

C-Reactive Protein as a Prognostic Marker in Hospitalized Patients with COVID-19

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ABSTRACT

Introduction: COVID-19 is a new infectious disease for which there is currently no treatment and has become a new threat for the populations. Therefore, it is necessary to explore biomarkers to determine disease severity which may help to identify patient at risk of prolonged intensive care or death. **Aims:** To evaluate the ability of C-reactive protein to predict the severity of COVID-19 infection. **Methods:** This study was conducted on 83 patients with COVID-19 admitted at COVID Unit of Nepalgunj Medical College Teaching Hospital, Kohalpur from April 2021 to June 2021. COVID-19 infection was diagnosed by Reverse Transcription Polymerase Chain Reaction of nasopharyngeal or throat Swab. The study population was divided into mild, moderate and severe cases. The data on demographic characteristics, clinical features and laboratory findings were collected and analyzed using SPSS version 26. P value less than 0.05 was taken as significant. **Results:** The mean levels of C-reactive protein in mild, moderate and severe cases were 2.75 mg/L, 9.87 mg/L and 84.48 mg/L respectively (P value = 0.003). This shows that CRP levels were significantly higher in severe cases and could be used as important biomarker to predict the severity of disease in COVID-19. **Conclusion:** The serum level of C-reactive protein can predict the severity and progression of disease in patient with COVID-19. Thus, C-reactive protein should be used as a prognostic marker in COVID-19.

Keywords: COVID-19, C-reactive protein, Prognostic marker

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INTRODUCTION

Since December 2019, a new type of corona virus called corona virus disease 2019 (COVID-19) has been identified in China.¹ The COVID-19 pandemic then spread quickly around the world^{2,3} and now has already become a challenge for the whole world which has drastically paralyzed the socio-economic life.⁴ Beyond isolated pulmonary disease COVID-19 has been associated with significant inflammation leading to coagulation, cardiovascular, neurologic and other end organ manifestations. Thus, identifying markers of disease severity may help to identify patients at risk of prolonged intensive care or death. Derangements in laboratory markers of inflammatory response including C-reactive protein (CRP) have been identified as predictors of clinical severity and complications.⁵⁻⁹ CRP is an acute phase, non specific markers of inflammation or infection and has been found to correlate with disease severity and treatment response across variety of infectious conditions.¹⁰ High CRP levels have been reported in severe acute respiratory syndrome, middle east respiratory

syndrome, H1N1 influenza.¹¹ Recent studies have reported that CRP levels are increased in patient with COVID-19 and may correlate with severity and disease progression.⁹⁻¹⁴ Thus, this study was conducted to evaluate CRP levels and disease severity to provide a guide for clinical management.

METHODS

This was a hospital based cross sectional study of 83 patients with COVID-19 admitted at COVID unit of NGMCTH, Kohalpur from April 2021 to June 2021. The study was approved by Institutional Review Committee (IRC) Nepalgunj Medical College and Teaching Hospital, Kohalpur, Banke. All patients enrolled in the study were diagnosed according to WHO interim guidance for COVID-19 (6th edition)¹⁵ i.e. all patients with laboratory confirmed {positive in nasopharyngeal or throat swab specimens by reverse transcription polymerase chain reaction (RT-PCR)} COVID-19 infection were included whereas suspected cases with similar clinical symptoms but RT-PCR negative were excluded.

Criteria to determine severity of COVID-19 infections are as follows:-

Mild	Moderate	Severe
Fever<6days	One of the following:	One of the following:
No dyspnea	Tachypnea(RR>24/min)	Tachypnea(RR>30/min)
SPO2> 94%	Hypoxia(SPO2 90%-93% persistent)	Hypoxia (SPO2 <90%)
No chest x-ray changes	Shortness of breath	Arterial oxygen partial pressure (PaO2)/Oxygen concentration (FI02) < 300mmhg.
	Fever(>100.4F)> 6 days	Intensive care unit (ICU) admission.
	Chest x-ray changes	

The epidemiological, clinical, laboratory findings and outcome data were collected. The data included demographic information, symptoms and past medical history. The data were analyzed using standard statistical method including SPSS 26. P value less than 0.05 was considered to be statistically significant. For comparing difference among different groups of severity, one way Anova test was used and to determine significance of difference between different pairs of groups, Tukey's Post hoc test was used.

RESULTS

A total of 83 patients infected with COVID-19 were enrolled in the study. Out of these, 11 patients (13.25%) were categorized as mild group, 12 patients (14.45%) as moderate and 60 patients (72.28%) as severe group. Demographic data and clinical characteristics are summarized in Table I. The mean age was 49.57±14.93. The mean age of severe group was higher than that of mild and moderate group. 61 patients (73.49%) were Male whereas 22 (26.51%) were Female. The average duration of hospital stay was 8.42± 7.39 days. Severe cases had more hospital stay days (9.13 ± 7.07) than that of mild and moderate cases (6.18±5.34, 6.92±10.14, respectively). 25 patients (30.12%) expired and all of them belonged to severe group. Overall, fever (68.67%) was the most common symptom, followed by dyspnea (66.26%) and dry cough (61.44%). However, dyspnea (90%) was the most common symptom in severe cases ,whereas dry cough (91.66%) and body ache (72.72%) in moderate and mild cases, respectively.

	Mild (n=11)	Moderate (n=12)	Severe (n=60)	Total (n=83)
Age,mean±SD	39.73±17.96	43.25±12.85	52.63±13.73	49.57±14.93
Sex				
Male	5	12	44	61
Female	6	0	16	22
Hospital Stay days (mean±SD)	6.18±5.34	6.92±10.14	9.13±7.07	8.42±7.39
Case Fatality				
Survived	11	12	35	58
Expired	0	0	25	25
Clinical Symptoms				
Fever	2	5	50	57
Fatigue	4	5	22	31
Dyspnea	0	1	54	55
Dry Cough	6	11	34	51
Sore Throat	5	6	2	13
Expectoration	0	1	26	27
Hemoptysis	0	2	4	6
Headache	5	4	15	24
Anorexia	7	5	18	30
Bodyache	8	4	23	35
Loss of smell and taste	4	0	0	4

Table I: Demographic data and baseline characteristics of patients infected with COVID-19

Hypertension (21 patients) and Diabetes (14 patients) were the most common co-morbidities which were 25.30% and 16.80% respectively, as shown in Table II.

Comorbidity	Mild (n=11)	Moderate (n=12)	Severe (n=60)	Total (n=83)
Hypertension	1	5	15	21
Diabetes	1	1	12	14
Cardiovascular Disease	0	0	5	5
Chronic Liver Disease	0	0	3	3
Chronic Kidney Disease	0	0	2	2
COPD	0	0	7	7
Cerebrovascular Accident	0	0	2	2

Table II: Comorbidites in patients of COVID 19

The mean CRP level among mild, moderate and severe group was 2.75 mg/L, 9.87 mg/L and 84.48 mg/L respectively and the difference was significant (p value - 0.003). The difference between mild and severe group was -81.73 mg/L (p value - 0.018) and between moderate and severe group was -74.61 (p value - 0.026) which were both significant. However, the difference between mild and moderate group was not found to be significant.

Severity	Number	CRP (mg/L)			P-value
		Minimum	Maximum	Mean	
Mild	11	1.00	7.82	2.75	0.003
Moderate	12	2.68	25.0	9.87	
Severe	60	14.49	685	84.48	

Table III: Laboratory findings of CRP in patients infected with COVID-19

DISCUSSION

In the present study, mean age of mild, moderate and severe cases was 39 years, 43 years and 52 years respectively which shows that elderly people are more vulnerable to severe COVID-19 infection. In the study done by Ali A et al¹⁶ mean age of severely infected COVID-19 patients was 70 years. The unequal ratio of males and females 61(73.49%) and 22 (26.51%) respectively shows that males are more targeted which is similar to the study done by Ali A et al¹⁶ Jin, J-M et al.¹⁷

In this study, average hospital stay was about 8 days. Similarly, in the study done by Sadeghi H et al,¹⁸ Guan W et al¹⁹ it was 7 days and 12 days respectively which is comparable to the present study.

In our study, the most common symptoms were fever (68.67%), dry cough (61.44%), dyspnoea (66.26%) which are similar to the study done by Ali A et al,¹⁶ Zhu N et al.²⁰ Likewise, Sadeghi H et al¹⁸ in his study also reported most common symptoms as fever (61.3%), dry cough (57.6%) and dyspnoea (72.5%).

Severity of COVID-19 disease also depends on underlying health condition of the infected patient. So, we also recorded the past medical history of all patients. We found hypertension (25.30%) and diabetes (16.86%) as the major comorbidities and majority of them had severe COVID-19 disease while some also had comorbidities like cardiovascular disease, chronic liver disease, chronic kidney disease, chronic obstructive pulmonary disease and cerebrovascular accident. Similarly Ali A et al¹⁶ Sadeghi H et al¹⁸ also reported hypertension and diabetes as the major comorbidities. This shows that patients with underlying medical conditions like hypertension and diabetes are more vulnerable to COVID 19 and may develop severe disease leading to death. Thus considering their past medical history, such patients should be given major priority for focused care.

The current study showed significantly higher CRP levels in severe cases than in mild and moderate cases. This suggests that CRP may be a biomarker of disease severity and progression in COVID-19 infection. Qin C et al²¹ reported higher CRP levels in severe COVID-19 patients compared to non-severe cases and suggested CRP may be monitored for evaluating disease

progression. Liu F et al²² revealed significantly higher level of CRP in severe cases infected with COVID-19 versus non-severe cases.

Sadeghi H et al¹⁸ also concluded that CRP level could be used as an important indicator of the severity of covid-19. In another study, Stringer D et al²³ reported CRP level ≥ 40 mg/l was associated with mortality. In our study, all expired cases belonged to severe group and severe group had an average CRP level 84.48mg/l.

Yitborek GY et al²⁴ found that routine investigation of CRP level had paramount contribution for predicting severity of covid-19 and responding timely and appropriately. Similarly Sharifpur M et al²⁵ found CRP levels significantly higher in patients who died compared to those who survived and concluded that high CRP correlates with disease severity and mortality. All of these studies show similarity to the results of the present study. Thus, CRP could be a predictive factor for disease severity and progression in COVID-19 infection.

LIMITATIONS

The limitation of the study was small sample size. Thus, further clinical studies with larger sample size are required. Another limitation was assessment of disease severity was done by using only CRP without Interlukin-6, procalcitonin, serum lactate and viral load, all of which may also contribute to disease severity.

CONCLUSION

CRP is widely available, inexpensive, easy to obtain marker that correlates with disease severity and progression in COVID-19 infection and it should be used as a key marker for disease monitoring.

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