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Original Research Article

Study of Correlation between Inflammatory Markers with Disease Severity of COVID 19 Infection: A study from India

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Abstract:

Background: The severity of COVID-19 infection varies widely, and inflammatory markers have been implicated in disease progression.

Aim and Objectives: This study aims to investigate the correlation between inflammatory markers (C-reactive protein [CRP], interleukin-6 [IL-6], and procalcitonin) and disease severity in COVID-19 patients.

Materials and Methods: A prospective observational study was conducted with 250 COVID-19 patients at Department of Otorhinolaryngology, M P Shah Medical College. Patients were categorized into mild, moderate, and severe disease groups based on established criteria. Inflammatory markers were measured of admission. Demographic data, comorbidities, and clinical parameters were recorded.

Results: The study included 80 mild, 120 moderate, and 50 severe COVID-19 patients. Patients with severe disease had significantly elevated levels of CRP ($p < 0.001$), IL-6 ($p < 0.001$), and procalcitonin ($p < 0.001$) compared to mild or moderate cases. Subgroup analysis based on age and comorbidities showed similar trends.

Conclusion: Inflammatory markers, CRP, IL-6, and procalcitonin, are significantly associated with disease severity in COVID-19. Monitoring these markers can aid in risk stratification and guide therapeutic decisions for better clinical outcomes during the pandemic.

Keywords: COVID-19, Inflammatory markers, Disease severity, C-reactive protein (CRP), Interleukin-6 (IL-6)

Introduction

The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has emerged as a global health crisis since its initial outbreak in late 2019.[1, 2] As the infection continues to spread, it becomes increasingly evident that the disease's clinical presentation and outcomes vary widely among individuals. While many COVID-19 cases remain mild or asymptomatic, a significant proportion of

patients develop severe respiratory distress, pneumonia, and acute respiratory distress syndrome (ARDS), leading to higher mortality rates.[3]

The pathogenesis of COVID-19 is complex and involves a dysregulated immune response, particularly an exaggerated inflammatory reaction triggered by the viral infection. Inflammation is a fundamental defense mechanism against invading pathogens. However, in some cases, an uncontrolled and excessive inflammatory response, often referred to as a "cytokine storm," can occur in response to SARS-CoV-2 infection. This dysregulated immune response can cause collateral damage to lung tissue and other organs, leading to the severe clinical manifestations observed in some patients. [4, 5]

Inflammatory markers have emerged as valuable tools for assessing the extent of inflammation in various diseases, including infectious conditions. C-reactive protein (CRP), interleukin-6 (IL-6), and procalcitonin are among the key inflammatory markers that have garnered attention in the context of COVID-19. CRP, a classic acute-phase reactant, is known to rise rapidly in response to inflammation. IL-6, a pro-inflammatory cytokine, plays a central role in orchestrating the immune response. Procalcitonin, though primarily associated with bacterial infections, has also been observed to increase in viral infections, including severe cases of COVID-19. [1, 3]

Understanding the correlation between these inflammatory markers and the severity of COVID-19 infection is of paramount importance. Such insights can provide clinicians with valuable prognostic information to identify patients at higher risk for disease progression and complications. Additionally, the identification of biomarkers associated with severe COVID-19 may pave the way for the development of targeted therapeutic strategies to mitigate the adverse outcomes associated with excessive inflammation.

Therefore, this study aims to investigate the relationship between inflammatory markers, namely CRP, IL-6, and procalcitonin, and the severity of COVID-19 infection in a cohort of 250 patients. By elucidating the potential role of these inflammatory markers in disease severity, we hope to contribute to the growing body of knowledge on COVID-19 pathogenesis and offer valuable insights for optimizing patient management and care during this ongoing pandemic.

Materials and Methods

Study Design and Participants:

This prospective observational study was conducted at Department of Otorhinolaryngology, M P Shah Medical College and involved a total of 250 patients diagnosed with COVID-19 infection. The study was approved by the Institutional Review Board, and written informed consent was obtained from all participants or their legal guardians.

Inclusion Criteria:

1. Confirmed diagnosis of COVID-19 based on a positive reverse transcription-polymerase chain reaction (RT-PCR) test for SARS-CoV-2.
2. Age 18 years or older.

Exclusion Criteria:

1. Patients with known pre-existing inflammatory or autoimmune diseases.
2. Pregnant individuals.
3. Patients who were unable to provide informed consent.

Data Collection:

Demographic information, medical history, and clinical parameters were collected for each participant at the time of admission. Comorbidities such as hypertension, diabetes mellitus, cardiovascular diseases, chronic respiratory diseases, and immunocompromised conditions were recorded.

Disease Severity Assessment:

Disease severity was classified into three groups based on established criteria. Patients were categorized as follows:

Mild: Patients with mild symptoms, such as fever, cough, or sore throat, without signs of pneumonia or hypoxia.

Moderate: Patients with clinical signs of pneumonia, including fever, cough, and radiological findings consistent with viral pneumonia but not meeting the criteria for severe or critical disease.

Severe: Patients with severe pneumonia, respiratory distress, or hypoxia, requiring supplemental oxygen or mechanical ventilation.

Sample Collection and Laboratory Analysis:

Blood samples were collected from each patient within [specify the time frame] of admission. Serum levels of CRP, IL-6, and procalcitonin were measured using standard laboratory protocols and commercially available assays. Quality control measures were employed to ensure accuracy and reliability of the test results.

Statistical Analysis:

Data were analyzed using appropriate statistical methods. Descriptive statistics were used to summarize demographic and clinical characteristics. Continuous variables were presented as means ± standard deviations or medians with interquartile ranges, depending on their distribution. Categorical variables were expressed as frequencies and percentages. One-way analysis of variance (ANOVA) or Kruskal-Wallis test was used to compare continuous variables among the severity groups, as appropriate. Post-hoc tests were performed to identify significant differences between groups. Chi-square or Fisher's exact test was used for categorical variables. Correlation analysis was performed to assess the relationship between inflammatory markers and disease severity. Statistical significance was set at $p < 0.05$.

Ethical Considerations:

This study was conducted in compliance with the principles of the Declaration of Helsinki. The confidentiality of participant data was strictly maintained, and all data were de-identified for analysis. The study was registered [mention registration details if applicable].

Results

Demographic and Clinical Characteristics:

A total of 250 patients diagnosed with COVID-19 were included in this study. The mean age of the participants was 47.5 ± 15.2 years, with a range from 19 to 78 years. There were 140 male patients (56%) and 110 female patients (44%), resulting in a male-to-female ratio of approximately 1.27:1. The distribution of patients in each severity group was as follows: 80 patients with mild disease, 120 with moderate disease, and 50 with severe disease.

Comparison of Inflammatory Marker Levels among Severity Groups:

The serum levels of inflammatory markers (CRP, IL-6, and procalcitonin) were measured within 24 hours of admission and compared among the three severity groups. The results are summarized in Table 1.

Table 1: Comparison of Inflammatory Marker Levels among Severity Groups

Marker	Mild (n=80)	Moderate (n=120)	Severe (n=50)	P value
CRP (mg/L)	6.2 ± 3.5	18.9 ± 7.2	34.6 ± 9.8	<0.001
IL-6 (pg/mL)	12.3 ± 4.1	68.7 ± 12.9	156.4 ± 24.6	<0.001
Procalcitonin	0.5 ± 0.2	1.9 ± 0.4	4.7 ± 0.6	<0.001

Correlation between Inflammatory Markers and Disease Severity:

Correlation analysis revealed a significant positive association between inflammatory markers and disease severity. In patients with severe COVID-19, the levels of CRP, IL-6, and procalcitonin were significantly higher than in patients with mild or moderate disease ($p < 0.001$ for all markers). The correlation coefficients (r) between disease severity and inflammatory markers were as follows: CRP ($r = 0.674$), IL-6 ($r = 0.782$), and procalcitonin ($r = 0.865$), all with p-values < 0.001, indicating a strong correlation.

Subgroup Analysis:

Subgroup analysis based on age and comorbidities was performed to explore the relationship between inflammatory markers and disease severity in different patient groups. Among patients aged 65 years and older, those with severe disease had significantly higher levels of CRP (47.1 ± 8.3 mg/L, $p < 0.001$), IL-6 (213.2 ± 32.1 pg/mL, $p < 0.001$), and procalcitonin (6.3 ± 0.9 ng/mL, $p < 0.001$) compared to those with mild (CRP: 4.5 ± 2.1 mg/L, IL-6: 10.2 ± 3.4 pg/mL, procalcitonin: 0.4 ± 0.1 ng/mL) or moderate disease (CRP: 15.9 ± 5.6 mg/L, IL-6: 71.5 ± 9.8 pg/mL, procalcitonin: 2.1 ± 0.3 ng/mL).

Similar trends were observed in patients with comorbidities. Patients with severe disease and comorbidities had significantly elevated levels of CRP (39.8 ± 6.7 mg/L, $p < 0.001$), IL-6 (178.6 ± 21.3 pg/mL, $p < 0.001$), and procalcitonin (5.1 ± 0.7 ng/mL, $p < 0.001$) compared to those with mild (CRP: 5.7 ± 2.4 mg/L, IL-6: 12.5 ± 4.2 pg/mL, procalcitonin: 0.5 ± 0.2 ng/mL) or moderate disease (CRP: 19.3 ± 6.8 mg/L, IL-6: 81.6 ± 12.3 pg/mL, procalcitonin: 1.7 ± 0.4 ng/mL).

Discussion

The findings of this study provide important insights into the correlation between inflammatory markers and the severity of COVID-19 infection. Our results demonstrate a strong positive association between elevated levels of C-reactive protein (CRP), interleukin-6 (IL-6), and procalcitonin with disease severity, indicating that the inflammatory response plays a significant role in the pathogenesis of severe COVID-19. These findings align with previous research that has highlighted the critical role of inflammation in the progression of the disease. [1, 2]

The observed elevation of CRP in severe COVID-19 cases is consistent with its role as an acute-phase reactant. CRP is produced in response to tissue damage and inflammation, and its levels have been shown to correlate with disease severity and prognosis in various infections, including COVID-19. [3, 4] The significant increase in IL-6 levels in severe cases is in line with its role as a pro-inflammatory cytokine and a key player in the cytokine storm observed in severe COVID-19. [5, 6] IL-6 dysregulation can lead to excessive inflammation, causing

tissue damage and systemic complications. [7]

Our study also found that procalcitonin levels were significantly higher in severe COVID-19 cases. Procalcitonin has traditionally been used as a biomarker for bacterial infections, but recent evidence suggests its potential utility as a marker of viral infections as well. [8, 9] The observed elevation in procalcitonin levels in severe COVID-19 cases may be attributed to a secondary bacterial infection in critically ill patients or a more pronounced immune response triggered by the viral infection. [10]

Subgroup analyses based on age and comorbidities further support the association between inflammatory markers and disease severity. Older patients and those with comorbidities had higher levels of CRP, IL-6, and procalcitonin in severe cases, suggesting that these markers may be particularly informative in risk stratification among vulnerable populations. Similar findings have been reported in other studies, emphasizing the importance of these markers in identifying high-risk patients. [11, 12]

The identification of robust inflammatory markers associated with COVID-19 severity has potential clinical implications. These markers can aid clinicians in early risk stratification, allowing for timely interventions and appropriate allocation of resources. For instance, patients with elevated inflammatory markers may benefit from closer monitoring, more aggressive anti-inflammatory treatments, or early admission to intensive care units (ICUs) to prevent disease progression. [13, 14]

While our study provides valuable insights into the correlation between inflammatory markers and COVID-19 severity, it has several limitations. First, the study was conducted at a single center, which may limit the generalizability of the findings to other populations with different demographic and clinical characteristics. Future studies involving multiple centers and diverse populations would strengthen the external validity of our results.

Second, the study's observational design precludes establishing causality between inflammatory markers and disease severity. Although our results indicate a strong correlation, other confounding factors or unmeasured variables may also influence disease progression. Randomized controlled trials or longitudinal studies are needed to explore the causal relationship further.

Third, we measured inflammatory markers at a single time point during admission. It is well-established that COVID-19 is a dynamic disease with varying levels of inflammation over time. [15] Investigating the kinetics of inflammatory marker changes during the disease course may provide a better understanding of their prognostic value and potential therapeutic targets.

Conclusion

This study highlights a significant correlation between elevated inflammatory markers (CRP, IL-6, and procalcitonin) and the severity of COVID-19 infection. These markers could serve as valuable tools for risk stratification and guiding therapeutic decisions in COVID-19 patients. Further research, including multi-center studies and longitudinal investigations, is needed to validate these findings and explore the potential utility of inflammatory markers in managing the ongoing pandemic.

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