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Journal of Medical and Life Science  
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## C-Reactive Protein as a Prognostic Indicator in COVID-19 mild infection Patients

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DOI: [10.21608/JMALS.2021.240126](https://doi.org/10.21608/JMALS.2021.240126)

### ABSTRACT

**Background:** the identification of a simple and effective prognosticator is crucial for high lightening and treating the potentially critical patients, to reduce the mortality rate, Serum CRP is a simple and effective prognosticator which casts light on potentially critical patients, Serum CRP has a predictive value of COVID-19. **Patients and methods:** This study included 328 out-hospitalized patients with confirmed COVID-19 infection, these study subjects were randomly selected irrespective of the age group and both genders were included, Assay procedure as manufactory instructions and Reagents of Cromatest Linear chemicals S.L.U. Barcelona Spain turbidimetric method is used. **Results:** Female gender was more frequent (n=192, 58.5%) than Male gender (n=136, 41.5%). This study reveals a high level of CRP in 296 patients (90.2%) with a sensitivity of 90.2%, which is divided into two groups the first have CRP levels 5-100 (56.1%) and the second group has CRP levels more than 100 (34.1%), the high-level CRP was a significant biomarker for COVID-19 diagnosis or prognosis in out-hospitalized patients (Outpatients and patients under home observation), with a p-value is  $p < .00001$  which less than 0.05. **Conclusion:** CRP levels were positively correlated with mild COVID-19 infection of lung lesions with a sensitivity of 90.2%. CRP levels could reflect disease severity and should be used as a key indicator for disease monitoring.

**Keywords:** CRP, C-reactive protein, COVID-19, out-hospitalized patients, biomarker.

### 1. Introduction:

Coronavirus disease-2019 (COVID-19) was first described in Wuhan in December 2019 which rapidly spread to 215 countries, areas, and territories leading to a pandemic <sup>(1)</sup>, The causative pathogen is now recognized as a novel coronavirus (nCoV), which was later renamed as severe acute respiratory syndrome

coronavirus-2 (SARS-CoV-2). The World Health Organization has raised the assessment of the risk of spread and the risk of the impact of COVID-19 to very high at a global level on February 28, 2020<sup>(2)</sup>, a subgroup of patients has suffered a severe illness, which often progressed into critical illness. regarded as having a multiorgan disease and disruption of

numerous physiological pathways, but many COVID-19 patients do not exhibit signs or symptoms, or just mild symptoms<sup>(3,4)</sup>. The vital role of abnormal laboratory parameters in patients with COVID-19 has become apparent, and published studies recommend that clinical laboratory parameters may help in risk stratification and prognosis of these patients<sup>(5,6)</sup>.

Some studies have reported that C-reactive protein (CRP) levels can be used in the early diagnosis of pneumonia and that higher CRP levels were associated with severe pneumonia<sup>(7)</sup>.

C-reactive protein (CRP) is an acute-phase reactant that is produced by the liver in response to inflammation. It is commonly secreted under the influence of cytokines such as interleukin-6 and tumor necrosis factor-alpha.

More specifically, a study including over 50,000 participants noted a significant association between elevated serum or plasma concentrations of CRP and ischemic vascular disease. In persons who had CRP levels above 3mg per liter, as compared with persons who had CRP levels below 1 mg per liter<sup>(8)</sup>.

Although an elevated CRP is not common in most viral infections, a study conducted in China with 1,099

COVID-19 patients demonstrated that 60.7% had CRP levels  $\geq 10$  mg/L<sup>(9)</sup>, and sensitive indicators able to reflect lung lesion changes and disease severity had to be explored. C-reactive protein (CRP) levels can be used in the early diagnosis of pneumonia<sup>(10)</sup>

Hence, the current study aims to evaluate the correlation between CRP levels in patients with mild COVID-19 infection, Outpatients and patients under home observation are included in this study, while hospitalized patients are not included.

## 2. Patients and methods

### 2.1. Study population Patients

This study included 328 out-hospitalized patients with confirmed COVID-19 infection, these study subjects

were randomly selected irrespective of the age group and both genders were included.

It was performed following the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All the studied population was informed about the purpose of sample collection, patients were free to refuse sample collection.

### 2.2. Data collection

In this cross-sectional study, we obtained data regarding 328 out-hospitalized patients with confirmed COVID-19 via real-time reverse transcription-polymerase chain reaction (PCR), the study population is customers who came to Alyamenny laboratory in Alexandria, Egypt for biomarkers and complete blood count investigations, and reviewed the medical records and compiled data between August 12 and December 30, 2020.

### 2.3. Collection and processing of blood samples:

1ml blood sample was collected for performing a CRP test turbidimetric method (Cromatest Linear chemicals S.L.U. Barcelona Spain) on 328 Positive COVID-19 patients for individuals matching in age and gender.

### 2.4. Assay procedure as manufactory instructions:

Reagents of Cromatest Linear chemicals S.L.U. Barcelona Spain for the human CRP test turbidimetric method and samples were allowed to be at room temperature before testing, (serum was separated from a blood sample by centrifugation), considered normal serum CRP level is 5 mg/L.

### 2.5. Statistical analysis

Data were analyzed using SPSS statistical software, version 20.0(SPSS, Chicago, Illinois, USA). All continuous data are presented as means and standard deviations, while categorical data are presented as numbers and percentages. Z Score Calculator for 2 Population Proportions test was used to compare categorical variables. Multivariate regression analysis was performed to analyze relationships between COVID-19 infected patients and CRP, Then, the best-fit model was generated without interaction variables.

A p-value of less than 0.05 was considered statistically significant for all calculations.

**3. Results:**

Table (1): shows the percentage of COVID-19 mild infected patients (out-hospitalized and home observation Patients) concerning CRP level, The present study included patients aged from 14 years to 75 years mean age was 44.5 ±30.5 who were confirmed to have Covid-19 based on real-time reverse transcription-polymerase chain reaction, female gender was more frequent (n=192, 58.5%) than

Male gender (n=136, 41.5%). This study reveals a high level of CRP in 296 patients (90.2%) with a sensitivity of 90.2%, which is divided into two groups the first have CRP levels 5-100 (56.1%) and the second group has CRP levels more than 100 (34.1%), the high-level CRP was a significant biomarker for COVID-19 diagnosis or prognosis in out-hospitalized patients (Outpatients and patients under home observation), with a p-value is  $p < .00001$  which less than 0.05.

**Table (1):** Association between CRP level and mild infection of COVID-19 Patients

COVID-19 POSITIVE Patients	Serum CRP level						Total	
	Normal		High-level CRP 5- 100		High-level CRP More than 100			
	No.	%	No.	%	No.	%	No.	%
Male	16	50	72	39.1	48	42.9	136	41.5
Female	16	50	112	60.9	64	57.1	192	58.5
Total	32		184		112		328	

Z Score Calculator for 2 Population Proportions. The value of  $p$  is  $< .00001$ . The result is significant at  $p < .05$ .

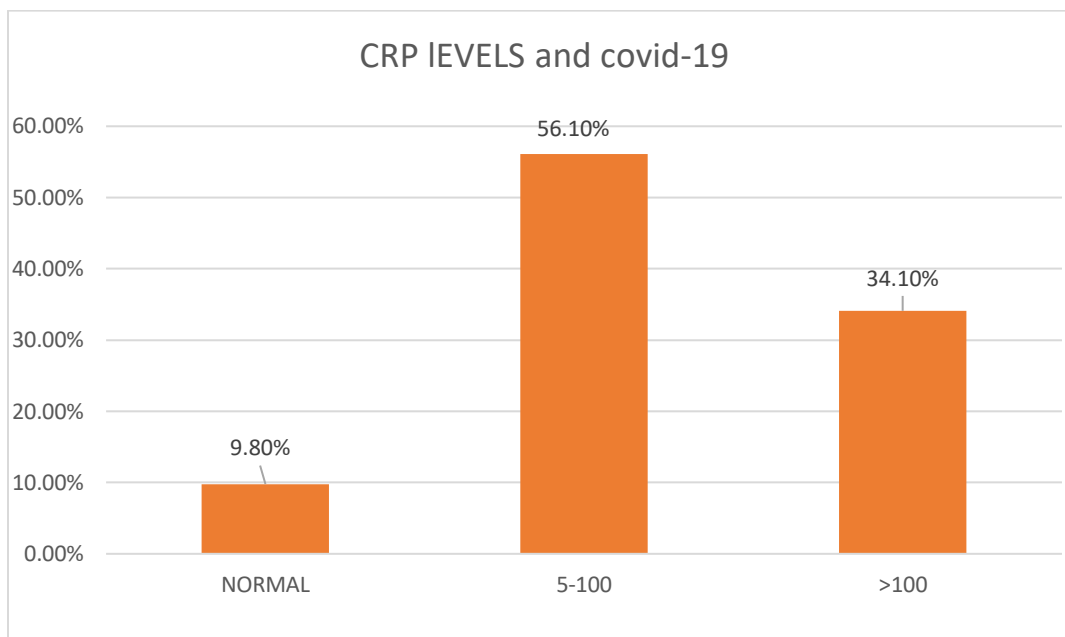


Figure 1; CRP levels with COVID-19 mild infection

#### 4. Discussion:

The inflammatory response plays a crucial role in COVID-19 progression. and inflammatory cytokine storm increases the severity of COVID-19<sup>(11)</sup>. Hence, the identification of a simple and effective prognosticator is crucial for high lightening and treating the potentially critical patients, intending to reduce the mortality rate<sup>(12)</sup>, Serum CRP is a simple and effective prognosticator which casts light on potentially critical patients, Serum CRP has a predictive value of COVID-19.

The present study included 328 patients with COVID-19 mild infection (out-hospitalized and home observation Patients) and included patients aged from 14 years to 75 years mean age was  $44.5 \pm 30.5$  who were confirmed to have Covid-19 based on real-time reverse transcription-polymerase chain reaction, female gender was more frequent (n=192, 58.5%) than Male gender (n=136, 41.5%). This study reveals a high level of CRP in 296 patients (90.2%) with a sensitivity of 90.2%, which is divided into two groups

the first have CRP levels 5-100 (56.1%) and the second group has CRP levels more than 100 (34.1%), the high-level CRP was a significant biomarker for COVID-19 diagnosis or prognosis in out-hospitalized patients (Outpatients and patients under home observation), with a p-value is  $p < .00001$  which less than 0.05.

CRP showed a sensitivity of 90.2% in COVID-19 mild infection patients which was more than other biomarkers such as ferritin which has a sensitivity of 71.4%<sup>(13)</sup>, LDH has a sensitivity of 67.7%<sup>(14)</sup>, and D-dimer has a sensitivity 36.4%<sup>(15)</sup> with mild COVID-19 infection patients.

Furthermore, a study of 27 COVID-19 patients from China found that CRP levels  $>20.4$  mg/L were 83.0% sensitive and 91.0% specific when predicting severe COVID-19 infection<sup>(16)</sup>.

Qin et al. observed higher CRP levels in severe COVID-19 patients than in non-severe cases, suggesting that

this biomarker can be monitored to evaluate disease progression<sup>(17)</sup>.

A study of 1834 COVID-19 patients from Italy and the United Kingdom found that CRP levels  $\geq 40.0$  mg/L were associated with 31.9% mortality compared with 15.0% mortality in patients with CRP levels  $< 40.0$  mg/L<sup>(18)</sup>.

CRP levels are correlated with the level of inflammation, and its concentration level is not affected by factors such as age, sex, and physical condition<sup>(19)</sup>.

Ruan et al., 2020 observed that C-reactive protein (CRP) levels are increased in COVID-19 patients, and it has been shown that survivors had median CRP values of approximately 40 mg/L, while non-survivors had median values of 125 mg/L, indicating a strong correlation with disease severity and prognosis<sup>(20)</sup>.

CRP levels can activate the complement and enhance phagocytosis, thus clearing the pathogenic microorganisms invading the body. CRP levels can be used for the early diagnosis of pneumonia<sup>(10)</sup>.

### Conclusions

CRP levels were positively correlated with mild COVID-19 infection of lung lesions with a sensitivity of 90.2%. CRP levels could reflect disease severity and should be used as a key indicator for disease monitoring.

### Conflict of interest

There are no conflicts of interest.

### Financial support and sponsorship

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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