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Association of C-reactive Protein with Disease Severity and Clinical Outcomes in Hospitalized Patients with COVID-19: A Multicentre study from Lahore, Pakistan

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ABSTRACT

Background: C-reactive protein (CRP) is an acute-phase inflammatory biomarker that has been associated with disease severity and adverse outcomes in patients with COVID-19. Early identification of patients at higher clinical risk is particularly important in resource-limited healthcare settings.

Objective: To assess the association of CRP levels with disease severity, ICU admission, ventilatory support, and in-hospital mortality among patients with PCR-confirmed COVID-19 in three public-sector tertiary care hospitals in Lahore, Pakistan.

Methodology: This retrospective multicenter study was conducted at Fatima Memorial Hospital, Jinnah Hospital, and Sir Ganga Ram Hospital, Lahore from April 1 to July 31, 2020. The final analytical sample comprised 635 patients with PCR-confirmed COVID-19. Demographic characteristics, comorbidities, CRP levels, disease severity, ICU admission, ventilatory support, and in-hospital outcomes were analyzed using SPSS version 24.0. Consecutive sampling was used.

Results: Of 635 patients, 145 (22.8%) had moderate disease and 490 (77.2%) had severe disease. Median CRP was higher in the severe group than in the moderate group (180 vs 58 mg/L). ICU admission occurred in 522 patients (82.2%). In-hospital mortality was 31.5% (200/635); 191 of 200 patients who died (95.5%) had severe disease, with a median CRP of 210 mg/L (IQR 170–280 mg/L).

Conclusion: Higher CRP levels were associated with severe disease and in-hospital mortality in this cohort. Because the study did not evaluate adjusted prognostic performance, receiver operating characteristic curve/area under curve, sensitivity, or specificity, interpret these findings should be interpreted as associations rather than evidence of independent predictive validity.

Keywords: COVID-19; C-Reactive Protein; Disease Severity; Mortality

Introduction

COVERID-19 results from infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was first identified in Wuhan, China, in late 2019. By early 2020, COVID-19 had escalated a global pandemic, characterized by significant morbidity and mortality as well as considerable variation in clinical presentation.¹⁻⁴ The pandemic has placed substantial strain on healthcare systems worldwide, particularly in low- and middle-income countries. Beyond respiratory symptoms, affected individuals may experience complications such as acute respiratory distress syndrome, multi-organ dysfunction, and thromboembolic events. The unpredictable clinical course of COVID-19 underscores the need for effective tools to identify patients at risk for severe outcomes early during hospitalization.

Since the onset of the pandemic, considerable research has focused on identifying biomarkers that can predict the clinical trajectory of COVID-19. Biomarkers that accurately reflect the underlying disease process are essential for early risk stratification, guiding treatment decisions, and optimizing healthcare resources utilization. Among various laboratory parameters, inflammatory markers such as CRP, ferritin, and D-dimer have received attention for their potential prognostic value. In some patients, initially mild or moderate COVID-19 can progress rapidly, necessitating increased oxygen support. Early identifying of patients at risk of clinical deterioration is therefore critical. CRP is a hepatic acute-phase protein that increases in response to inflammation and decreases as the inflammatory stimulus resolves.⁵ Its biological kinetics support its use as a marker of inflammatory activity. Because CRP reference intervals vary by assay and laboratory, a universal normal value should not be assumed.

The pathophysiology of severe COVID-19 is characterized by a dysregulated immune response and a hyperinflammatory state, often termed the 'cytokine storm.' This intense inflammatory environment can result in clinical deterioration, multi-organ dysfunction, and increased mortality. CRP, as a downstream marker of interleukin-6 (IL-6) activity, is particularly relevant because IL-6 is implicated in the cytokine storm associated with severe COVID-19. Elevated CRP may therefore serve as an accessible and cost-effective marker for identifying patients at risk for severe disease. However, CRP can also be elevated in infectious, autoimmune, and other inflammatory conditions, and is not specific to COVID-19. Current WHO severity definitions emphasize clinical features such as oxygen saturation, respiratory distress, and the need for life-sustaining therapies.⁶ Laboratory markers including CRP have also been investigated in relation to disease severity. Several studies have reported higher CRP levels in

patients with more severe COVID-19.⁷⁻⁹ This association may reflect increased systemic inflammatory activity during severe infection. Excessive inflammatory activation can contribute to tissue injury and may be accompanied by further elevation of CRP. Additionally, some reports indicate that serial measurement of CRP may assist in tracking disease progression or response to therapy.¹⁰⁻¹¹ However, the interpretation of CRP trends should consider comorbid conditions and secondary infections, which may also influence CRP levels. Despite these limitations, CRP remains a widely available and relatively inexpensive laboratory test in most hospital settings, making it a practical tool for clinical assessment. Further studies in diverse populations are needed to clarify its prognostic significance across different healthcare environments.

Despite extensive international research, limited data exist regarding association between CRP levels and clinical outcomes in COVID-19 patients in Pakistan, particularly within public-sector hospitals. Understanding the prognostic value of CRP in this context is crucial for informing clinical management and resource allocation. Accordingly, this multicentre study aims to assess the association of CRP levels with disease severity, ICU admission, need for ventilatory support, and in-hospital mortality among PCR-confirmed COVID-19 patients admitted to three public-sector tertiary care hospitals in Lahore, Pakistan.

Objective

To assess the association of CRP levels with disease severity, ICU admission, ventilatory support, and in-hospital mortality among hospitalized patients with COVID-19 in the local population.

Operational definition

COVID-19 infection: SARS-CoV-2 infection confirmed by a positive polymerase chain reaction (PCR) test.

CRP: CRP was treated as a quantitative laboratory variable and reported in mg/L. A CRP value ≥ 100 mg/L was also listed among the biochemical criteria used in the study's disease-severity classification; it was not evaluated as a standalone prognostic threshold in the present analysis.

Disease severity: Patients were categorized as having moderate or severe disease according to the clinical and biochemical criteria recorded in the study protocol, as detailed below.

Moderate Disease: Moderate disease: Patients were aged < 65 years, had low risk or no comorbidities, and met the three listed clinical criteria: (1) hypotension or a fall in

mean arterial pressure >10 mmHg; (2) worsening hypoxia requiring >5 L/min of supplemental oxygen; and (3) persistent respiratory rate >30 breaths/min. In addition, at least two of the following three biochemical criteria were listed: D-dimer ≥ 1000 ng/mL, CRP ≥ 100 mg/L, and serum ferritin ≥ 600 ng/mL.

Severe Disease: Severe disease is defined by the presence of at least one of the following clinical features: high-grade fever with a temperature of 39°C or higher, hypotension, indicated by a decrease in mean arterial pressure greater than 10 mmHg, worsening hypoxia requiring more than 5 liters per minute of supplemental oxygen, or a sustained respiratory rate exceeding 30 breaths per minute.

The study protocol defined severe disease as the presence of any of the following three biochemical abnormalities: a D-dimer level of at least 1000 ng/mL, a C-reactive protein (CRP) concentration of at least 100 mg/L, and a serum ferritin level of at least 600 ng/mL. The presence of any two of these laboratory criteria, together with clinical features, was considered indicative of a severe biochemical inflammatory response in patients.

Methodology

This retrospective study was conducted at three tertiary care hospitals in Lahore, Fatima Memorial Hospital, Jinnah Hospital, and Sir Ganga Ram Hospital from April 1, 2020 to July 31, 2020. During this time, all PCR-confirmed COVID-19 cases meeting the inclusion criteria were included in the analysis. Clinical and laboratory data were extracted from patient records, with a focus on C-reactive protein (CRP) levels and their association with disease severity. Severity was categorized as moderate or severe according to predefined clinical and biochemical criteria. The final analytical cohort comprised 635 patients, selected through consecutive sampling to minimize selection bias and ensure comprehensive representation of hospitalized COVID-19 cases during the study period. This sampling strategy enabled robust comparison of CRP levels and other relevant parameters across severity categories, offering insights into the prognostic significance of CRP within the local healthcare context. The inclusion criteria for this study comprised patients with COVID-19 confirmed by a positive PCR test and those whose records met the study's consent or participation requirements. Patients were excluded if they had a documented bacterial infection, as indicated by elevated procalcitonin levels in the original records, or if their records contained incomplete data. This methodology ensured that the study population included only accurately diagnosed COVID-19 cases with adequate information for analysis, thereby reducing confounding from concurrent bacterial infections. Records of hospitalized patients admitted to designated

COVID-19 blocks and the intensive care units (ICUs) of the three participating tertiary care hospitals were reviewed. Clinical data, laboratory data, treatment details, and in-hospital outcomes were collected and compared. Data were entered and analyzed using SPSS version 24.0. Categorical variables were summarized as frequencies and percentages. CRP was summarized using the median and interquartile range (IQR), as reported in the source analysis. Chi-square tests were used for categorical comparisons. A two-sided p-value <0.05 was considered statistically significant. The original analysis did not include ROC/AUC analysis or multivariable prognostic modelling; accordingly, results are described as associations rather than causal or predictive effects.

Results

A total of 635 patients were included in this study. Majority of the study cases were male 427 (67.2%) and 208 (32.8%) were female (Figure 1).

Among 635 patients, 145 (22.8%) were classified as having moderate disease and 490 (77.2%) as having severe disease (Figure 2). The reported median CRP was 58 mg/L in the moderate group and 180 mg/L in the severe group (reported IQR values 13 and 18, respectively; $p=0.0472$). Severe disease was recorded in 333 of 427 men (78.0%) and 157 of 208 women (75.5%) ($p=0.048$).

Diabetes mellitus was present in 269 patients (42.4%); 202 (75.1%) were classified as having severe disease, with a reported median CRP of 191 mg/L (reported IQR 21; $p=0.029$). Obesity was present in 74 patients (11.7%); 64 (86.5%) had severe disease, with a reported median CRP of 199 mg/L (reported IQR 17; $p=0.054$). These findings represent associations and should not be interpreted as evidence that the comorbidities caused higher CRP levels or poorer outcomes.

ICU admission occurred in 522 of 635 patients (82.2%); 490 of 522 ICU-admitted patients (93.9%) were classified as having severe disease, with a median CRP of 184 mg/L (IQR 150–280 mg/L). Among the 522 ICU patients, 346 (66.3%) were recorded in the NIPPV category; 224 of 346 (64.7%) had severe disease, with a reported median CRP of 119 mg/L (reported IQR 97; $p=0.002$). IPPV was recorded in 176 of 522 ICU patients (33.7%); 143 of 176 (81.3%) had severe disease, with a reported median CRP of 181 mg/L (reported IQR 109; $p<0.001$). In-hospital mortality was 31.5% (200/635). Of the 200 patients who died, 191 (95.5%) had severe disease. The reported median CRP among patients who died was 210 mg/L (IQR 170–280 mg/L; $p<0.001$) (Table 1).

CRP, C-reactive protein; IQR, interquartile range; DM, diabetes mellitus; HTN, hypertension; CVD, cardiovascular disease; CKD, chronic kidney disease; ICU, intensive care unit; IPPV, invasive positive-pressure ventilation; NIPPV, non-invasive positive-pressure

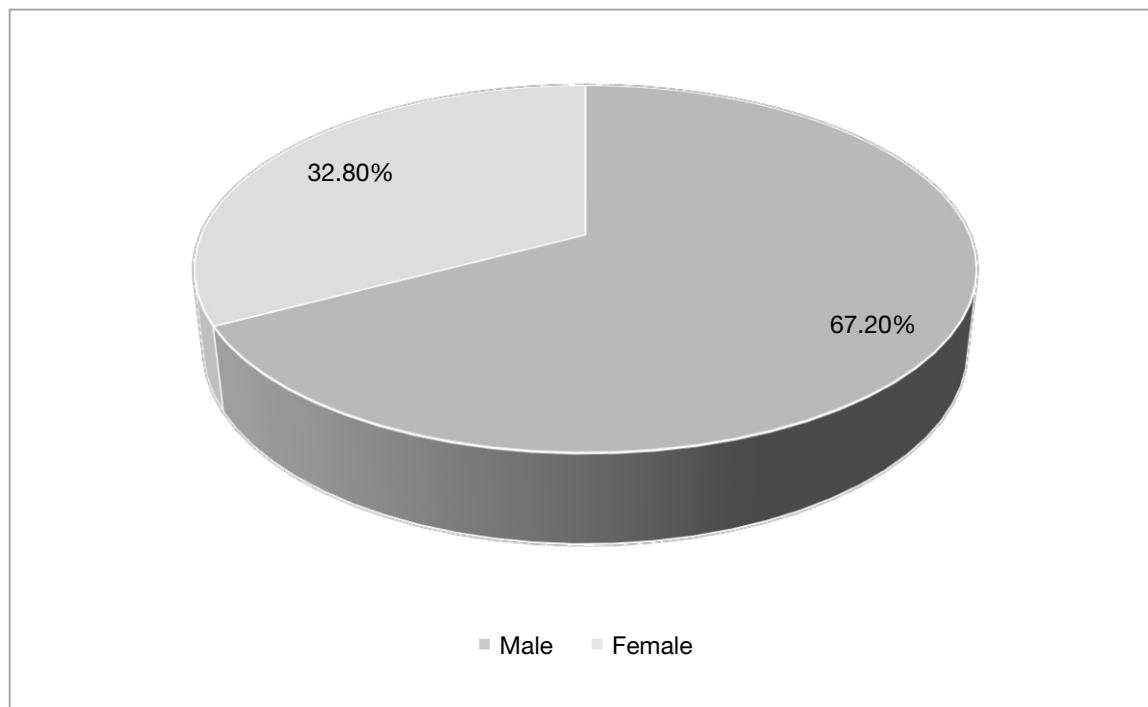


Figure 1. Gender based distribution of study cases

ventilation. CRP values are reported in mg/L. Where the source manuscript supplied only a single IQR value rather than lower and upper quartiles, that value has been retained pending verification against the original SPSS output.

Discussion

This multicentre retrospective study assessed the association between C-reactive protein (CRP) levels, disease severity, and clinical outcomes in 635 hospitalized patients with PCR-confirmed COVID-19 at three tertiary-care hospitals in Lahore, Pakistan. Severe disease was prevalent in this cohort (77.2%), with ICU admission in 82.2% of patients and an overall in-hospital mortality rate of 31.5%. CRP concentrations were significantly higher among patients with severe disease compared to those with moderate disease, and the highest CRP levels were observed in patients who died. A similar pattern emerged across respiratory support categories, with higher CRP concentrations in patients requiring invasive positive-pressure ventilation than in those receiving non-invasive support. Collectively, these results demonstrate an association between higher CRP levels, increased clinical severity, and adverse outcomes in this hospitalized population. However, because CRP was included in the study's definition of disease severity and the analysis did not adjust for potential confounding,

these results should be interpreted as associations rather than evidence that CRP independently predicts outcome. The observed association between C-reactive protein (CRP) levels aligns with CRP's established biological function as a sensitive acute-phase marker of systemic inflammation. Hepatocytes primarily synthesize CRP in response to inflammatory cytokines, particularly interleukin-6, and its concentration can rise markedly during acute infection and tissue injury.⁵ In cases of severe COVID-19, heightened innate and adaptive immune responses may lead to endothelial injury, pulmonary inflammation, tissue damage, and systemic inflammatory reactions, all of which contribute to elevated CRP concentrations. These findings are biologically plausible and corroborate previous evidence indicating that inflammatory biomarkers increase with escalating COVID-19 severity. Liu et al. reported that CRP, interleukin-6, and procalcitonin were associated with disease severity and prognosis in patients with COVID-19. At the same time, Tan et al. showed CRP correlated with radiological findings and could help identify risk of severe disease.^{7,8} Wang also reported rising CRP concentrations during the early stages of COVID-19, and Chen et al. found a positive association between plasma CRP and clinical severity.^{12,13}

The magnitude of the difference observed in this study is substantial. The median C-reactive protein (CRP) concentration was 58 mg/L in patients with moderate

Table 1. Association of CRP levels with demographic characteristics, comorbidities, ICU admission, ventilatory support, and in-hospital outcomes

Variables	Categories	Moderate disease, n (%) and CRP median (reported IQR), mg/L	Severe disease, n (%) and CRP median (reported IQR), mg/L	Total	P-value
Age categories (Years)	≤ 30	10 (6.9)	48 (9.8)	58 (9.1)	0.0472
	31 -45	29 (20)	118 (24.1)	147 (23.1)	
	46-60	51(35.2)	166 (33.9)	217 (34.2)	
	61-75	46 (31.7)	125 (25.5)	171 (27)	
	>75	9 (6.2)	33 (6.7)	42 (6.6)	
	Total	145 (22.8) – 58 (13)	490 (77.2) – 180 (18)	635 (100)	
Gender	Male	94 (22.0) – 50 (19)	333 (78.0) – 177 (17)	427 (67.2)	0.048
	Female	51 (24.5) – 49 (25)	157 (75.5) – 198 (19)	208 (32.8)	
	Total	145 (22.8)	490 (77.2)	635 (100)	
Comorbidities	DM [®]	67 (24.9) – 39 (11)	202 (75.1) – 191 (21)	269 (42.4)	0.029
	HTN [®]	68 (23.2) – 57 (13)	225 (76.8) – 170 (16)	293(46.1)	0.85
	CVD ^μ	24 (24.0) – 44 (10)	76 (76.0) – 210 (11)	100(15.7)	0.079
	CKD ^π	8 (19.5) – 54 (21)	33 (80.5) – 180 (12)	41(6.5)	0.703
	Obesity	10 (13.5) – 55 (11)	64 (86.5) – 199 (17)	74(11.7)	0.054
Outcome of patients	Discharged	388 (89.2) – 71 (13)	47 (10.8) – 129 (27)	435 (68.5)	0.027
	Death	9 (4.5) – 160 (79)	191 (95.5) – 210 (170–280)	200 (31.5)	<0.001
Ventilatory support	Admitted to ICU	32 (6.1) – 98 (67)	490 (93.9) – 184 (150–280)	522 (82.2)	
	IPPV among ICU patients	33 (18.8) – 98 (57)	143 (81.3) – 181 (109)	176/522 (33.7)	<0.001
	NIPPV among ICU patients	122 (35.3) – 80 (99)	224 (64.7) – 119 (97)	346/522 (66.3)	0.002

disease and 180 mg/L in those with severe disease. This finding supports the hypothesis that CRP reflects the intensity of systemic inflammatory activity in hospitalized patients. Previous studies have reported similar trends. Liu et al. found that inflammatory biomarkers, including CRP, were elevated in patients with severe disease, while

Tan et al. reported that CRP correlated with computed tomography (CT) findings and severe clinical disease.^{7,8} A meta-analysis by Huang et al. also demonstrated that CRP, along with procalcitonin, D-dimer, and ferritin, was associated with severe COVID-19.¹⁰ These consistent observations across diverse populations strengthen the

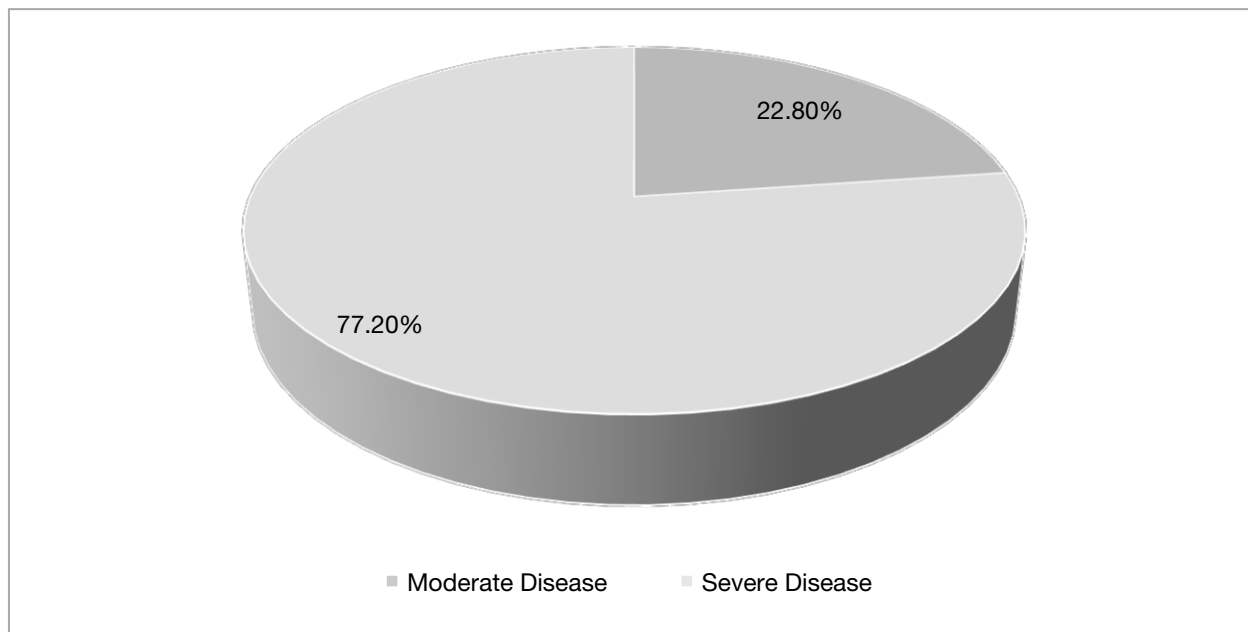


Figure 2. Disease based distribution of study cases

evidence that increased CRP is associated with more severe clinical phenotypes. However, the present study does not determine whether CRP elevation independently contributes to disease progression or merely reflects the severity of the inflammatory response in advanced disease.

A key finding was the association between C-reactive protein (CRP) levels and the requirement for intensive respiratory support. Among patients admitted to the intensive care unit (ICU), most exhibited severe disease, and those receiving invasive positive-pressure ventilation demonstrated a higher median CRP compared to patients managed with non-invasive ventilation. This observation is consistent with the clinical understanding that progression to respiratory failure in COVID-19 is often accompanied by extensive pulmonary involvement. These results corroborate previous studies linking CRP to clinical severity and adverse outcomes. Luo et al. reported an association between CRP and prognosis among hospitalized COVID-19 patients, while Villard et al. similarly identified a relationship between CRP and COVID-19 severity.^{11,14} The present study contributes additional evidence from Pakistani public-sector tertiary hospitals, indicating that higher CRP concentrations are observed in patients requiring more intensive respiratory support.

Caution is warranted when interpreting this relationship, as CRP and respiratory deterioration may have been assessed at different times during hospitalization. The available records lack standardized information regarding the precise timing of CRP measurement relative to

symptom onset, ICU transfer, initiation of non-invasive ventilation, or intubation. As a result, it remains unclear whether elevated CRP levels preceded clinical deterioration and could serve as an early warning marker, or if CRP increased as a result of established severe illness. This distinction is critical, since biomarkers measured after significant clinical deterioration offer limited utility for early prognostic stratification. Future prospective studies should obtain CRP measurements at predefined intervals, particularly at admission and prior to major clinical deterioration.

The observed association between C-reactive protein (CRP) levels and mortality constitutes a significant finding. Within this cohort, 200 patients died, resulting in an in-hospital mortality rate of 31.5%. Notably, 95.5% of deaths occurred among patients classified as having severe disease. The median CRP concentration among deceased patients was 210 mg/L, substantially exceeding the value observed among survivors. This observation aligns with previous research. Abdullah et al., in a retrospective study of 88 patients, reported higher CRP concentrations among non-survivors compared to survivors.¹⁵ Similarly, Hafeez et al., in a cohort of 136 patients, found that inflammatory biomarkers were associated with mortality.¹⁶ Luo et al. also identified prognostic associations between CRP concentrations and adverse outcomes in hospitalized COVID-19 patients.¹¹ The consistency of these findings across multiple studies indicates that marked CRP elevation serves as a clinically relevant indicator of inflammatory burden in hospitalized patients.

However, these should not be interpreted as evidence that C-reactive protein (CRP) concentration independently predicts mortality. The study did not conduct multivariable regression analyses to adjust for potential confounders, including age, sex, diabetes, hypertension, cardiovascular disease, chronic kidney disease, baseline respiratory status, or illness duration before hospitalization. Furthermore, receiver operating characteristic (ROC) analysis, area under the curve (AUC), sensitivity, specificity, and predictive values were not evaluated. Consequently, although the median CRP was higher among non-survivors, this study cannot establish an optimal prognostic threshold or determine CRP's accuracy in discriminating between survivors and non-survivors.

The findings related to comorbidities are noteworthy. Diabetes mellitus was identified in 42.4% of the cohort, with a substantial proportion of these patients exhibiting severe disease and elevated CRP concentrations. Prior studies have established associations between diabetes, other metabolic comorbidities, and increased severity of COVID-19 as well as adverse outcomes. Fachri et al. documented relationships among comorbidities, radiographic abnormalities, and CRP levels in patients with COVID-19.¹⁷ Similarly, Shoukat et al. observed differences in CRP concentrations across non-comorbid, comorbid, and multimorbid hospitalized COVID-19 patients.¹⁸ These findings are biologically plausible, as diabetes and other chronic diseases are linked to altered immune responses, endothelial dysfunction, and a heightened baseline inflammatory state. Nevertheless, the current study should not be interpreted as evidence that diabetes or other individual comorbidities directly caused higher CRP concentrations, given that the analysis was primarily unadjusted.

The association between CRP and hypertension, cardiovascular disease, chronic kidney disease, and obesity was less consistent in this cohort. This inconsistency may be attributable to variations in sample size among comorbidity groups, differences in the inflammatory contributions of specific conditions, or confounding by age and disease severity. Chronic diseases often coexist in older hospitalized patients, complicating efforts to isolate the independent effect of each comorbidity without multivariable analysis. Consequently, the observed associations should be considered descriptive and hypothesis-generating rather than indicative of causality.

A key methodological consideration is that this study used CRP as a biochemical marker to classify disease severity. Specifically, a CRP concentration of 100 mg/L or greater was among the laboratory criteria for severity classification. As a result, the strong association observed between CRP and moderate or severe disease is partly attributable to study design. This introduces a risk of incorporation bias, as the biomarker under evaluation directly contributes to the outcome definition. The

associations between CRP and mortality, ICU admission, and ventilatory support are less susceptible to this bias, since these outcomes were not defined by CRP. However, CRP did not define those outcomes used in the comparisons, so residual confounding cannot be excluded. Future research should use externally defined clinical severity criteria that exclude the biomarker under investigation when assessing CRP's independent prognostic value.

This study is particularly relevant to resource-limited healthcare settings. During the early stages of the pandemic, tertiary hospitals in Pakistan experienced significant strain as the number of patients requiring oxygen therapy, ICU care, and mechanical ventilation rose rapidly. In these contexts, a routinely available laboratory marker such as CRP may offer valuable supplementary information when considered alongside oxygen saturation, respiratory rate, clinical examination, and other laboratory parameters. CRP is generally more accessible than specialized cytokine assays and may therefore serve a practical role in clinical risk assessment. Nonetheless, the current findings do not support using CRP as the sole determinant for treatment allocation or ICU admission. Potempa et al. emphasized that while CRP can provide useful information regarding disease severity, it should always be interpreted within the broader clinical context.¹⁸

The interpretation of these findings must consider the characteristics of the study population. Over three-quarters of participants were classified as having severe disease, 82.2% required ICU admission, and nearly one-third died. These rates are substantially higher than those observed in unselected community populations with COVID-19, as the study focused on hospitalized patients from tertiary referral hospitals. Consequently, the results primarily reflect the relationship between CRP and outcomes among severely ill hospitalized patients, rather than the broader population of individuals with SARS-CoV-2 infection. The elevated severity and mortality rates may also be influenced by referral patterns, delayed presentation, limited critical-care capacity, and the clinical characteristics of patients treated in public-sector tertiary hospitals during the study period.

This study demonstrates that higher CRP concentrations were consistently associated with severe clinical status, increased respiratory support requirements, ICU admission, and in-hospital mortality among hospitalized patients with COVID-19. These results align with previous international and regional evidence and contribute additional data from tertiary public-sector hospitals in Pakistan.^{19,20} However, the findings should be interpreted as indicative of an association between inflammatory burden and adverse clinical status, rather than as definitive evidence of independent prognostic validity. Specifically, the inclusion of CRP in the severity definition and the lack of adjusted prognostic modeling limit the

strength of causal or predictive inferences. Nonetheless, CRP may serve as a valuable adjunctive inflammatory marker when interpreted in conjunction with clinical findings and other laboratory parameters. Prospective studies employing externally defined severity outcomes, standardized CRP measurement timing, serial assessment, multivariable modeling, and ROC/AUC analysis are necessary to establish its independent prognostic utility in Pakistani patients with COVID-19.

Strengths

Several strengths of this study warrant acknowledgment. First, the research was conducted across three tertiary-care hospitals, enhancing clinical heterogeneity and minimizing reliance on a single center's experience. Second, the inclusion of 635 hospitalized patients provided a substantial sample size for examining associations between CRP and multiple clinically significant outcomes. Third, the study assessed several meaningful outcomes, including disease severity, ICU admission, ventilatory support, and in-hospital mortality. The consistent direction of association across these outcomes reinforces the descriptive evidence that higher CRP levels are associated with more severe clinical illness.

Limitations

Important limitations are the retrospective design, the high proportion of ICU admissions, and the absence of ROC/AUC analysis, effect-size estimates with confidence intervals, and multivariable adjustment for potential confounding. The timing of CRP measurement relative to clinical deterioration and initiation of respiratory support is not documented in the submitted manuscript and should be verified from the original records. In addition, CRP ≥ 100 mg/L was included among the biochemical criteria used for disease-severity classification; analyses relating CRP to the severity category are therefore susceptible to incorporation bias and should be interpreted cautiously. Finally, the exact procalcitonin threshold used to exclude bacterial co-infection and the site-specific participant flow also require confirmation from the original study records.

Conclusion

Higher CRP levels were associated with severe disease and in-hospital mortality in this hospitalized cohort. These findings support an association between inflammatory burden and adverse clinical status but do not, by themselves, establish CRP as an independent prognostic biomarker. Prospective studies using clearly timed CRP measurements, externally defined severity criteria, ROC analysis, and adjusted multivariable models are needed

to determine prognostic performance.

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