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Original Article

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C-Reactive protein and chest x-ray morphology in COVID-19 patients: Our single center experience

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Abstract

***Background & Aims*:** Coronavirus disease-2019 (COVID-19) is a newly discovered viral illness for which there is no proven cure at this time. We sought to establish the value of C-reactive protein (CRP) levels and chest X-ray morphology in determining the severity of COVID-19 disease and to correlate them with related mortality.

***Materials & Methods*:** Data of COVID-19 patients with clinical outcomes in a small-designated hospital in Nadiad (Gujarat, India), collected retrospectively from March 15 to May 31, 2020. Patients with COVID-19 had their admission CRP's prognostic value, and chest X-ray morphology assessed.

***Results*:** Out of 85 patients enrolled, 72 survived and 13 died. With an area under the curve (AUC) of 0.808 (95 percent CI, 0.708–0.885; P=0.001), the ROC curve analysis revealed moderate accuracy to identified mortality. Our model had an elevated CRP value of 0.105 units, which corresponded to an increased mortality rate of 1.11 times (Wald=12.73, 1.11(1.05, 1.18).

***Conclusion*:** In contrast to the RT-PCR test, our investigation found that CRP and chest X-ray morphology were excellent predictors of earlier diagnosed COVID-19 patients. We want to require a larger sample size and to identify an additional biomarker that reduces mortality.

***Keywords*:** C-reactive protein (CRP), Chest X-ray Morphology, Covid-19, mortality

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Introduction

On December 31, 2019, Wuhan, China, experienced an outbreak of severe pneumonia cases from an unknown source. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was discovered and a virus isolated from the epithelial cells of infected persons' respiratory systems, and the outbreak was named coronavirus disease (COVID-19) (1). The COVID-19 outbreak spread quickly over the world (2, 3). The World Health Organization (WHO) labeled it a pandemic in January 2020 (4). By March 30, 2021, there were 127,349,248 confirmed COVID-19 cases, with 2,787,593 deaths reported to the World Health Organization (WHO) (5). SARS- CoV's rapid spread, rapid changes in clinical characteristics, and higher mortality have become the world's most serious concern nowadays. Furthermore, there are no reliable prognostic

indicators for predicting disease severity and progression.

C-reactive protein (CRP) levels can be employed in the early identification of pneumonia, according to certain studies, and greater CRP levels are linked to severe pneumonia (6). CRP, an acute phase glycoprotein produced by the liver in response to interleukin 6 (IL-6), is a commonly used marker of inflammation in clinical practice (7). It is also a sign of serious bacterial infection, trauma, and various chronic diseases, commonly encountered in older adults, such as malignancies. Although elevated levels of CRP linked to lower mortality in the patients with acute lung damage, experimental results suggest that CRP may have a protective function in alveolitis, and earlier clinical evidence has linked elevated levels of CRP to lower mortality in the patients with acute lung injury (8).

Fever, cough, dyspnea, fatigue, and myalgia are the most common COVID-19 symptoms. Less common symptoms include sputum, hemoptysis, headache, and gastrointestinal symptoms (5). A chest X-ray was found to be of limited use in the initial diagnosis of COVID-19, with a sensitivity of about 69% (9, 10). Patients with COVID-19 had typical radiological findings on chest imaging, including multifocal and bilateral ground glass opacities, and consolidations with peripheral and basal predominance. Less common were septal thickening, bronchiectasis, pleural effusion, lymphadenopathy, and cavitation (4, 12-16). The aim of the present cohort study was to determine whether raised CRP levels along with chest X-ray morphology in the early phases of COVID-19 were linked with mortality in hospitalized patients.

Materials & Methods

Study Design, Participants, and Definition:

The Dr. N.D. Desai Faculty of Medical Science and Research was the site of the current retrospective investigation. Patients with COVID-19 had to be treated at this hospital. Between 15 March 2020 to 31 May 2020, 105 adult cases confirmed at this institute. The WHO interim recommendation for COVID-19 (6th edition) was used to diagnose all COVID-19 patients who participated in the most recent trial (6). We mean that all patients with physician- laboratory-confirmed COVID-19 infection were included by using reverse transcription-polymerase chain reaction (RTPCR) of nasopharyngeal/throat swab specimens, whereas suspicious cases with comparable clinical symptoms were excluded. One of the following standards determined severe COVID-19 sickness: arterial oxygen partial pressure (PaO2)/oxygen concentration (FiO2) (PaO2/(FiO2) equal to 300 mm Hg, respiratory rate of 30 bpm, and oxygen saturation of 93%.

Data Collection:

An experienced team from our institute examined the patient's medical records. Using an electronic medical record data-collecting checklist, information on epidemiological, clinical, laboratory, radiological and other findings and outcome have collected. Additionally, recorded patient information was gathered, including demographic details, prior medical histories (PMH), underlying illnesses, symptoms, and indicators.

CRP level and lung morphology:

Pulmonary morphology and CRPs of the patients had been noted. We were looked for a connection between mortality, lung lesion morphology, and CRP levels.

Statistical Analysis:

The statistical data were analysed using SPSS version 26.0 (IBM, Chicago, IL, USA). Continuous and categorical variables were presented as Mean±SD and n(%), respectively. Logistic regression performed on mortality as dependent variable with CRP. The predictive value of the CRP evaluated by measuring the area under the receiver operating characteristic (AUC) curve. The optimal threshold value obtained by calculating the Youden index.

Results

Table 1. summarizes the demographic characteristics of all patients. The patients' average age was 47.26±16.73 years, with no significant difference in

age (p=0.5483) between males and females (46.55±14.83 vs. 48.96±20.86), respectively. We enrolled 85 individuals in our study who tested positive for COVID using the RT-PCR assay. 70.59% of the patients were males in our study and 29.41% were females. All COVID positive patients had their CRP levels and X-ray morphology assessed. Table 2. summarizes descriptive statistics for the analytic dataset, which is separated into patients who lived (n=72) and those who died (n=13).

Table 1. Overall Characteristic:

Sr. No	Variable	Sub variable	Mean ± SD/Number (%)
1	Age		47.26 ± 16.73
2	Gender	Male	60(70.6)
		Female	25(29.4)
3	Ward	General Ward	43(50.6)
		Causality Ward	26(30.6)
		ICU Ward	16 (18.8)
4	CRP		6.01 ± 9.38
5	Mortality		13(15.3)

Table 2. Mortality based Overall Characteristic:

Sr. No	Variable	Sub variable	Survived(72)	Mortality(13)	p-Value
1	Age		45.93 ± 16.89	54.62 ± 15.89	
2	Gender	Male	24(33.33)	1(7.69)	
		Female	48(66.67)	12(92.31)	
3	Ward	General Ward	40 (55.6)	3 (23.1)	
		Causality Ward	17 (23.6)	9 (69.2)	
		ICU Ward	15 (20.8)	1 (7.7)	
4	CRP		4.16 ± 7.44	16.24 ± 12.43	

CRP and Mortality:

Length of stay and the earliest and highest levels of CRP were of significant interest in analyzing of the predicting death. Age, BMI, sex, and the number of comorbidities were entered as covariates in all analyses, but they only slightly changed the solutions, and none of them were significantly predictive of the outcomes (i.e., they did not change the confidence intervals or parameter coefficients), so they were removed. Because the results of the analyses using these two factors differed only little, only the first CRP's results are reported.

We performed logistic regression on CRP values based on mortality. According to the analysis, our model was 87.1% correctly classified, and if our model was 0.105 units of CRP value elevated, corresponding 1.11 times increase had been observed in mortality (Wald=12.73,1.11(1.05,1.18) (Table 3).

Table 3. Logistic Regression Based Mortality

	B	**Wald**	**Sig.**	**Exp(B)(95% L-95%U)**
Constant	-2.641	32.139	<0.0001	
Result Value	0.105	12.728	<0.0001	1.11 (1.05 , 1.18)

Next, the ROC curve analysis indicated moderate accuracy, with an area under the curve (AUC) of 0.808 (95% CI, 0.708–0.885; P <0.001) for CRP to predict the mortality in COVID-19 patients (Figure 1A). Defined by the ROC curve, the optimal threshold value was 14.1 mg/L, and was associated with a sensitivity of 69.23% and specificity of 94.4 % (Figure 1 & Table 4).

Table 4. Area under the ROC curve (AUC) between CRP and Mortality

Area under the ROC curve (AUC)	
Area under the ROC curve (AUC)	0.808
95% Confidence interval	0.708 to 0.885
z statistic	4.35
Significance level P (Area=0.5)	<0.0001
Youden index	
Youden index J	0.6368
Associated criterion	>14.1
Sensitivity	69.23
Specificity	94.44

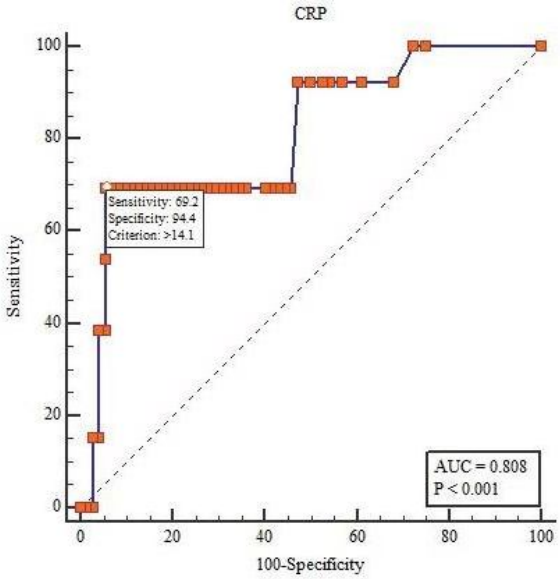

Fig. 1. Area under curve(AUC) between CRP and mortality

X-ray and mortality:

We observed 33.33% Bronchovascular thickening in the right middle zone and 9.72% consolidation in both middle and lower zone of lungs in the survived patients, whereas there was 46.15% consolidation on both lower zone, more over the right side, with pulmonary edema as well as 30.77% haziness or ground glass opacities in right lung in the died patients.

We observed 46.15% consolidation on both lower zone more over the right side with pulmonary edema, 30.77% haziness or ground glass opacities in right lung field in the died patients, while there was a 33.33% of

observed Broncho vascular thickening in the right middle zone type in most of the survived patients.

Discussion

In this retrospective analysis, we looked at the role that CRP and X-ray morphology had in determining the severity of COVID-19 sickness. The CXR can assist in the quick identification of patients who have suspected to COVID-19 in the course of the ongoing epidemic. RT-PCR of viral nucleic acid is regarded as the gold standard diagnostic test for SARS-CoV-2. Due to reporting delays and an increase in false negative results, this test does have certain drawbacks. A high clinical suspicion of COVID-19 and a report of RT-PCR for SARS-CoV-2 are awaited for diagnosis. Therefore, a quick radiological assessment and laboratory tests should be necessary to begin early optimal treatment. A computed tomography (CT) scan should still be the imaging modality of choice in some situations, but the CXR should be advised as the first-line imaging option (17, 18). Despite the fact that the baseline CXR in our study participants had a sensitivity of 63.3%, recent research found variability ranging from 69 to 90% (6). In our facility, COVID-19 cases usually managed for treatment first by performing CXR and CRP values.

In our study, we observed that the COVID-19 patients showed elevated CRP levels, which is in agreement with other studies (6, 19). According to our study, CRP levels can well be associated with disease severity. This is in accordance with a study, which reported that the patients with severe disease had an average CRP concentration of 15.46 mg/L, whereas those with mild symptoms had a CRP concentration of 2.71 mg/L (20). Another study also reported higher levels of CRP in the severe group at the initial stage than in those in the mild group (21). Another study discovered that the mean CRP concentration was significantly higher in the severe patients than in non-severe patients (22). Another study conducted in China showed that the patients who died due to COVID-19 had about 10-fold higher levels of CRP than the survivors (23). According to our findings, every 1.05 mg/L increase in CRP is associated with an 11.1-fold increase in mortality.

Limitations

A few restrictions applied to this study. First, the very low number of patient population in our study. Since illness development is typically a dynamic process, the CRP values we have solely collected at the time of hospital admission might not accurately describe changes in the patient's condition. Analysis of biomarkers on a regular basis needed to do that. In this study, we did not assess the relationship between the severity of COVID-19 and other serological markers such as procalcitonin, lactate dehydrogenase, and ferritin.

Conclusion

From the explanation above, it may be inferred that CRP levels and CXR morphology are closely associated to the severity of COVID-19 sickness. As a result, coupled with other clinical characteristics, it might be a useful marker for evaluating a patient's condition. High inflammatory stress may be indicated by elevated CRP values in COVID-19 patients, which may contribute to serious sickness or even death. Patients should therefore receive immediate attention and appropriate therapy if their CRP levels noticeably raised. The precise function of CRP in COVID-19 individuals is still unknown.

Acknowledgments

No Declared

Conflict of interest

There is no conflict of interest for the authors of this investigation.

Ethical statement

The study followed the WHO interim recommendation for COVID-19 diagnosis and the Declaration of Helsinki for ethical principles12. The study was approved by the Ethics Committee of the institute. All patients or their legal representatives provided written informed consent for their data to be used for research purposes.

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