C- REACTIVE PROTEIN LEVELS AMONG COVID-19 POSITIVE CASES PRESENTING IN GULAB DEVI HOSPITAL LAHORE: A DESCRIPTIVE CROSS-SECTIONAL STUDY

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Abstract

Background & Objectives: Severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) is a highly infectious virus associated with the development of COVID 19. Lack of valid biomarkers makes it difficult to predict disease severity. C-reactive protein (CRP) is an acute phase inflammatory marker that which may predict COVID-19 infection and its severity. The aim of this study was to describe the CRP levels in COVID-19 positive cases presenting in Gulab Devi hospital Lahore.

Methods: In this cross sectional study conducted in Gulab Devi Hospital Lahore for six month, 100 COVID-19 positive cases were selected using convenient sampling technique. About 3 ml of venous blood was drawn for qualitative and semi-quantitative titration analyses to determine CRP concentration in blood. Descriptive analysis was performed using SPSS version-26 to describe the levels of CRP in relation to clinical features and disease severity.

Results: CRP levels were elevated above normal range in 93% COVID-19 positive cases. Patients with severe infection had high levels of CRP (>6mg/L, range: 12-96 mg/L), mildly infected patients had moderate values of CRP and recovering patients of COVID-19 showed lowest value of CRP (<3mg/L).

Conclusion: The serum CRP level was substantially higher in COVID-19 positive cases in this study. CRP is an inexpensive, rapid test available to physicians for early detection of COVID-19 severity. Determining CRP levels can also help physicians to identify patients at higher risk of mortality and complications.

Keywords: COVID-19, biomarker, C-reactive protein, Severe COVID-19 disease

C- reactive protein (CRP) is an acute phase protein produced and released from hepatocytes in response to acute infection or inflammation. It is a pentameric, annular structural protein found in the blood. Inflammation causes its levels to grow. Its physiological role is to attach to lysophosphatidyl choline receptors on the surface of dead or dying cells, as well as some infections, to activate the complement system's classical pathway and improve phagocytosis.[1] Main biological function of CRP appears to be a host defense mechanism against pathogens and the clearance of apoptotic and necrotic cells from the body. The typical concentration of CRP in blood is less than 10 mg/L. Its level increases fast within 6 to 8 hours of exposure to foreign antigens and peaks 48 hours after the commencement of the disease.[2] The level of CRP has been linked to the severity of inflammation, and its concentration is unaffected by age, gender, race, physical condition, or geographic location.[3]

Severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) was named due to its approximately 80 percent similarity to severe acute respiratory syndrome virus (SARS-CoV), which causes severe acute respiratory distress syndrome (ARDS). SARS-CoV-2 is responsible for significant mortality in the year

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2019-2021.[4] This virus causes a disease named as COVID 19, which was declared a pandemic by World Health Organization (WHO) in March, 2020. In the start of the pandemic, COVID -19 was pre-dominantly seen in elderly people because they have a limited immune response to pathogens. Individuals aged 65 years or above are mostly affected by this virus, but as the outbreak advanced, it also affected younger people under the age of 18 years.[5] Risk factors for COVID-19 are older age, underlying medical co-morbidities, high levels of inflammatory markers, pregnancy and a higher sequential organ failure assessment (SOFA) score.[6] As a result, patient care is adapted according to the severity of the signs and symptoms.

COVID-19 can be diagnosed by signs and symptoms, CT chest and reverse transcriptase polymerase chain reaction (RT-PCR), but other biomarkers provide useful information which can impact significantly on patient care. Many studies have assessed the clinical, biological, and radiological features of COVID-19 infection. Several inflammatory and hematologic analytical biomarkers can be used as important diagnostic tool and identification of severe forms of COVID-19. Different diagnostic and prognostic factors have been studied e.g. lymphocyte count, lactate dehydrogenase (LDH), interleukin 6 (IL-6), pro-calcitonin, CRP, D-dimer, ferritin, (pro BNP), but their role in prediction, prognosis and disease classification still remains to be established.[7,8]

Inflammatory cytokines fight the virus, but when the system is overactive, it can harm the tissue of the lungs. The creation of CRP is triggered by cytokines and tissue damage. CRP levels show rapid increase when there is more lung tissue damage by SARS-COV-2.[9] In severe cases, this virus causes a hyper-inflammatory reaction that leads to a pathological dysfunction of the innate host defences. Multiple organ failure and cytokine release syndrome (cytokine storm) are two of the most common complications. Tissue damage is at the core of all pathologies, and if it is severe enough, it can lead to organ dysfunction and death. Acute phase response activation in COVID-19 patients correlates with CRP levels in blood, therefore, CRP can be used

as a rapid and cost-effective method of determining the degree of tissue damage occurring in patient at the time of observation.[10] As a result, elevated blood CRP levels indicate severe tissue damage and a pathological inflammatory response. CRP levels were 10 times greater in COVID-19 patients who died than in recovered patients.[11,12] It is tempting to believe that the membrane-associated pentameric shape of CRP isoform may play a vital role in COVID-19 infection pathophysiology and its consequences, notably in boosting pro-inflammatory and pro-coagulant symptoms. The aim of this study was to describe clinical features and the CRP levels in COVID-19 positive cases .

METHODS

This cross-sectional study was conducted at the Pathology Laboratory of Gulab Devi Teaching Hospital, Lahore. The duration of the study was six months. About 3ml blood samples of 100 COVID-19 positive cases were collected using convenient sampling technique and processed for CRP level. Data were analyzed using SPSS version 26. We used latex agglutination slide method with diagnostic kit to detect the level of CRP. Descriptive analysis was performed to describe the levels of CRP in relation to clinical features and disease severity. Results were presented in the form of frequency distribution and percentages.

RESULTS

The mean age of the sample of 100 COVID-19 positive cases in this study was 38.2±9.8 years. Of these participants, 30% were females and 70% were males. About 15% patients had CRP concentration of 12 mg/L, whereas 33% had CRP concentration of 24 mg/L, 32% patients had 48 mg/L concentration of CRP and 13% patients had 96 mg/L concentration of CRP (Table 1). Minimum value of CRP was 6 mg/L and maximum value of CRP was 96 mg/L in this study. Regarding gender based differences, those with normal CRP levels (<6mg/L), three were female patients and four were male patients; 15 patients had CRP levels of 12 mg/L in which 2 were female patients and 13 were male COVID-19 positive patients; 33 patients had

CRP levels of 24 mg/L among where 9 were females and 24 patients were male COVID-19 positive patients. Patients with CRP levels of 32 mg/L, 11 were females and 21 were males COVID-19 positive patients. Thirteen patients had CRP levels of 96 mg/L including 5 females and 8 males patients (Table 1). Table 2 shows frequency of clinical features in these patients. About 91% patients presented with dry cough, 93% with fever, and 16% presented with difficulty of breathing. Regarding CRP levels, 7% patients had normal CRP levels (<6 mg/L), and 93% had high CRP concentrations in blood (Table 2).

DISCUSSION

Tillett and Francis were two scientists who dis-

Table 1: *Frequency Distribution of C-reactive protein levels among COVID-19 positive cases presented in Gulab Devi Chest Trust Teaching Hospital, Lahore (n=100)*

C-reactive protein (mg/L)	Frequency	Percentage
< 6	07	7.0%
12	15	15.0%
24	33	33.0%
48	32	32.0%
96	13	13.0%

Table 2: *Clinical features of C0VID-19 positive cases presenting in Gulab Devi Chest Trust Teaching Hospital Lahore stratified by gender (n=100)*

Clinical feature		Male	Female	Total
Dry Cough				
	Yes	63%	28%	91%
	No	07%	02%	09%
Fever				
	Yes	66%	27%	93%
	No	04%	03%	07%
Shortness of Breath				
	Yes	10%	06%	16%
	No	60%	24%	84%
C-reactive Protein				
	Yes	66%	27%	93%
	No	04%	03%	07%

covered C-reactive protein (CRP) in 1930.[13] It is a pentameric, annular (ring-shaped) protein that rises in response to inflammation in blood plasma. CRP concentration declines when inflammation or tissue damage is repaired, making it a helpful marker for monitoring disease severity.

In early December 2019, first case of COVID-19 was reported in Wuhan, city of China. It has quickly spread around the world and became a pandemic. Early diagnosis of COVID-19 is important for effective clinical therapy and control measures to be implemented.[14] The WHO recommends using RNA in a real-time reverse transcriptase-PCR (RT-PCR) as the gold standard approach for diagnosing COVID-19. However, some studies have shown an issue of false-negative outcomes.[15] SARS-CoV-2 virus when enters infected patient's lungs by the oral or nasal route, it proliferates among the parenchymal cells of lung, which leads to severe inflammation in patient's lungs with release of different inflammatory mediators e.g. cytokines and the disease progresses to cell death of lung parenchyma.[16]

World Health Organization provides standard procedures for the parity of the assay from time to time. Furthermore, most diagnostic assays are expensive, are equipment-dependent, consume more time and necessitate biological competence. Missed diagnoses of a significant number of clinically suspected individuals could let the virus spread, which could lead to rapid disease progression. However, researchers have identified serum CRP as an important biomarker whose levels change considerably in COVID-19 patients. It has been shown in studies to be a useful index for diagnosing and assessing severity.[17,18] Therefore, CRP level in blood of COVID-19 patients correlates with the level of inflammation and damage to lung parenchyma of patients, activation of acute phase response, making them a quick and cost-effective biomarker to estimate the degree of damage to lung tissue.

The present study comprised 100 patients suffering from COVID-19. Out of 100 COVID-19 patients, 70 (70%) are male patients and 30 (30%) are female patients. C-RP levels were measured in all patients. C-RP levels were elevated in 93 (93%) COVID-19 positive and 7(7%) patients were with normal C-reactive protein levels. These patients may or may not have symptoms of COVID-19. Symptomatic patients in this study show fever, dry cough, shortness of breath, drop satu-

ration etc. In this study 81 (81%) patients were with fever, 16 (16%) with shortness of breath, 91 (91%) with dry cough.

In this study minimum value of C-RP was 6 mg/L and maximum value was 96mg/L in COVID-19 positive cases. Patients with more disease severity have high level of C-RP and mild stage patients have low C-RP value. The mean and standard deviation of C-RP value was 410.3±28.63 mg/L. Out of the total patients 100 have C-RP values <6 (7%), 12 (26%), 24 (24%), 48(31%), 96 (12%).

There is a positive correlation of C-RP levels with lung lesion and disease severity. As a result there is a significant association between C-RP levels and disease severity in patients with corona virus disease-19. So, we can use C- RP as an inflammatory marker and to check the disease severity in COVID-19 positive cases. It can also be utilized as a disease monitoring key indicator. As a result of this the levels of C-RP in blood can be used as inexpensive, easily measured and non invasive biomarker to assess the severity of activated acute phase response, inflammation and damage in lung parenchyma of patients suffering from COVID-19 at the time of measurement.

CONCLUSION

CRP is an inexpensive, rapid test available to physicians for early detection of COVID-19 severity. The serum CRP levels were substantially higher in COVID-19 positive cases in this study. Determining CRP levels can help physicians to identify patients at high risk of mortality and complications. Moreover, the severity of the disease can be monitored by using serial CRP levels.

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