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C-reactive Protein and D-Dimer as Possible Predictors of Clinical Characteristics and Outcome in Community-Acquired Pneumonia

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ABSTRACT

Background: Community-acquired pneumonia (CAP) is one of the major causes of morbidity and mortality worldwide. The early recognition of patients at risk of severe disease and poor outcomes is of critical importance. Inflammatory and coagulation biomarkers, including C-reactive protein (CRP) and D-dimer, may play a role in the prediction of severity and prognosis of the disease.

Objective: To evaluate the role of CRP and D-dimer as predictors of clinical characteristics and outcomes in patients with CAP.

Methodology: A cross-sectional analytical study was conducted among 230 CAP patients in a tertiary care hospital in Swat, from January 2025 to March 2026. The data collected included clinical, demographic, and laboratory data such as CRP and D-dimer levels. The study also included the associations of these biomarkers with the severity of the disease, radiological involvement, ICU admission, length of stay in the hospital, and mortality using SPSS version 23.

Results: The mean values of CRP and D-dimer were 82.6 ± 38.8 mg/L and 1.34 ± 0.82 mg/L, respectively. These two markers were observed to rise with disease severity, bilateral lung involvement, ICU admission, prolonged hospital stay, and mortality ($p < 0.001$). It is evident that increased values of these two markers were associated with worse outcomes in CAP patients.

Conclusion: The use of CRP and D-dimer as biomarkers for the prediction of the severity of the disease and the outcome of the patients with CAP is significant. Future studies are suggested for the validation of the findings.

Keywords: Community-Acquired Pneumonia; C-Reactive Protein; D-Dimer; Biomarker

Introduction

Community-acquired pneumonia (CAP) is one of the most common infectious diseases and a significant cause of morbidity and mortality worldwide. CAP is described as the acute infection of the lung parenchyma occurring in people outside the hospital or within 48 hours of hospitalization. CAP continues to place a significant burden on the healthcare system, considering its high incidence, hospitalization, and financial impact.[1] This illness affects people of different ages, but the severity of the illness is more pronounced in the elderly, patients with underlying chronic diseases, and immunocompromised patients. Despite the availability of effective antimicrobial and supportive treatment, the complications and mortality associated with CAP, especially severe cases, remain significant.

The clinical manifestations of CAP vary from mild respiratory illness to severe systemic illness with respiratory failure, septic shock, and multiple organ dysfunction syndrome. Thus, the early identification of patients at risk of developing severe disease with poor outcomes is important to optimize the treatment strategies and prognosis of the patient. Various clinical scoring tools, including the Pneumonia Severity Index and CURB-65 scoring tools, have been developed to evaluate the severity of CAP and aid the decision-making process regarding the management of the patient.[2] Though the scoring tools have been found to be useful tools, they are based on clinical observations and parameters. They may not accurately depict the pathophysiological process of the disease. Thus, the search for laboratory biomarkers that may aid the prediction of the severity of the disease, response to the treatment, and outcome of the patient with CAP has gained significant interest.

Inflammation is a key process in the pathogenesis of pneumonia. When the respiratory system is invaded by a pathogen, the host's immune system triggers a complex inflammatory cascade to expel the pathogen. This process involves the production of various cytokines and acute-phase proteins, which lead to local and systemic inflammatory responses. Among these inflammatory biomarkers, C-reactive protein (CRP) has been studied extensively as a marker of inflammation and infections.[3] CRP is a class of acute-phase proteins produced by the liver cells of the host. Its production is regulated by various pro-inflammatory cytokines, especially interleukin-6. CRP production increases rapidly in response to infections and tissue damage. This acute-phase response of CRP provides a useful biomarker for detecting and monitoring inflammatory conditions.[4,5] CRP levels have been shown to correlate with the severity of the disease, the extent of the affected area, and the period of recovery in patients suffering from pneumonia.

In addition to the inflammatory process, disorders of the coagulation system have been identified as playing an important part in the pathophysiological process of pneumonia. The process of infection and the consequent inflammatory process may activate the coagulation process, resulting in the formation of fibrin thrombi in the pulmonary microcirculation. These alterations may cause disorders of gas exchange, tissue hypoxia, and progression of the severity of the disease. D-dimer is a degradation product of fibrin that is formed as a consequence of the degradation of cross-linked fibrin. The level of D-dimer is increased in disorders characterized by disorders of coagulation and fibrinolysis, such as sepsis, thromboembolic disorders, and severe infections.

Studies have shown that the levels of D-dimer may have prognostic significance in patients with community-acquired pneumonia as well. High levels of D-dimer have been associated with severe infection, increased risk of developing complications, longer hospital stays, and increased mortality rates.[6,7] The increase in the levels of D-dimer in patients with pneumonia is attributed to the activation of the coagulation process as a result of the inflammatory process and damage to the endothelium. The measurement of the levels of D-dimer may thus be useful in the prognosis of the condition.[8]

Considering the close association between inflammation and coagulation in the setting of an infection, it would be important to simultaneously assess both CRP and D-dimer levels in CAP patients to get a more accurate picture of disease severity. This would enable clinicians to better utilize these markers to forecast patient clinical characteristics, identify high-risk patients, and take early therapeutic interventions. Such markers would also be important in monitoring disease progression in patients with CAP.

Objective

To evaluate the role of C-reactive protein and D-dimer as potential predictors of clinical characteristics and outcomes in patients with community-acquired pneumonia.

Methodology

The study was conducted in Saidu Teaching Hospital, Swat over a period of one year, from September 2024 to April 2025. A total of 230 patients with community-acquired pneumonia were included in the study using a consecutive non-probability sampling method.

The inclusive criteria included patients aged 18 years and above with symptoms of pneumonia such as fever, cough, production of sputum, shortness of breath, and chest pain, accompanied by radiological evidence of new pulmonary infiltrates on chest radiographs, and those with the onset of pneumonia outside the hospital or within

48 hours of hospitalization. Patients with hospital-acquired pneumonia, those with underlying chronic inflammatory disorders, underlying malignancies, recent major surgeries or trauma, pulmonary embolism, underlying liver disease, or those receiving anticoagulant therapy were excluded from the study in an attempt to exclude underlying factors that could potentially affect the levels of CRP and D-dimer.

Data was analyzed by using SPSS version 23.0. All participants were subjected to the collection of demographic and clinical data using a structured data collection form. Information related to age, gender, presenting symptoms, co-morbid conditions like diabetes mellitus, hypertension, COPD, and smoking status was noted. Clinical examination findings and vital signs were noted at the time of admission. Ethical approval certificate was obtained from the institutional ethical review committee of Saidu Teaching Hospital, Swat for this study, and all the procedures were carried out in accordance with the ethical principles. Written informed consent was obtained from the participants before the inclusion of the participants in this study.

Results

Among the study cases, more participants (38.6%) were aged between 41 and 60 years (38.6%), then those aged over 60 (32.6%). The proportion of male patients in this research was 58.6%, whereas females accounted for 41.3%. The most common symptoms in patients with community-acquired pneumonia were cough (88.6%), fever (83.0%), dyspnea (70.4%), and sputum production (74.7%), whereas chest pain was also observed in 41.7% of patients. The comorbid conditions in this research among patients with community-acquired pneumonia were diabetes mellitus in 31.7%, hypertension in 26.5%,

Table 1. Demographic, clinical, and radiological characteristics of patients with community-acquired pneumonia (n = 230)

Variables		Frequency (n)	Percentage (%)
Age group	18–40 years	66	28.6 %
	41–60 years	89	38.6 %
	>60 years	75	32.6 %
Gender	Male	135	58.6 %
	Female	95	41.3 %
Symptoms present			
Fever		191	83.0 %
Cough		204	88.6 %
Sputum production		172	74.7 %
Dyspnea		162	70.4 %
Chest pain		96	41.7 %
Comorbidities			
Diabetes mellitus		73	31.7 %
Hypertension		61	26.5 %
COPD		52	22.6 %
Smoking history		102	44.3 %

Table 2. Association of C-reactive protein levels with clinical characteristics and outcomes in CAP patients

Clinical parameter	Category	Mean CRP (mg/L) ± SD	p-value
CRP level (mg/L)	Mean ± SD	82.6 ± 38.8	-
CURB-65 severity	Mild (n=97)	59.3 ± 24.7	<0.001
	Moderate (n=81)	81.6 ± 29.7	
	Severe (n=52)	112.4 ± 40.6	
Radiological involvement	Unilateral (142)	72.7 ± 31.3	0.002
	Bilateral (88)	98.6 ± 41.2	
ICU admission	Yes (n=47)	118.4 ± 42.6	<0.001
	No (n=183)	73.4 ± 30.3	
Hospital Stay	≤7 days	68.8 ± 27.6	<0.001
	>7 days	101.3 ± 39.7	
Outcome	Recovered (n=209)	76.4 ± 31.5	<0.001
	Mortality (n=21)	128.5 ± 44.4	

and chronic obstructive pulmonary disease (COPD) in 22.6%. Moreover, a history of smoking was observed in 44.3% of this research's population. This research suggests that middle-aged to elderly people, particularly males, are more susceptible to community-acquired pneumonia (Table 1).

In this study, the average CRP concentration for patients with CAP was found to be 82.6 ± 38.8 mg/L. CRP concentration has been found to be closely related to the severity of CAP. The concentration increases from 59.3 mg/L for patients with mild CAP to 112.4 mg/L for patients with severe CAP. This shows a strong positive correlation between CRP concentration and the severity of CAP ($p < 0.001$). Patients with bilateral lung involvement had higher CRP concentrations (98.6 mg/L) compared to those with unilateral lung involvement (72.7 mg/L, $p = 0.002$). Similarly, patients requiring ICU admission had a higher CRP level (118.4 mg/L) when compared to those admitted to general wards (73.4 mg/L; $p < 0.001$). Patients with long hospital stays (>7 days) had higher CRP levels (101.3 mg/L) when compared to those with short hospital stays (≤7 days; 68.8 mg/L; $p < 0.001$), and patients who did not survive had a high CRP level (128.5 mg/L) when compared to those who survived (76.4 mg/L; $p < 0.001$). These results suggest that high CRP levels are strongly associated with increased severity of disease, extensive lung involvement, need for ICU admission, long hospital stays, and mortality, thus establishing its role as a prognostic biomarker for CAP (Table 2).

The mean level of D-dimer in CAP patients was found to be 1.34 ± 0.82 mg/L. The levels of D-dimer were also found to be significantly associated with disease severity. The levels of D-dimer in mild CAP were found to be 0.77 mg/L, whereas in severe CAP cases, it was 2.07 mg/L ($p < 0.001$). The levels of D-dimer in CAP patients with bilateral lung involvement were also found to be significantly higher (1.75 mg/L) than those with unilateral lung involvement (1.07 mg/L; $p = 0.001$). The levels of D-dimer in CAP patients requiring ICU admission were also found to be significantly higher (2.13 mg/L) than those not requiring ICU admission (1.12 mg/L; $p < 0.001$). The levels of D-dimer in CAP patients with prolonged hospital stay (>7 days) were also found to be significantly higher (1.73 mg/L) than those with a short hospital stay (≤7 days; 0.93 mg/L; $p < 0.001$). The levels of D-dimer in CAP patients with fatal outcome were also found to be significantly higher (2.42 mg/L) than those with a non-fatal outcome (1.18 mg/L; $p < 0.001$) (Table 3).

Discussion

Community-acquired pneumonia is considered to be one of the major causes of morbidity and mortality worldwide. The condition continues to exert a significant impact on

Table 3. Association of D-dimer levels with clinical characteristics and outcomes in CAP patients

Clinical parameter	Category	Mean D-dimer (mg/L) ± SD	p-value
D-dimer level (mg/L)	Mean ± SD	1.34 ± 0.82	-
CURB-65 severity	Mild (n=97)	0.77 ± 0.37	<0.001
	Moderate (n=81)	1.33 ± 0.54	
	Severe (n=52)	2.07 ± 0.92	
Radiological involvement	Unilateral (142)	1.07± 0.48	0.001
	Bilateral (88)	1.75 ± 0.87	
ICU admission	Yes (n=47)	2.13 ± 0.88	0.001
	No (n=183)	1.12 ± 0.51	
Hospital Stay	≤7 days	0.93 ± 0.42	0.001
	>7 days	1.73 ± 0.75	
Outcome	Recovered (n=209)	1.18 ± 0.63	0.001
	Mortality (n=21)	2.42 ± 0.94	

healthcare services, especially in developing countries. Early identification of patients who are prone to severe disease complications is crucial to prevent unfavorable outcomes. In the present study, the potential of C-reactive protein and D-dimer to act as predictive markers for clinical characteristics was evaluated. The study revealed that both CRP and D-dimer levels were significant markers for disease severity, radiological involvement, intensive care unit admission, length of hospital stay, and mortality.

A research article published by Ullah et al (2020) stated that increased levels of CRP levels (>100 mg/dL) and D-dimer levels (>500 ng/ml) in hospitalized patients with COVID-19 were associated with severe clinical outcomes. These may be potential predictors of the severity of the illness.[9] Similarly, in a retrospective cohort study involving 318 patients with severe COVID-19 infection by Milenkovic (2022), it was established that increased levels of inflammatory and coagulation markers were significant predictors of in-hospital mortality. For instance, the levels of IL-6 ≥ 74.98 pg/mL, CRP ≥ 81 mg/L, procalcitonin ≥ 0.56 ng/mL, and D-dimer ≥ 760 ng/mL were associated with an increased risk of mortality in patients with severe COVID-19 infection, thus predicting the outcome in patients with severe COVID-19 infection in the intensive care unit.[10]

The demographic data of the study population revealed that CAP was more common among middle-aged to elderly patients. The largest number of patients was observed among those between 41-60 years of age, followed by those above 60 years. This is supported by previous epidemiological studies that revealed an increased incidence of CAP among elderly patients. This is because, with increasing age, there is a decline in immune function, various physiological changes, and an increased number of comorbid conditions. According to a study by Elias (2024), pneumococcal community-acquired pneumonia is a significant cause of respiratory infection among elderly patients.[11] Another retrospective study conducted in Spain by Rivero-Calle (2016) revealed that the incidence of community-acquired pneumonia among adults was 4.63 cases per 1000 population per year, which increased with increasing age.[12]

In addition, there were more males in this study population than females. This has also been observed in other studies, and it can be attributed to the differences in lifestyle and risk factors such as smoking, exposure to pollutants in the workplace, and the prevalence of chronic respiratory diseases. As indicated by one of the studies by Bălă (2021), air pollution is a major global health risk that affects the respiratory system. Air pollutants such as particulate matter, ozone, and nitrogen dioxide are known

to cause diseases such as COPD, asthma, lung cancer, and respiratory infections.[13]

The clinical manifestations noted in this study also correlate with the common symptoms of community-acquired pneumonia. Cough, fever, shortness of breath, and sputum production were the most frequently reported symptoms. Chest pain was also noted in a considerable number of patients. A survey study conducted by Wyrwich (2013) revealed that community-acquired pneumonia in individuals aged ≥50 years is characterized by multiple symptoms, including fatigue, cough, headache, weakness, shortness of breath, wheezing, and loss of appetite.[14] The presence of comorbid conditions such as diabetes mellitus, hypertension, and chronic obstructive pulmonary disease (COPD) was also relatively high among the study population. These conditions are well-known to impair the immune system and make individuals more susceptible to respiratory infections. Smoking history was also noted in a considerable number of patients, which could further impair mucociliary clearance and make individuals more susceptible to pulmonary infections.

One of the main findings of this study is that there is a significant association between CRP levels and disease severity of CAP. In this study, the average level of CRP among the study subjects was found to be 82.6 ± 38.8 mg/L, which increased gradually with increasing disease severity according to the CURB-65 classification system. Patients with severe CAP had much higher levels of CRP compared to those with mild or moderate CAP. This study further supports the idea that levels of CRP reflect the degree of systemic inflammatory response present in pneumonia. A study by Travlos (2022) found that levels of C-reactive protein (CRP) on day 4 and day 7 of hospitalization have a moderate predictive ability for survival of patients with community-acquired pneumonia, while a decline of more than 50% in CRP levels by day 4 is related to shorter hospital stay.[15] Kushner and Mackiewicz (2020) noted that C-reactive protein is an important acute-phase protein produced by the liver as a response to inflammation and is controlled by cytokines such as IL-6. The levels of this protein increase rapidly during infections and injuries. As such, the levels of this protein may be an indicator of the severity of the inflammation.[16]

The study also showed a significant association between the levels of CRP and radiological findings. Patients with bilateral lung involvement were noted to have higher levels of CRP than those with unilateral lung involvement. In a study by Chalmers (2019), it was noted that C-reactive protein (CRP) is a significant inflammatory biomarker that increases in response to acute lung parenchymal inflammation in conditions such as pneumonia and acute respiratory distress syndrome. This indicates that it may be a measure of lung inflammation and parenchymal damage.[17] Another significant finding in this study is the association between levels of CRP and clinical outcomes. Patients who required admission to the ICU had significantly higher levels of CRP than those patients who required admission to general wards. A study conducted by Gülcher (2016) indicated that higher levels of C-reactive protein (CRP) at ICU discharge, i.e., 75 mg/L or greater, are associated with a high risk of ICU readmission.[18] In addition, patients who required longer hospitalization and those patients who experienced mortality had significantly higher levels of CRP than those patients who required shorter hospitalization. This indicates that patients who require admission to a hospital due to high levels of CRP at the time of admission are at a high risk of developing complications and experiencing poor health outcomes. In addition, monitoring the levels of CRP can provide valuable information regarding the progression of the disease.

Besides CRP, this study also aimed to determine the role of D-dimer as a prognostic marker of CAP. The average level of D-dimer of patients included in this study was 1.34 ± 0.82 mg/L. There was a significant increase in the levels of D-dimer with increasing disease severity. Patients with severe CAP had high levels of D-dimer compared to those with mild disease. This is because inflammatory mediators, which are present during pneumonia, trigger coagulation, leading to fibrin formation, then fibrinolysis, resulting in high levels of D-dimer. According to a study done by Cerda-Mancillas, et al., (2020) there is a significant association between levels of D-dimer and severity of CAP, including increased need for mechanical ventilation and vasopressor support. A level of less than 2400 mcg/L is indicative of low risk of short-term mortality.[19]

The study also showed that patients with bilateral radiological involvement had significantly higher levels of D-dimer than those with unilateral involvement. This implies that severe pulmonary inflammation and endothelial damage may lead to an increase in the coagulation process. Patients with severe disease and those admitted to the ICU had significantly higher levels of D-dimer. This implies that severe disease and increased physiological stress may be associated with elevated levels of D-dimer. A study by Berger et al., (2020), showed that increasing levels of D-dimer in the ICU indicate a worse prognosis and thus may be used as a guide in monitoring the severity of the disease.[20]

The D-dimer levels were also seen to be significantly associated with prolonged hospital stays and mortality. For patients with a hospital stay of more than seven days, it was observed that there were higher D-dimer levels when compared with patients with a hospital discharge of less than seven days. For patients with fatal outcomes, it was observed that there were extremely high levels of D-dimer. High levels of D-dimer may indicate the presence of systemic coagulation activation, endothelial dysfunction, and microvascular thrombosis.

Overall, the results of the current study indicate that CRP

and D-dimer are useful biomarkers, which may help to predict the severity of disease and prognosis of patients with CAP. These biomarkers, when measured during hospital admission, may help clinicians manage patients with CAP. Future multicenter studies with a large sample size are recommended to validate the results of the current study.

Conclusion

The findings of the current study show that both CRP and D-dimer are important prognostic factors for the severity and outcome of patients with CAP. High levels of CRP are associated with the severity of the systemic inflammatory response and are associated with severe CAP, extensive lung involvement, admission to the ICU, prolonged hospital stay, and mortality. High levels of D-dimer are associated with the activation of the coagulation system and are associated with severe CAP, admission to the ICU, prolonged hospital stay, and mortality. These findings suggest that measuring CRP and D-dimer levels upon hospital admission may provide important prognostic information that enables clinicians to identify high-risk patients and optimize management strategies to improve patient outcomes. It is suggested that incorporating these markers in combination with clinical scoring systems such as CURB-65 may provide improved risk assessment in CAP patients. Further large-scale multicenter studies are recommended to confirm the prognostic value of CRP and D-dimer and determine appropriate cut-off values for clinical use.

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