics, comorbidities, reasons for admission, duration of ICU or ward stay, routine investigations like CBC, LFT, KFT and serum samples for CRP, procalcitonin and pentraxin-3 levels were obtained on the day of microbiological confirmation. HAP and VAP were managed according to clinical practice guidelines of IDSA and ATS 2016 [3] and latest guidance for management of multidrug resistant organisms [19].

Patient's venous samples were collected to measure serum PTX-3 levels. Thirty minutes after drawing blood, tubes underwent centrifugation for 8 mins at 4000 rpm. Samples were then aliquoted and serum portions were preserved at –80°C. Serum PTX-3 levels were measured using a commercial ELISA kit (Elabscience Human PTX 3/TSG-14) according to manufacturer's instructions. Serum PCT levels were measured by chemiluminescence immunoassay (CLIA) on

Siemens Advia Centaur XP; serum CRP levels were determined by immunoturbidimetric assay on Beckman Coulter AU series (AU 680). The patients were followed for 28 days to assess the outcome. Depending on the outcomes, patients were grouped into survivors and non survivors. Those who died within 28 days were grouped as non-survivors and those who survived for atleast 28 days after the diagnosis of pneumonia or were discharged from the ICU or ward within 28 days were considered as survivors.

Statistical analysis

Categorical variables were presented as number and percentage (%) whereas quantitative data were presented as means ± SD. The final analysis was done via SPSS software, IBM manufacturer, Chicago, USA, version 25.0. The comparison of not normally distributed quantitative variables was analysed using Mann-Whitney Test and normally distributed quantitative variables were analysed via Independent-t test. Qualitative variables were analysed using Chi-Square test. ROC curves were obtained to assess cut off point, sensitivity, specificity, positive predictive value and negative predictive value of procalcitonin, CRP and pentraxin-3 for predicting nosocomial pneumonia mortality. Multivariate logistic regression was utilized to find out significant risk factors of VAP non survivors. For statistical significance, p value < 0.05 was considered statistically significant.

Results

In this study, 58 VAP and 14 HAP patients were included, out of which 58.33% (n= 42) survived while 41.67% (n=30) died. The mean age of study subjects was 52.78 ± 16.98 years and majority (68.06%) were males. Most common pathogen isolated was CRAB (*Carbapenem-Resistant Acinetobacter baumannii*) (44.44%) followed by CRE *Klebsiella pneumoniae* (*Carbapenem-Resistant Enterobacteriaceae)* (25%) followed by ESBL (*Extended-Spectrum Beta-Lactamase*) (20.83%). The demographic, clinical and laboratory parameters are compiled and represented in Table 1. The average day of expiry was 11.03 ± 6.58 days.

In univariate analysis, male gender, smoking, opium addiction, neurological diseases as comorbidity, septic shock during pneumonia, raised blood urea and high serum pentraxin-3 levels were significantly associated with 28-day mortality. Multivariate regression showed none of the above variable as significant risk factors of mortality. However, after subgroup analysis in VAP patients, in multivariate analysis, pentraxin-3 was found to be a significant

independent risk factor of mortality after adjusting for confounding factors with adjusted odds ratio (OR) of 1.038 (1.001 to 1.076) (Table 2).

ROC curves above the diagonal line are considered to have reasonable discriminating ability to predict mortality. Discriminatory power of PTX-3 (AUC 0.833; 95% CI: 0.727 to 0.911) was excellent (Figure 1). On the other hand, discriminatory power of procalcitonin (AUC 0.587; 95% CI: 0.465 to 0.702) (Figure 2) and CRP (AUC 0.629; 95% CI: 0.507 to 0.740) was non-significant (Figure 3). Amongst all biomarkers, PTX-3 was the best predictor of mortality at cut off point of > 62.657 pg/ml with AUC of 0.8333 and high sensitivity and specificity of 76.67% and 83.33% respectively.

Discussion

Nosocomial pneumonia remains a significant contributor of morbidity and mortality despite advancements in antimicrobial therapy [20]. Early identification of individuals at high risk of mortality due to hospital acquired pneumonia is crucial for improving patient care, outcomes and optimizing healthcare resources utilization. Exploring inflammatory biomarkers as prognostic tools could offer more practical advantages over complex severity indices like SOFA (Sequential Organ Failure Assessment) and APACHE II (Acute Physiology and Chronic Health Evaluation II) and highlights the need for further research to validate the effective application of blood biomarker measurement in clinical decision-making. CRP and PCT are widely studied parameters for diagnosing infections and monitoring clinical response in VAP [5,20-23]. However, their uncertain prognostic relevance calls for additional research into alternative biomarkers.

Pentraxin-3, an acute phase secretory protein of the long pentraxin subfamily, is produced by innate immune system at various inflammatory sites. Particularly, in the lungs, it is produced by leucocytes, endothelial cells and epithelial cells. In contrast to C-reactive protein (CRP), rapid elevation of PTX-3 following lung infection, emphasizes its significance in early diagnosis and assessment of disease severity [24]. Pentraxin-3 levels correlates with acute lung injury, acute respiratory distress syndrome severity and systemic involvement [25]. High plasma PTX3 levels have been shown to predict poor outcomes in sepsis and septic shock [12-17]. Furthermore, the diagnostic significance of PTX3 levels in serum, pleural fluid, and alveoli has been investigated in patients with pneumonia [24-26]. Bronchoalveolar lavage (BAL) PTX3 levels demonstrated greater diagnostic potential, showing significantly higher levels and an earlier peak in VAP patients compared to serum CRP, highlighting PTX3's superior potential

among various biomarkers [25]. Similarly, research identified that PTX3 threshold level of >16.43 ng/ml yielded 74.0% specificity and 68.6% sensitivity for diagnosing VAP [23]. However, its role as a prognostic marker in nosocomial pneumonia needs further exploration. This study comprehensively analysed prognostic role of demographic profile, comorbidities, laboratory parameters, microbiological results and blood biomarkers such as CRP, procalcitonin and pentraxin-3 in predicting the outcomes of nosocomial pneumonia.

We found that male gender, smoking, opium addiction, neurological comorbidities, septic shock and elevated blood urea & serum pentraxin-3 levels were significantly higher in non-survivors. Conversely, favourable outcomes were associated with female gender, absence of addictive behaviour, trauma as a cause of hospitalization and ESBL microorganisms as infectious aetiology. Multivariate analysis revealed raised serum pentraxin-3 levels as an independent risk factor for mortality in VAP patients. The overall mortality of nosocomial pneumonia was 41.67%, aligning with previous reports where mortality rate ranged from 9.2 to 53.3% [20].

Higher in-hospital mortality among men was observed, consistent with prior literature. Gender significantly impacts the incidence and outcomes of CAP (community acquired pneumonia), HAP and VAP, with higher mortality observed in males [27]. This can be attributed to men's higher addictive potential and more severe existing comorbidities relative to women. Substance abuse, particularly smoking and opium addiction, correlated with higher mortality rates, possibly due to the detrimental effects on the immune system and respiratory function. Mechanically ventilated patients with opioid use disorders require higher sedative and analgesic dose, resulting in excessive sedation and respiratory depression, thereby prolonging ventilatory support [28]. Prior research has similarly observed extended ventilation and hospitalization among opioid users although their results did not translate into higher mortality [29]. Implementing opioid-sparing agents for sedation might be beneficial for these patients.

Neurological comorbidities were associated with an increased mortality risk, likely due to complications like immobility, dysphagia, and respiratory muscles weakness. Prior studies have consistently reported a higher incidence of hospital-acquired pneumonia, particularly from multi-drug resistant gram-negative bacteria (MDR GNB) in neurological patients [30]. Septic shock has emerged as a significant contributor of mortality, also evidenced by research showing that 60% of ICU admissions with nosocomial infections had septic shock with exceptionally high mortality rates [31].

Drug-resistant gram-negative bacteria (GNB), notably CRAB (*Carbapenem resistant Acinetobacter baumannii*) emerged as the predominant pathogen (44.44%) followed by *Carbapenem-Resistant Enterobacteriaceae* (CRE) (25%) and ESBL (*Extended Spectrum Beta-lactamase*) organisms (20.83%). Several studies have highlighted that GNB accounted for 89% of VAP infections with *Acinetobacter baumannii* being the most frequently isolated pathogen, followed by *Pseudomonas aeruginosa* [32-34]. Overall mortality was higher for A. baumannii infections (83.33%) and K. pneumoniae (71.42%) consistent with our findings [35,36]. In our study, ESBL organisms were significantly less prevalent among non survivors compared to survivors likely influenced by the widespread use of carbapenems as the empirical antibiotic for nosocomial infections which are also recommended for ESBL infections [37].

Amongst various laboratory parameters, elevated blood urea levels significantly predicted mortality outcomes. This observation corroborates previous studies which highlighted mortality association with blood urea nitrogen levels exceeding 11 mmol/L and serum creatinine levels above 1.1 mg/dl further emphasizing the clinical relevance of monitoring renal function in assessing patient outcomes [38,39].

CRP is a highly sensitive inflammatory biomarker, however not specific, increases in both infectious and non-infectious inflammation. Although our study revealed higher mean CRP levels in non-survivors compared to survivors, it was not statistically significant. Similar results were reported where no significant association between serial CRP measurements was found between two groups of VAP patients [40].

PCT is widely acknowledged as a specific biomarker in diagnosing bacterial infections [41]. Its association with severity of infection has been extensively studied in community acquired pneumonia with higher levels as a predictor of mortality [42]. Research into PCT and CRP kinetics in Ventilator-Associated Pneumonia (VAP) highlighted that elevated PCT levels by Day 4 of VAP strongly correlate with higher mortality, whereas CRP levels did not significantly affect mortality rates [40,43]. In our study, PCT demonstrated a sensitivity of 83.33% as a mortality predictor, consistent with previous findings, albeit with a lower specificity of 42.86%. Another study [44] reported no significant differences in the mean serum PCT or CRP levels at ICU admission between VAP survivors and non survivors. Thus, serial measurements of PCT rather than the single value at the onset of nosocomial pneumonia were found to carry prognostic value [45].

PTX3 emerged as a significant independent risk factor for mortality, outperforming CRP and PCT in VAP patients, however not in nosocomial pneumonia, possibly due to higher

inflammation in more critically ill VAP patients. Amongst all parameters, Pentraxin-3 was found to be the best predictor of mortality with high specificity of 83.33%, highest positive predictive value and highest negative predictive value of 76.70% and 83.30% respectively as compared to PCT and CRP in predicting VAP mortality. Our results support previous researches indicating that pentraxin-3 is strongly associated with lung injury [46,47]. As a single unique biological marker, PTX3 emerged superior in predicting mortality as compared to frequently used others markers including CRP, IL-6, and TNF-α [48]. Recent findings have highlighted significantly elevated levels of PTX3 and other inflammatory proteins in individuals previously infected with COVID-19, supporting the validity of PTX3 as a systemic biomarker in prolonged systemic inflammatory responses [49]. These results emphasize the potential of PTX3 as a valuable tool in assessing prognosis and guiding therapeutic interventions in severe cases.

Our study extensively examined the prognostic value of a single measurement of Pentraxin-3, in patients with nosocomial pneumonia, complemented by comprehensive demographic, clinical and microbiological profiles. The prospective design of our study ensured complete data capture until the end of follow-up, enhancing the study's reliability. However, it is important to acknowledge certain limitations. Conducted at a single centre, our findings may have limited generalizability across broader regional populations. Being a single centre study, the spectrum of microbiological profile was limited as it does not reflect the variability in microbial prevalence and resistance patterns in different settings. More research involving pooled data from multiple centres would enhance the robustness of the results. Another limitation was the lack of consideration of baseline disease severity, which could impact mortality outcomes. Furthermore, the absence of baseline PTX-3 level measurements before VAP onset highlights the need for comprehensive baseline assessments in future studies for better understanding of predictive biomarkers.

Notwithstanding these constraints, PTX-3 has demonstrated a strong association with mortality in pneumonia, surpassing CRP and PCT. Therefore, as a dynamic inflammatory marker, PTX3 levels could complement traditional scoring systems, providing a real-time indicator of worsening infection and guiding timely antibiotic stewardship. This further emphasizes the need for additional research to establish optimal threshold of PTX-3 levels for accurately predicting mortality risk in cases of hospital-acquired infections and informing decisions on antibiotic de-escalation strategies. This research holds promise for refining clinical practices and optimizing treatment outcomes in patients with hospital acquired pneumonia.

Conclusions

Pentraxin-3 emerged as a novel biomarker, offering promising prognostic value in nosocomial pneumonia outperforming traditional markers like procalcitonin and CRP. This emphasizes the importance of future research to validate its application and further broaden our understanding of morbidity and mortality in nosocomial infections.

References

1. Magill SS, Edwards JR, Fridkin SK, Emerging Infections Program Healthcare-As- sociated Infections Antimicrobial Use Prevalence Survey Team. Survey of health care-associated infections. N Engl J Med 2014;370:2542-3.
2. Melsen WG, Rovers MM, Groenwold RH, et al. Attributable mortality of ventilator associated pneumonia: a meta-analysis of individual patient data from randomised prevention studies. Lancet Infect Dis 2013;13:665-71.
3. Kalil AC, Metersky ML, Klompas M, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis 2016;63:e61-111.
4. Kollef MH: Ventilator-associated pneumonia. JAMA 1993;270:1965-70.
5. Ugarte H, Silva E, Mercan D, et al. Procalcitonin used as a marker of infection in the intensive care unit. Crit Care Med 1999;27:498-504.
6. Yentis SM, Soni N, Sheldon J. C-reactive protein as an indicator of resolution of sepsis in the intensive care unit. Intensive Care Med 1995;21:602-5.
7. Luyt CE, Guerin V, Combes A, et al. Procalcitonin kinetics as a prognostic marker of ventilator-associated pneumonia. Am J Respir Crit Care Med 2005;171:48-53.
8. Pettila V, Hynninen M, Takkunen O, et al. Predictive value of procalcitonin and interleukin 6 in critically ill patients with suspected sepsis. Intensive Care Med 2002;28:1220-5.
9. Wanner GA, Keel M, Steckholzer U, et al. Relationship between procalcitonin plasma levels and severity of injury, sepsis, organ failure, and mortality in injured patients. Crit Care Med 2000;28:950-7.
10. Guo S, Mao X, Liang M. The moderate predictive value of serial serum CRP and PCT levels for the prognosis of hospitalized community-acquired pneumonia. Respir Res 2018;19:193.
11. Rhee C. Using procalcitonin to guide antibiotic therapy. Open Forum Infect Dis 2016;4:ofw249.

12. Perez-San Martin S, Suberviola B, Garcia-Unzueta MT, et al. Prognostic value of plasma pentraxin 3 levels in patients with septic shock admitted to intensive care. PLoS One 2020;15:e0243849.
13. Vega CA, Mommert M, Boccard M, et al. Source of circulating pentraxin 3 in septic shock patients. Front Immunol 2018;9:3048.
14. Hansen CB, Bayarri-Olmos R, Kristensen MK, et al. Complement related pattern recognition molecules as markers of short-term mortality in intensive care patients. J Infect 2020;80:378-87.
15. Hu C, Zhou Y, Liu C, Kang Y. Pentraxin-3, procalcitonin and lactate as prognostic markers in patients with sepsis and septic shock. Oncotarget 2018;9:5125-36.
16. Song J, Moon S, Park DW, et al. Biomarker combination and SOFA score for the prediction of mortality in sepsis and septic shock: A prospective observational study according to the Sepsis-3 definitions. Medicine 2020;99:e20495.
17. Ronanki K, Bairwa M, Kant R, et al. Pentraxin 3 (PTX3) as a predictor of severity of sepsis in patients admitted to an intensive care unit: a cross-sectional study from North India. Cureus 2022;14:e28282.
18. Uusitalo-Seppälä R, Huttunen R, Aittoniemi J, et al. Pentraxin 3 (PTX3) is associated with severe sepsis and fatal disease in emergency room patients with suspected infection: a prospective cohort study. PLoS One 2013;8:e53661.
19. Tamma PD, Heil EL, Justo JA, et al. Infectious Diseases Society of America 2024 guidance on the treatment of antimicrobial-resistant Gram-negative infections. Clin Infect Dis. 2024. doi:10.1093/cid/ciae403.
20. Sangmuang S, Nuntnarumit P, Phukerd S, et al. Factors associated with mortality in immunocompetent patients with hospital-acquired pneumonia. J Glob Infect Dis 2019;11:13-8.
21. Lee JY, Jaye DL, Waites KB, et al. Procalcitonin in patients with pneumonia. Korean J Lab Med 2010;30:406-13.
22. Duflo F, Debon R, Monneret G, et al. Alveolar and serum procalcitonin diagnostic and prognostic value in ventilator-associated pneumonia. Anesthesiology 2002;96:74-9.
23. Luyt CE, Combes A, Reynaud C, et al. Usefulness of procalcitonin for the diagnosis of ventilator-associated pneumonia. Intensive Care Med 2008;34:1434-40.
24. Lin Q, Fu F, Shen L, et al. Pentraxin 3 in the assessment of ventilator-associated pneumonia: an early marker of severity. Heart Lung 2013;42:139-45.

25. Mauri T, Coppadoro A, Bellani G, et al. Alveolar pentraxin 3 as an early marker of microbiologically confirmed pneumonia: a threshold-finding prospective observational study. Crit Care 2014;18:562.
26. Ozsu S, Abul Y, Mentese A, et al. Pentraxin-3: a novel biomarker for discriminating parapneumonic from other exudative effusions. Respirology 2013;18:657-62.
27. de Miguel-Yanes JM, Lopez-de-Andres A, et al. Incidence, outcomes and sex-related disparities in pneumonia: a matched-pair analysis with data from Spanish hospitals (2016-2019). J Clin Med 2021;10:4339.
28. Yamanaka T, Sadikot RT. Opioid effect on lungs. Respirology 2013;18:255-62.
29. Park YJ, Yo CH, Hsu WT, et al. Use of opioids and outcomes of pneumonia: results from the US Nationwide Inpatient Sample. J Acute Med 2021;11:113-28.
30. Lee H, Moon J, Shin HR, et al. Pneumonia in hospitalized neurologic patients: trends in pathogen distribution and antibiotic susceptibility. Antimicrob Resist Infect Control 2019;8:25.
31. Baharoon S, Telmesani A, Tamim H, et al. Community- versus nosocomial-acquired severe sepsis and septic shock in patients admitted to a tertiary intensive care in Saudi Arabia, etiology and outcome. J Infect Public Health 2015;8:418-24.
32. Dey A, Bairy I. Incidence of multidrug-resistant organisms causing ventilator-associated pneumonia in a tertiary care hospital: a nine months' prospective study. Ann Thorac Med 2007;2:52-7.
33. Chawla R. Epidemiology, etiology and diagnosis of hospital acquired pneumonia and ventilator associated pneumonia in Asian countries. Am J Infect Control 2008;36:93-100.
34. Goel V, Hogade SA. Ventilator-associated pneumonia in a medical intensive care unit: Microbial aetiology, susceptibility patterns of isolated organisms and outcome. Indian J Anaesth 2012;56:558-62.
35. Patil HV, Patil VC. Incidence, bacteriology, and clinical outcome of ventilator-associated pneumonia at tertiary care hospital. J Nat Sc Biol Med 2017;8:46-55.
36. Rice LB. Challenges in identifying new antimicrobial agents effective for treating infections with Acinetobacter baumannii and Pseudomonas aeruginosa. Clin Infect Dis 2006;43:100-5.
37. Tamma PD, Aitken SL, Buehrle DJ, et al. Infectious Diseases Society of America antimicrobial-resistant treatment guidance: gram-negative bacterial infections. Clin Infect Dis 2023;ciad428.
38. Carrabba M, Zarantonello M, Bonara P, et al. Severity assessment of healthcare-associated pneumonia and pneumonia in immunosuppression. Eur Respir J 2012;40:1201-10.

39. Celikhisar H, Kucuk H, Yilmaz N, et al. Prognostic factors in elderly patients admitted to the intensive care unit with community-acquired pneumonia. Aging Male 2020;23:1425-31.
40. Tanriverdi H, Tor MM, Kart L, et al. Prognostic value of serum procalcitonin and C-reactive protein levels in critically ill patients who developed ventilator-associated pneumonia. Ann Thorac Med 2015;10:137-42.
41. Guo SY, Zhou Y, Hu QF, et al. Procalcitonin is a marker of gram-negative bacteremia in patients with sepsis. Am J Med Sci 2015;349:499-504.
42. Kim DH, Jung HW, Kang HK. Prognostic value of procalcitonin in pneumonia among patients admitted to intensive care unit. Kosin Med J 2019;34:15-23.
43. Seligman R, Seligman BG, Teixeira PJ. Comparing the accuracy of predictors of mortality in ventilator-associated pneumonia. J Bras Pneumol 2011;37:495-503.
44. Meisner M, Tschaikowsky K, Palmaers T, Schmidt J. Comparison of procalcitonin (PCT) and C-reactive protein (CRP) plasma concentrations at different SOFA scores during the course of sepsis and MODS. Crit Care 1999;3:45-50.
45. Ahmed E, Abu Elkhashab RS, Swelem RS, et al. Etiological and prognostic values of procalcitonin in hospital-acquired pneumonia. Egyptian J Chest Dis Tuberc 2014;63:201-6.
46. Kao SJ. Plasma long pentraxin 3 (PTX3) concentration is a novel marker of disease activity in patients with community-acquired pneumonia. Clin Chem Lab Med 2013;51:907-13.
47. Mauri T, Coppadoro A, Bellani G et al. Pentraxin 3 in acute respiratory distress syndrome: an early marker of severity. Crit Care Med 2008;36:2302-8.
48. Liu S, Qu X, Liu F, Wang C. Pentraxin 3 as a prognostic biomarker in patients with systemic inflammation or infection. Mediators Inflamm 2014;2014:421429.
49. Capra AP, Crupi L, Pantò G, et al. Serum pentraxin 3 as a promising biomarker for the long-lasting inflammatory response of COVID-19. Int J Mol Sci 2023;24:14195.

Table 1. Comparison of demographic, clinical and laboratory parameters between survivors and non survivors. Data are mean ± standard deviation or n (%).

Variable	Overall (n=72)	Survivors (n=42)	Non survivors (n=30)	p value
Demographics				
Age (mean ± SD)	52.78±16.98	50.45±16.63	56.03±17.21	0.171
Male, n (%)	49 (68.06)	23 (54.76)	26 (86.67)	**0.005**
Female, n (%)	23 (31.94)	19 (45.24)	4 (13.33)	
Addiction, n (%)				
Nil	29 (40.28)	25 (59.52)	4 (13.33)	**<0.0001**
BMFE	8 (11.11)	5 (11.90)	3 (10)	1
Smokers	24 (33.33)	7 (16.67)	17 (56.67)	**0.0004**
Opium	9 (12.50)	2 (4.76)	7 (23.33)	**0.029**
Tobacco	7 (9.72)	3 (7.14)	4 (13.33)	0.44
Alcoholic	6 (8.33)	1 (2.38)	5 (16.67)	0.076
Comorbidities, n (%)				
Diabetes	26 (36.11)	13 (30.95)	13 (43.33)	0.281
Hypertension	24 (33.33)	18 (42.86)	6 (20)	0.043
Respiratory problems	29 (40.28)	18 (42.86)	11 (36.67)	0.597
CKD	7 (9.72)	5 (11.90)	2 (6.67)	0.692
Neurological	23 (31.94)	9 (21.43)	14 (46.67)	**0.024**
Cardiac	7 (9.72)	4 (9.52)	3 (10)	1
Post-operative	9 (12.50)	7 (16.67)	2 (6.67)	0.288
Post Trauma	6 (8.33)	6 (14.29)	0 (0)	**0.037**
Complications, n (%)				
No complications	43 (59.72%)	27 (64.29%)	16 (53.33%)	0.35
Septic shock	15 (20.83%)	5 (11.90%)	10 (33.33%)	**0.027**
AKI	12 (16.67%)	9 (21.43%)	3 (10%)	0.336
Thrombocytopenia	10 (13.89%)	6 (14.29%)	4 (13.33%)	1
MODS	3 (4.17%)	1 (2.38%)	2 (6.67%)	0.567
Encephalopathy	2 (2.78%)	0 (0%)	2 (6.67%)	0.17
Microbes, n (%)				
CRAB	32 (44.44)	15 (35.71)	17 (56.67)	0.078
CRE	18 (25)	10 (23.81)	8 (26.67)	0.783
DTR Pseudomonas	4 (5.56)	2 (4.76)	2 (6.67)	1
ESBL	15 (20.83)	15 (35.71)	0 (0)	**< 0.0001**
Serratia	1 (1.39)	0 (0)	1 (3.33)	0.417
MRSA	1 (1.39)	0 (0)	1 (3.33)	0.417
Stenotrophomonas	1 (1.39)	0 (0)	1 (3.33)	0.417
Lab Parameters				
TLC (/µL)	18750±7202.7	1770±7544	20210±6539	0.147
Platelet(thousand/µL)	244.82±167.77	255±143	230±198	0.16
Total bilirubin(mg/dL)	1.04±1.47	0.88±1.11	1.26±1.86	0.068
Albumin (g/dL)	2.44±0.6	2.54±0.61	2.32±0.58	0.13
Urea (mg/dL)	67.91±50.18	56.37±43.2	84.07±55.34	**0.008**
Creatinine (mg/dL)	1.63±1.61	1.44±1.46	1.9±1.79	0.095
CRP (mg/L)	132.98±80.43	118.97±78.56	152.58±80.18	0.063§
Procalcitonin (ng/mL)	9.32±20.58	6.31±14.37	13.55±26.71	0.211§
Pentraxin-3 (pg/mL)	62.12±39.2	44.98±20.93	86.12±46.07	**<0.0001**
Day of Expiry (Mean)	-	-	11.03±6.58	

SD, standard deviation; BMFE, biomass fuel exposure; CKD, chronic kidney disease; AKI, acute kidney injury; MODS, multiorgan dysfunction syndrome; CRAB, Carbapenem resistant Acinetobacter baumannii; CRE, Carbapenem Resistant Enterobacteriaceae ; DTR, difficult to treat resistant; ESBL, extended spectrum beta lactamases; MRSA, Methicillin resistant Staphylococcus aureus; TLC, Total leucocyte count; CRP, C-reactive protein.

Table 2. Multivariate logistic regression to find out significant risk factors of VAP non-survivors.

Variables	Odds Ratio (95% CI)	P value
Urea (mg/dL)	1.006 (0.989-1.024)	0.485
Pentraxin 3 (pg/mL)	1.038 (1.001-1.076)	**0.043**
Gender		
Female (reference)	1.000	-
Male	4.367 (0.790-24.132)	0.091
Neurological	4.532 (0.862-23.824)	0.074
Trauma	0.499 (0.015-16.731)	0.698
Organism		
ESBL	0.521 (0.026-10.320)	0.669

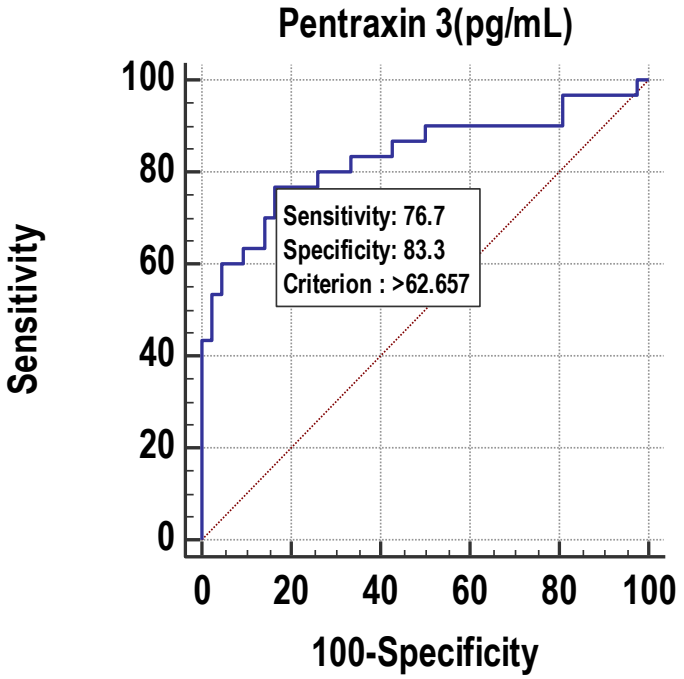

Figure 1. Receiver operating characteristic curve of pentraxin 3 (pg/mL) for predicting mortality.

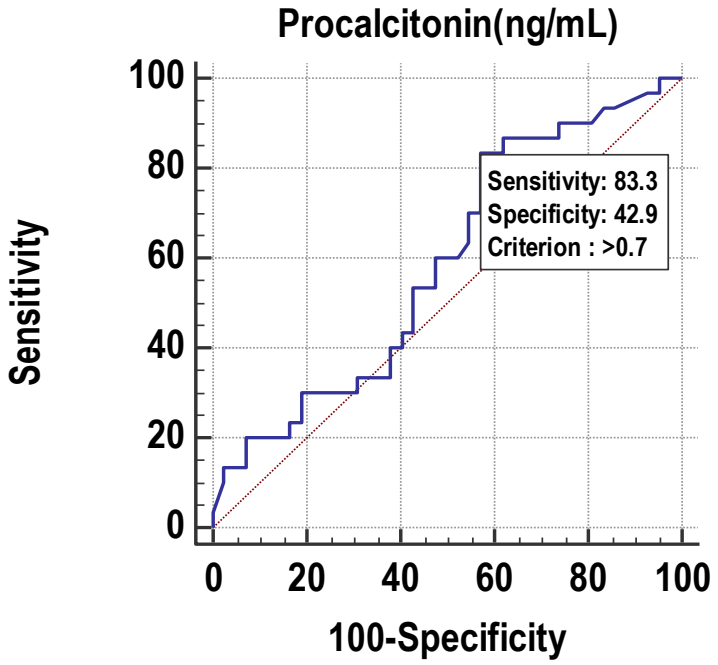

Figure 2. Receiver operating characteristic curve of procalcitonin (ng/mL) for predicting mortality.

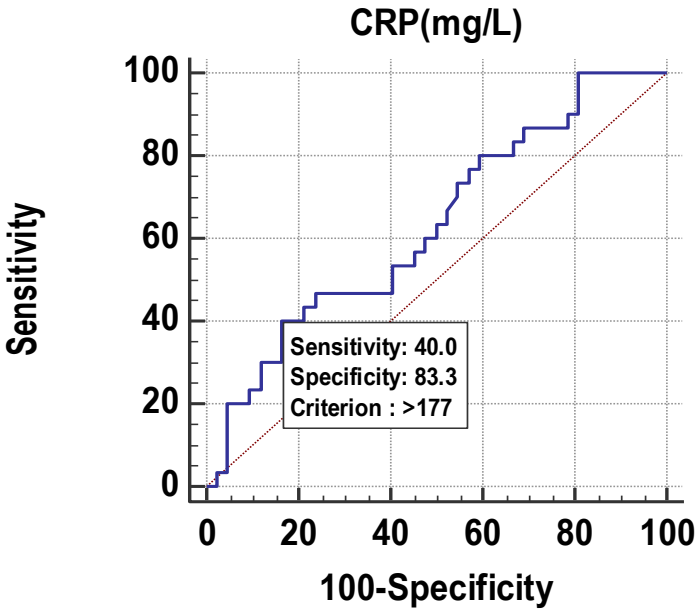

Figure 3. Receiver operating characteristic curve of CRP (mg/L) for predicting mortality.