Assessing serum C-reactive protein as a predictor of COVID-19 outcomes: a retrospective cross-sectional study

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Background: Despite being very infectious and fatal, the coronavirus disease 2019 (COVID-19) lacks a reliable and practical biomarker to assess how serious it will be.

Aim: The current study aims to conclude the possibility of C-reactive protein (CRP) level serving as a biomarker for early prediction of COVID-19 infections.

Methods: In this retrospective cross-sectional study, 88 people participated who were infected with COVID-19, aged from 25 to 79 years old. Compare the CRP test range of all samples from patients who visited the hospital between January and April 2022.

Results: All participants were confirmed to have COVID-19 through nasopharyngeal swab analysis and real-time polymerase chain reaction real-time polymerase chain reaction testing. Results showed that the majority of infected individuals had elevated CRP levels. A *P*-value of less than 0.05 indicated a significant difference in CRP levels between alive and dead patients. No significant difference in CRP levels was found between male and female patients. The average CRP level of deceased patients was 137.79 mg/l, while the average CRP level of survivors was 14.37 mg/l. The median interquartile range of deceased patients was also found to be significantly higher compared to survivors.

Conclusion: In conclusion, serum CRP levels potentially predict the severity and development of sickness in patients with COVID-19 infections.

Keywords: coronavirus, covid-19, inflammatory markers, SARS-COV-2, serum CRP

Introduction

The coronavirus disease 2019 (COVID-19) pandemic, caused by the highly infectious severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, was first identified in China in December 2019. Due to the high fatality rate among severe cases

HIGHLIGHTS

- Serum C-reactive protein levels could help distinguish individuals with moderate to severe coronavirus disease 2019 infections.
- A significant difference in C-reactive protein levels between alive and dead patients.
- Inflammatory marker measurements help to assess the coronavirus disease 2019 infection's severity.

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and its high rate of transmission, COVID-19 is considered a public health emergency. Symptoms of SARS-CoV-2 infection can range from mild to severe and may include cough, fever, headache, diarrhea, muscle aches, shortness of breath, coughing up blood, and respiratory issues[1–4]. However, some of the patients experience a severe form, such as acute respiratory distress syndrome. Furthermore, nonsevere patients could progress to serious illness. The little droplets that develop while sneezing and coughing quickly spread this illness from one person to another. Although a person's illness is when it is most infectious, the transmission may occur even before the patient's symptoms start to manifest. The average time between exposure and the onset of symptoms is 5 days, ranging from 2 to 14 days. A cough might produce up to 3000 droplets. Some little molecules will stay in the environment even if these droplets may touch other persons and coat nearby surfaces[5,6].

Recent research revealed a strong correlation between C-reactive protein (CRP) and the severity of various infections. Hepatocytes in the liver create a plasma protein called CRP, and a

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The relation of CRP with COVID-19 infection for 88 patients, including age, sex, and life status

Variables	Patients ($n = 88$)	CRP levels (mg/l)
Age groups		
25–35 years old	17 (19.3)	4.34 (4.60)
36–46 years old	23 (26.1)	30.34 (72.14)
47–57 years old	29 (33)	46.86 (75.40)
58–68 years old	14 (15.9)	71.80 (71.65)
69–79 years old	5 (5.7)	119.48 (112.42)
Sex		
Male	55 (62.5)	48.33 (82.78)
Female	33 (37.5)	32.57 (51.99)
Total	88 (100)	42.42 (72.84)
Normal (0–5 mg/l)		
Male	18 (20.5)	2.24 (1.27)
Female	13 (14.8)	2.37 (1.28)
Total	31 (17.65)	2.30 (1.28)
Increased		
Male	37 (42)	70.76 (93.27)
Female	20 (22.7)	52.19 (59.34)
Total	54 (64.7)	64.36 (76.30)
Alive		
Male	42 (47.7)	16.22 (22.71)
Female	26 (29.5)	11.38 (11.76)
Total	68 (77.2)	13.8 (17.23)
Dead		
Male	13 (14.8)	152.08 (117.50)
Female	7 (8)	111.25 (68.35)
Total	20 (22.8)	131.66 (92.92)

variety of inflammatory mediators including, IL-6 could stimulate its production. It has been shown that this biomarker is also linked to chronic inflammation such as diabetes mellitus and cardiovascular disease. Moreover, plasma leakage is more likely to occur when plasma CRP elevates early. Regarding this, several blood indicators seem to correlate with severity and mortality. The CRP levels are significantly elevated in patients with severe SARS-COV-2 infections. During the examination, the use of a biological marker like CRP allows for a clearer interruption of the clinical aspects. Therefore, determining serum CRP levels could be crucial for making an early diagnosis and managing symptoms connected to COVID-19[7].

COVID-19's pathogenic, physiologic, and diagnostic processes are currently being investigated. Clinical monitoring and efficient treatment options were critical in reducing case
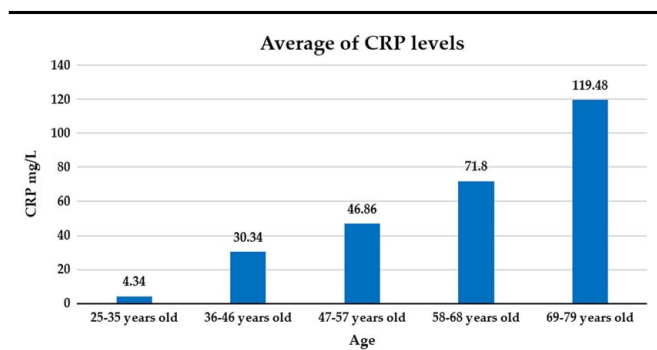
mortality. The computed tomography scan was critical in evaluating the severity of the condition. Another delicate marker that may reflect changes in lung lesions and the severity of the sickness had to be examined. People with severe pneumonia had elevated levels of CRP, which might aid in the early detection of pneumonia[8]. Thus, the goal of this research is to investigate the association between CRP levels and disease development in order to give therapeutic recommendations for COVID-19 individuals.

Methods

This study has been reported in line with the Strengthening the Reporting of cohort, cross-sectional and case-control studies in Surgery (STROCSS) criteria[9].

Study design and materials

A total of 88 patients who visited the Baxshin hospital diagnosed with COVID-19 ages from 25 to 79 years old retrospectively enrolled in this study between January and April 2022 and exclude the patients who had acute cardiac injury, acute kidney injury. A variety of instruments and equipment, including a test tube, real-time PCR, Cobas-e411, rack, cotton, disinfection, syringe, compression bandage, and plaster, were used.

Data collection

Some demographic data, a CRP test (0–5 mg/l), age and sex were taken into account in accordance with the ethics of laboratory knowledge. A real-time polymerase chain reaction was used to confirm and the findings were encouraged.

Statistical analysis

Categorical variables are reported as frequencies and percentages and were subjected to analysis using either the Fisher's exact test or the Pearson's χ^2 test, as applicable. Depending on the variable distribution, continuous variables were represented using means and SD or medians and interquartile ranges. Depending on the situation, the Mann–Whitney U test or Student's t-test was used to assess continuous data. The statistical analyses were conducted using the IBM SPSS software (version 26), with a significance threshold of 0.05.

Results

In the present study, 88 COVID-19 patients were enrolled. Generally, COVID-19 symptoms such as fever, shortness of breath, fatigue, loss of taste and appetite, headache, body ache, sore throat, sneezing, nausea, vomiting, and difficulty sleeping

Figure 1. The level of CRP in COVID-19 patients according to the age ($n = 88$).

Two-sample distribution with gender-based variances

CRP	Male	Female
Mean	48.33	32.57
Observations	55	33
Median interquartile range	14.15	12.28
Hypothesized mean difference	0	
t-test	1.097	
P (T < t) two-tail	0.328	> 0.05
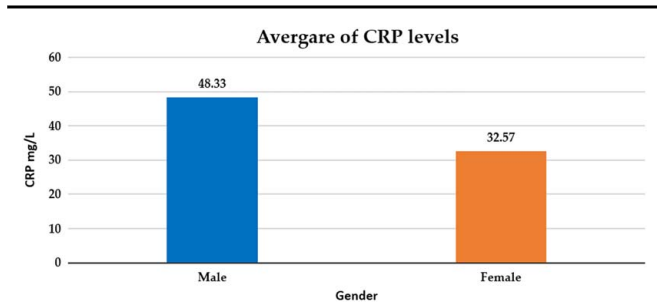
Figure 2. The variation of CRP levels along with gender ($n = 88$).

Table 3

Two samples assuming unequal variance according to life status

Serum CRP	Dead	Alive
Mean	137.79	14.37
Variance	793.95	382.6
Observations	20	65
Hypothesized Mean Difference	0	
df	25	
t Stat	7.5	
Median interquartile range	164.68	13.65
P(T < = t) one-tail	3.78×10^{-8}	
t Critical one-tail	1.7	
P(T < = t) two-tail	7.55×10^{-8}	< 0.05
t Critical two-tail	2.05	

were fixed among these patients. In this study, 55 (62.5%) were male, whereas 33 (37.5%) were female. The mean ages were 48.41 years old. The vast majority of patients 52 (59.1%) were between 36 and 57 years old, and the mean CRP level was 53.77. Higher values of CRP were found among older patients. Also, a higher CRP value was recorded in male patients compared to females, with means of 48.33 and 32.57, respectively. The data shown in Table 1 about the demographic relationship between SARS-CoV-2 infection and CRP levels were found to be quite significant. However, among 88 COVID-19 patients, 20 deaths were reported, with a gender distribution of 13 (14.8%) males and 7 (8%) females. The highest CRP values were recorded among dead patients, with a mean of 152.08.

In addition, of 88 patients, 31 (17.65%) of them had a normal (0–5 mg/l) CRP value with a mean of 2.30. Therefore, the CRP value increased in 57 (64.7%) out of 88 patients with a mean of 64.36. The sex distribution of 37 (42%) males and 20 (22.7%) females was recorded among increased CRP patients (see Table 1).

Figure 1 presents the results, demonstrating the CRP values for each age group. Age was found to be a significant factor in the increase in CRP levels. CRP levels ranged from 4.34 to 119.48 mg/l across age groups, with the highest levels found in patients aged 69–79 years old. Interestingly, the mean CRP levels for men and women are different. Figure 2 shows that men tend to have substantially greater CRP levels than women. CRP levels are reported to be 48.33 mg/l among male patients and 32.57 mg/l among female patients on average. Table 2 depicts the two-sample distribution with gender-based variances. Males had a median interquartile range of 14.15 mg/l, while females had a value of 12.28 mg/l. In addition, the likelihood P-value is higher than the alpha ($P > 0.05$), which indicates that there is not a significantly different level of CRP between the sex.

Table 3 shows the two samples under the assumption of unequal variance based on life status. It can be shown that if the t-statistic is greater than the two-tailed value, the null hypothesis (H0) is rejected. The H0 is disproved in this situation since the

t-statistic of 7.5 is more than 2.05; however, the H1 is supported. A P-value of less than 0.05 indicates that there is a significant difference between the CRP levels of surviving and deceased patients. The mean CRP levels between men and women are also shown in Table 3.

Table 4 displays the association between age groups and CRP levels in 88 patients. It can be observed that as age increases, the CRP level also increases continuously. Patients aged between 25 and 35 years exhibit lower CRP levels than those aged between 36 and 46 years, and so on. Moreover, the highest CRP level among all age groups is found to be 119.48 mg/l, which is observed in the age group of 69–79 years.
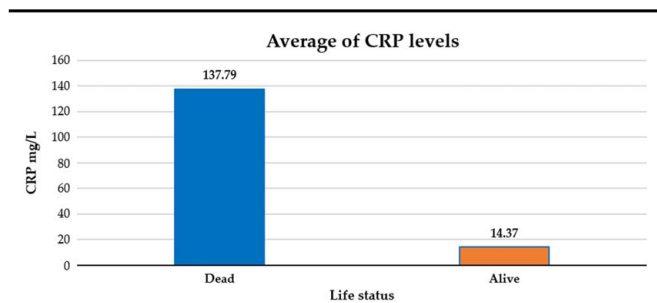
In addition, the table illustrates the regression analysis for the variable of age groups against the level of CRP. The analysis reveals that a P-value less than 0.05, particularly P values between 0.01 and 0.001, signifies statistical significance or strong evidence against the null hypothesis (H0). The P-value for the association between age groups and CRP level was estimated to be 0.003, which lies between 0.01 and 0.001. This result indicates very strong evidence against the null hypothesis, and consequently, the null hypothesis (H0) is rejected, while H1 is accepted. Thus, there is a significant difference between age groups and the level of CRP.

Furthermore, since there is a correlation between the CRP level and the survival rate of COVID-19 patients, it can be inferred that age, along with CRP, plays a significant role in the survival of COVID-19 patients.

Curiously, there is a disparity between the mean CRP levels of patients who have passed away and those who are still alive. According to Figure 2, CRP levels are typically much higher in deceased patients than in living ones. The average levels of CRP of deceased patients are 137.79 mg/l, while the average levels of CRP of patients who are still alive are 14.37 mg/l (Fig. 3).

Table 4

Regression analysis for the association between age groups and level of C-reactive proteins

Age groups (years)	Patients ($n = 88$)	CRP levels (mg/l)	P	t-stat	Multiple R	Upper % 95 (C.I)	Lower 95% (C.I)
25–35	17 (19.3)	4.34 (4.60)	0.00324 < 0.05	8.65	0.980571	3.37	1.56
36–46	23 (26.1)	30.34 (72.14)					
47–57	29 (33)	46.86 (75.40)					
58–68	14 (15.9)	71.80 (71.65)					
69–79	5 (5.7)	119.48 (112.42)					

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Figure 3. The variation of CRP levels along with Life status ($n = 88$).

Discussion

The COVID-19 pandemic is spreading rapidly across the world, with even asymptomatic individuals serving as carriers of the virus. Furthermore, the mortality toll is quickly increasing, making COVID-19 a serious danger to population growth. The development of effective treatment options is critical, and early monitoring of key indicators is crucial in guiding treatment strategies. Early assessment of a patient's condition is also highly valuable[10,11]. The most frequent sequelae seen in COVID-19 individuals who did not survive are acute cardiac injury, shock, acute respiratory distress syndrome, acute kidney injury, and significant changes in serum CRP levels. The liver produces a protein called CRP, which rises in reaction to infection, tissue damage, and inflammation. Elevated levels of CRP in the blood indicate an acute-phase response and can be used as an indicator of inflammation[12].

CRP levels have also been linked to the occurrence of acute renal damage, and the degree of cardiac injury. This is most likely due to the fact that the immune system reacts more aggressively to viral infections by releasing numerous immunological molecules, and excessive CRP production over normal limits may induce organ dysfunction in COVID-19 patients. Since a person's genetic composition controls how much CRP they produce, it is important to look at potential genetic factors in a variety of populations in order to get useful findings[7,13,14]. In addition to serum CRP, additional inflammatory indicators may also positively connect with the severity of COVID-19 individuals, including serum ferritin[15], hypocalcemia[5], procalcitonin[16], and erythrocyte sedimentation rate[17]. Although the CRP levels were not significantly different between the nonsevere and severe groups, Chen *et al.*[18] found that the severe group had a higher mean CRP level. According to different research, CRP levels and the severity of COVID-19 are connected. This study has a small sample size, which may limit its ability to be generalized. Additionally, the retrospective design and missing clinical data are limitations that should be addressed in future studies. Clinical investigations with bigger sample numbers and numerous CRP level assessments at various treatment periods are required to validate our findings.

Conclusions

According to our research, serum CRP levels could be a crucial sign of the severity and development of COVID-19. Moreover, serum CRP levels increased with ages among COVID-19 patients and this level could help distinguish individuals with moderate to severe COVID-19 infections. This suggests that CRP testing may

be helpful as an early warning sign for serious disease and assist doctors in stratifying patients for transfer to ICU.

Ethical approval

The current retrospective cross-sectional work was approved by the ethics board of Baxshin Research Center (No. BRC0202022, 01/02/2022) at Baxshin hospital.

Consent

None.

Author contribution

J.M.H. and J.M.A.A.: conceptualized this study; A.J.A., H.A.R., and K.O.S.: drafted the manuscript; J.M.H., A.M.M. and A.T.A. critically reviewed the manuscript; S.S.T.: collection and data analysis.

Conflicts of interest disclosure

None.

Research registration unique identifying number (UIN)

As per the International Journal of Surgery policies, this study is a Retrospective Cross-sectional Study -based study and didn't include neither patients nor human experiments or involvement of any kind. Therefore, does not include or require a research registration unique identifying number (UIN) or registration ID. As the above-mentioned registries target clinical trials, our research does not meet their criteria.

Guarantor

Dr Jeza Muhamad Abdul Aziz.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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