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Research Paper

C-Reactive Protein as a prognostic marker of severity of SARS-CoV-2 Pneumonia among hospitalized patients in Eastern Nepal

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ABSTRACT: ***Background****: C-reactive protein (CRP) is an acute-phase protein that is raised in response to infection or inflammation. Higher levels suggest a more serious infection and have been used to predict the severity of COVID-19 disease. The evidence supporting CRP as a prognostic marker has yet to be determined.* ***Methods:*** *Patients with SARS-CoV-2 viral nucleic acid using qRT-PCR, patients with SARS-CoV-2 symptoms, and comorbidtis were included. In SARS-CoV-2, severe differences in oxygen and CRP levels were compared. The relationship between C-reactive protein (CRP) levels and COVID-19 pneumonia severity was then investigated using linear regression and correlation models.* ***Results:*** *CRP could be used as an independent factor in predicting the severity of COVID-19 infection. Dry cough and difficulty in breathing were most common symptoms in SARS-COV-2 patients. Analysis of the ROC curve showed that oxygen level could also be used to predict disease severity.* ***Conclusions****: CRP levels are linked with the severity of COVID-19 pneumonia in the early stages of illness.*
KEYWORDS*: SARS-CoV-2, Pneumonia, CRP, Severity*

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I. INTRODUCTION

Corona virus is a member of the *Ortho-coronavirinae* subfamily of the *Coronavirinae* family and the Order *Nidovirale*s. SARS-CoV-2 caused an outbreak of severe acute respiratory syndrome in 2003 [1]. In December 2019, an outbreak of "unknown viral pneumonia" was reported. Finally, a new *corona virus* was discovered; the isolated virus was given the name SARS-CoV-2 and was described as highly contagious and fatal. More than 78,631 SARS-CoV-2 illnesses and 2747 deaths were verified in China by the end of February 2020, prompting the World Health Organization to proclaim COVID-19 a pandemic. Some patients infected with SARS-CoV-2 did not develop hypoxemia or respiratory stress during COVID-19, demonstrating that SARS-CoV-2 infection is a diverse disease. Therefore, one accurate and simple biomarker is needed to predict the severity of COVID-19 pneumonia. Several studies have recently found that C-reactive protein (CRP) is linked to severe dengue infection, and that patients with greater plasma CRP during the early stages of the disease are more likely to develop plasma leakage [2] and [3]. CRP could be used to predict the severity of COVID-19 pneumonia, according to our hypothesis. And, as far as we know, this is the first study to look at CRP's prognostic value in predicting the severity of COVID-19 pneumonia.

II. MATERIALS AND METHODS

2.1 Study design, participants and definition

The Institutional Review Committee (IRC-PA-155/2077-78) of Birat Medical College Teaching Hospital has accepted the current cross-sectional study protocol (BMCTH). From July 2021 to September 2021, the BMCTH confirmed a total of 108 adult COVID-19 cases. The WHO Interim guideline for COVID-19 was used to diagnose all COVID-19 patients who enrolled in the recent trial (6th edition) [4]. Within 7 days of clinical symptoms, and within 7 days of a positive viral nucleic acid test for a symptomatic patient, COVID-19 is defined. COVID-19 was confirmed by a positive viral nucleic acid test, which was the only criterion for inclusion. Patients with bacterial illness, those who began symptoms more than 7 days before, and those who had incomplete data were also removed [5]. In other words, all patients with COVID-19 infection were included if it was confirmed by a clinician and a laboratory (positive nasopharyngeal/throat swab specimens by reverse transcription-polymerase chain reaction (RTPCR)), while suspicious cases with comparable clinical symptoms were removed. From the patients' medical records, all sociodemographic, clinical, laboratory, and outcome data were retrieved. The Pneumonia Severity Index (PSI) of Fine et al. was used to categorize the clinical severity of patients on admission [6]. CRP levels were monitored depending on individual medical decisions, and we documented all results within the first seven days of hospital admission to ensure that no bacterial infection developed during this time.

The SPSS 24.0 software was used to conduct the statistical analysis. The mean standard deviation (mean SD) is used to express measurement data having a normal distribution. Spearman correlation analysis was used to examine correlation. A statistically significant P value was less than 0.05. The area under the receiver operating characteristic curve was used to assess the CRP's predictive value (AUROC).

III. RESULTS

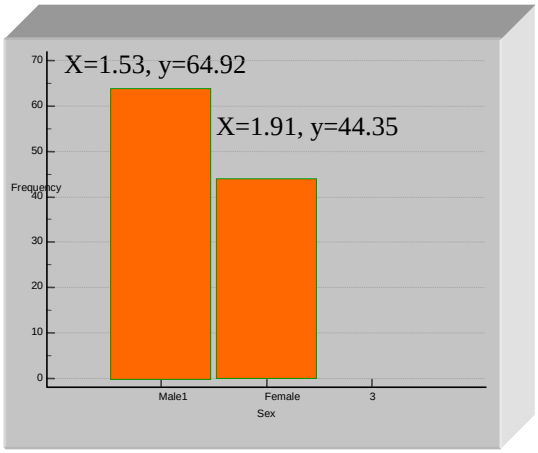


Figure 1: Gender distribution in COVID-19

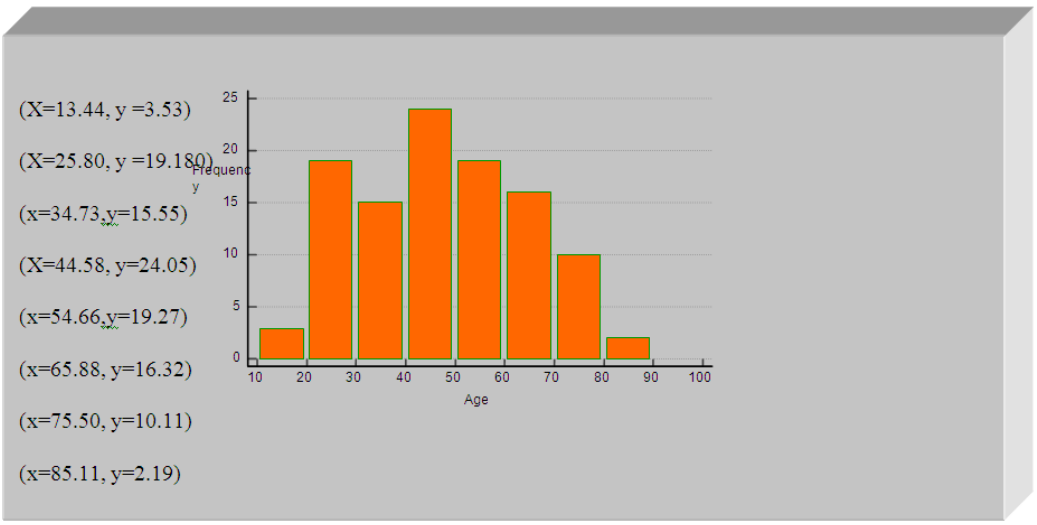


Figure 2: Distribution of age groups in COVID-19

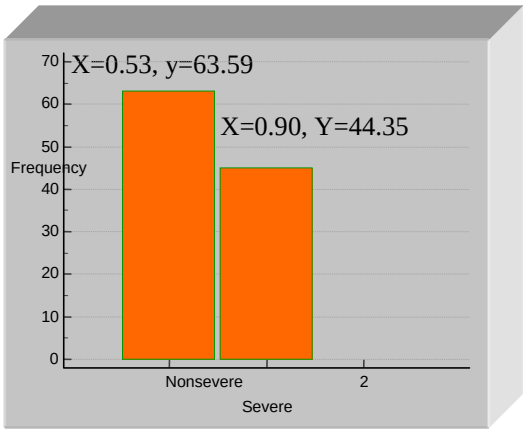


Figure 3: COVID-19 Severity Frequency

Co morbidities	Total sample	Early Stage CRP level		
	Yes/ no	Mean	Std. Deviation	(p < 0.05)
Hypertension	34/73	109.4/83.808	81.5684/68.022	0.054
Cardiovascular disease	8/100	119.5/89.07	104.66/70.279	0.036
Diabetes	25/83	104.16/87.457	81.204/70.616	0.20
Cancer	0/108	0/91.324	0/73.148	-
Chronic liver disease	2/106	34/92.405	19.79/73.38	0.061
Chronic kidney disease	7/101	52.285/94.029	32.627/74.480	0.0046
Brain disease	1/107	192/90.383	0/72.833	0
Asthma/COPD	7/101	98.857/90.801	85.812/72.657	0.278

Table 1: Patients with COVID-19 had the following demographic and baseline characteristics.

Total Severe	Age		Early Stage CRP level		Late Stage CRP level		Lowest Oxygen level	
	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std. Deviation
45 Yes (41.7%)	55.533	15.5850	117.28	79.09735	60.311	60.9343	75.3289 %	21.97383
63 No (58.3%)	41.079	16.2384	72.778	62.8922	39.079	37.6222	94.9206 %	3.19930
(p < 0.05)			.006		.042		.000	

Table 2: COVID-19 patients' demographic and baseline features

Symptoms	Asymptomatic	Symptomatic
Fever	61(56.5)	47(43.5)
Dry cough	29(26.85)	79(73.1)
Expectoration	102(94.4)	6(5.6)
Hemoptysis	101(93.5)	7(6.5)
Chest pain	57(52.8)	51(47.2)
Difficulty in breathing	44(40.7)	64(59.3)

Table 3: The distribution of symptoms of patients with COVID-19

Comorbiditis	Without comorbiditis	With comorbiditis
Hypertension	74(68.5)	34(31.5)
Cardiovascular disease	100(92.6)	8(7.4)
Diabetes	83(76.9)	25(23.1)
Cancer	108(100)	0(0.0)
Chronic liver disease	106(98.1)	2(1.9)
Chronic kidney disease	101(93.5)	7(6.5)
Brain disease	107(99.1)	1(.9)
Asthma/COPD	101(93.5)	7(6.5)

Table 4: Patients with COVID-19 have a wide range of co-morbidities

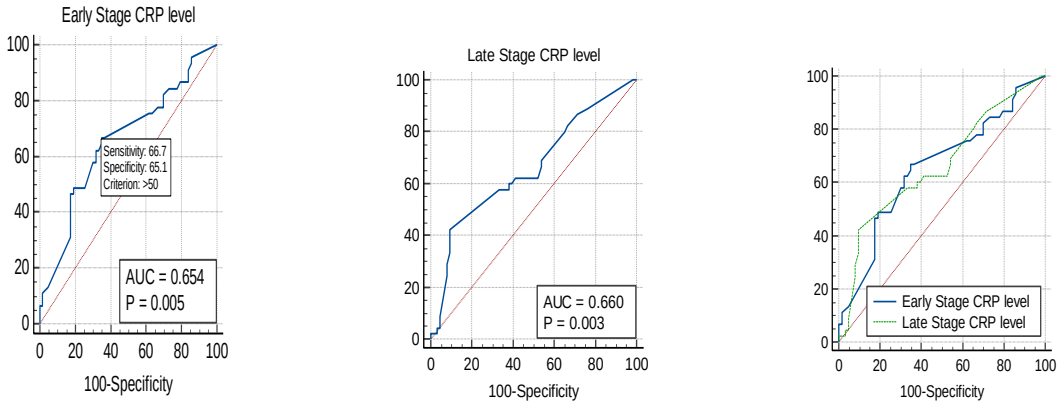


Figure 4: C-reactive protein receiver operating characteristic (ROC) curves for predicting disease severity in COVID-19 patients

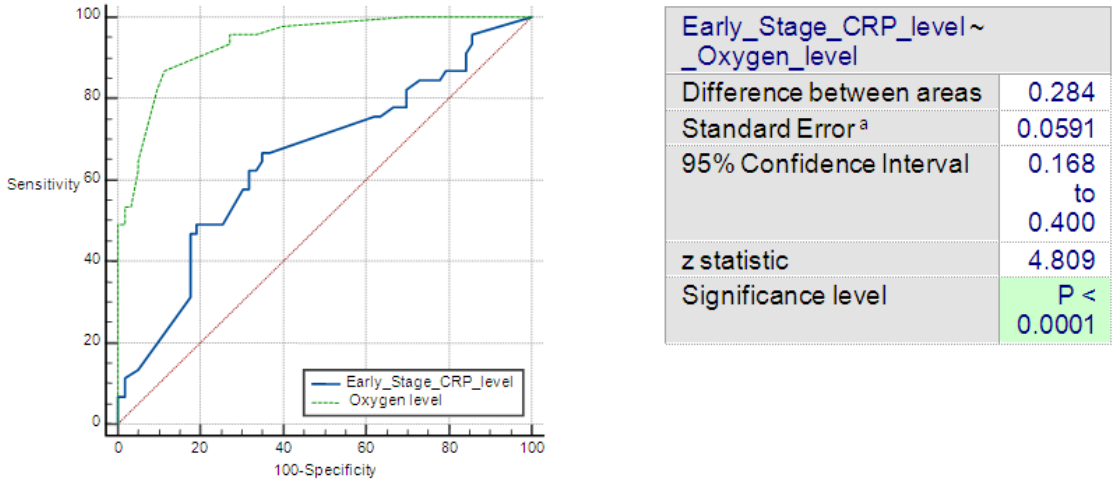
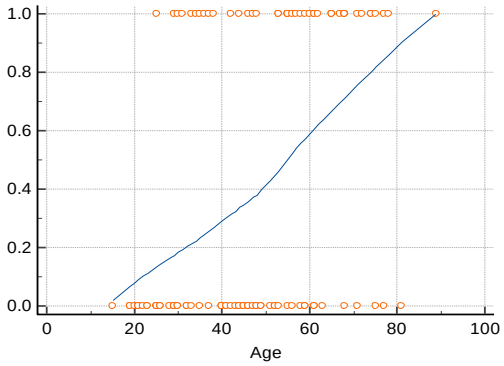
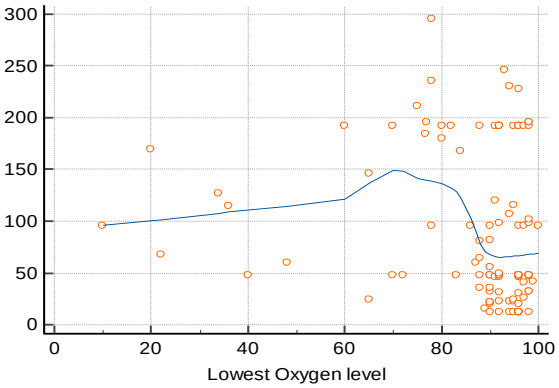


Figure 5: C-reactive protein and oxygen level Receiver Operating Characteristic (ROC) curves for predicting disease severity in COVID-19 patients



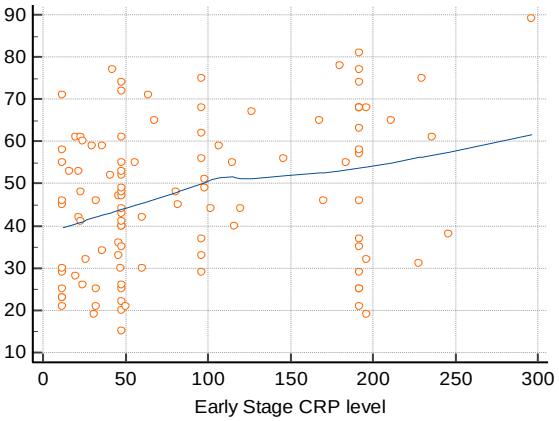
Sample size	108
Correlation coefficient r	0.4107
Significance level	P<0.0001
95% Confidence interval for r	0.2403 to 0.5564

Figure 6: Correlation of severity with age



Sample size	108
Correlation coefficient r	-0.1650
Significance level	P=0.0878
95% Confidence interval for r	-0.3433 to 0.02470

Figure 7: Correlation of CRP on admission with oxygen requirement



Sample size	108
Correlation coefficient r	0.2999
Significance level	P=0.0016
95% Confidence interval for r	0.1176 to 0.4627

Figure 8: The correlation of CRP with age

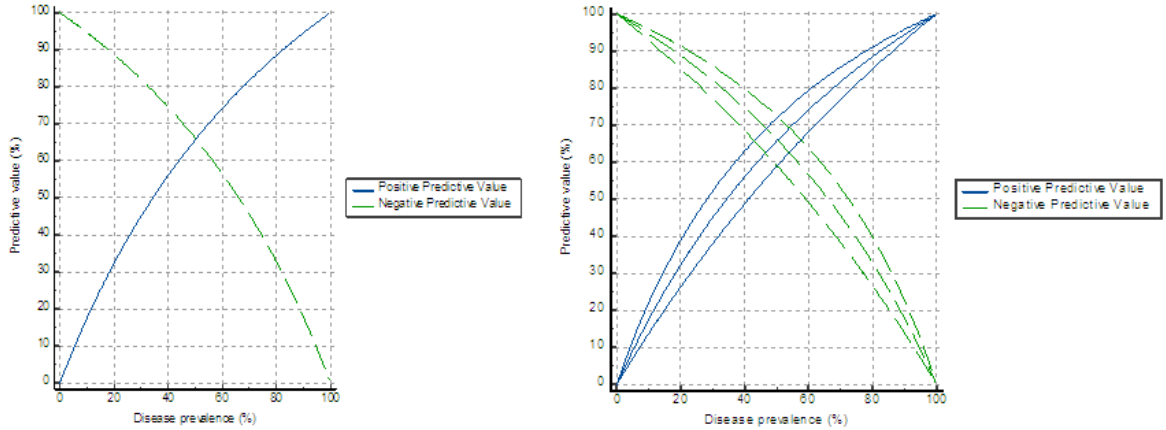


Figure 9: COVID-19 has a high positive predictive value when it comes to prevalence

IV. DISCUSSION

Globally, the number of COVID-19 patients is steadily increasing, and asymptomatic persons are also a source of infection [7]. COVID-19-related case fatalities are also on the rise. COVID-19 is a new public health issue, and treatment alternatives must be assessed [8],[9]and[10]. Early monitoring of key markers was critical for guiding treatment methods, as was an early assessment of the severity of the patients' condition [11]. CRP levels are linked to the severity of inflammation, and their concentration is unaffected by age, gender, or physical condition [12]. CRP levels can activate complement and increase phagocytosis, ridding the body of harmful germs. Patients with severe pneumonia had elevated CRP levels, which can be used to diagnose pneumonia early. It's a crucial metric for diagnosing and assessing severe lung infectious illnesses [13] and [14]. Matsumoto's research also demonstrated the importance of CRP levels in cases of severe pneumonia. CRP levels were shown to be linked to lung lesions and disease severity [15]. The clinical characteristics of severe COVID-19 patients were compared to those of nonsevere patients in this cross-sectional study, which looked at the possible factors linked to illness progression and severity. In addition, the CRP's predictive usefulness in the advancement of COVID-19 patients has been discovered. To put it another way, ROC analysis proved that CRP is a good predictor of COVID-19 development and severity. Furthermore, during inflammatory responses, serum CRP levels rise. This biomarker can be elevated by viral or bacterial infections, as previously stated. It's worth noting that CRP levels in bacterial infections were much higher than in viral infections [16]. The current study found that severe patients had considerably higher CRP levels than non-severe patients, suggesting that CRP may be a biomarker of disease severity and progression in COVID-19 patients. According to Liu et al., more severe COVID-19-infected individuals had considerably higher CRP levels than non-severe patients [17]. Qin et al. observed greater CRP levels in severe COVID-19 patients than in nonsevere instances, suggesting that this biomarker can be monitored to evaluate disease progression [18]. CRP levels were assessed as a potential biomarker of COVID-19 prognosis in a meta-analysis by Sahu et al. CRP concentrations remain high in expired individuals, according to their findings, and could be a viable diagnostic for determining mortality [19]. Furthermore, other studies found that some common COVID-19 consequences, such as shock, ARDS, acute renal injury, and acute cardiac injury, were linked to increased CRP levels in severe and expired COVID-19 patients [20]. Higher levels of interleukin–6 have recently been discovered in the serum of patients requiring mechanical ventilation, but its measurement is not as readily available as CRP, a well-known non-specific acute-phase protein induced by IL–6 in the liver, and higher CRP values have been reported in severe cases [17] and [21]. CRP is thought to be a reflection of the inflammatory status of lungs illness. Similarly, Ruan et al. discovered that patients who died had greater CRP levels than those who were discharged [21].This could be explained by the fact that CRP is a key regulator of inflammatory processes as well as a marker of inflammation and infection [22]and [23] . Furthermore, we discovered that CRP levels were linked to respiratory assistance, such as oxygen consumption and the need for mechanical ventilation, as well as death. In addition, the CRP kinetics during the first week of hospitalization differed significantly depending on whether or not patients required mechanical breathing. As a result, CRP could be a useful marker for predicting the onset of respiratory failure and, as a result, aid in the proper allocation of patients at an early stage.

V. CONCLUSIONS

Our data imply that serum CRP levels could be an important indication of COVID-19 development and severity. Patients with higher CRP levels should also be closely evaluated throughout their disease course, according to the findings.

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