

Comparison of inflammatory markers in COVID-19 patients- a study based on disease severity groups

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Abstract

Objective: To compare different inflammatory markers in various coronavirus disease 2019 severity groups.

Method: The cross-sectional, retrospective, comparative study was conducted at the Central Park Teaching Hospital, Lahore, Pakistan, and comprised data from April to June 2021 of coronavirus disease 2019 inpatients. The data was divided into mild, moderate and severe/critical category using the World Health Organisation interim guidelines. Data was analysed using SPSS 22.

Results: Of the 50 patients, 29(58%) were males and 21(42%) were females. The overall mean age was 54.12±21.23 years. The mean age was 62±17.1 years in critical group compared to 50±19.7 years in mild and 52±15.9 years in moderate groups. There were 8(16%) patients in the mild group, 16(32%) in the moderate group and 26(52%) in the critical severity group. Mortality was the outcome in overall 19(38%) cases, and 14(73.7%) of them were in the critical group ($p=0.03$). C reactive protein, interleukin-6, serum ferritin and D-dimer levels were significantly different among the groups ($p<0.05$).

Conclusion: Older people were found to have experienced coronavirus disease 2019 in more severe forms. The inflammatory markers were significantly high in patients with severe disease and were associated with high mortality.

Key Words: COVID-19, SARS CoV-2, SARS coronavirus, C-reactive protein, Ferritin, Interleukin-6, Acute-phase protein, Severity of illness. (JPMA 73: 2379; 2023) DOI: 10.47391/JPMA.7938

Submission completion date: 26-10-2022— **Acceptance date:** 22-07-2023

Introduction

After having started in China in late 2019, the coronavirus disease 2019 (COVID-19) destroyed normal lifestyle and health globally.¹ It was declared a pandemic that threatened the biosecurity of countries across the world.² Due to the rapid and being wide spread, there was an urgent need of clinical and laboratory parameters for quick diagnosis.³ The list of clinical symptoms included elevated body temperature, headache, loss of appetite, loss of sense of smell and taste, cough, breathlessness, nausea, vomiting, diarrhoea and multi-organ failure.⁴

Majority of the patients developed mild symptoms and recovered. A few patients developed serious complications that included acute respiratory tract infection (RTI), sepsis, acid-base disturbances, heart failure, renal failure and encephalopathy.⁴

Coronavirus is a ribonucleic acid (RNA) virus, having an envelope. It resides in the epithelial cells and primarily causes severe RTI. It is regarded as a multisystem disease that affects heart, vessels, lungs, gastrointestinal tract,

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brain, haematopoietic system and immune system.⁵ The virus is transmitted through respiratory droplets or direct contact from person to person.⁶

It is a routine practice to use a variable number of biochemical and haematological parameters as diagnostic and prognostic markers of various diseases. Most potent and easily available tests in routine laboratories are complete blood count (CBC) and biochemical markers.¹ A study conducted on 852 COVID-19 patients observed that in 77 patients who died, blood tests majorly manifested leucocytosis, neutrophilia and eosinophilia as well as elevated levels of D-dimer, serum ferritin, C-reactive protein (CRP) and interleukin-6 (IL-6).⁴ A Romanian study concluded that inflammatory markers can be utilised to determine the severity of COVID-19 since they are linked to lung damage.⁷ A meta-analysis also found that severe COVID-19 was related with higher levels of inflammatory markers than a mild condition.⁸

The current study was planned to compare different inflammatory markers in various COVID-19 severity groups.

Materials and Methods

The cross-sectional, retrospective, comparative study was conducted at the Central Park Teaching Hospital (CPTH),

Lahore, Pakistan, and comprised data from April to June 2021 of COVID-19 inpatients. The sample was raised using convenience sampling technique. Patients of both genders with positive polymerase chain reaction (PCR) test for COVID-19 admitted to the COVID-19 ward and the COVID-19 intensive care unit (ICU) were included.

Patients aged <18 years, pregnant women and those taking medication for reducing inflammatory response were excluded from the study.

Demographic and clinical data was taken from the patient record, and laboratory data was obtained from the institutional laboratory's online records. Spectrophotometric technique had been used for CRP, and chemiluminescence immunoassay technique for serum ferritin and IL-6. The data was divided into mild, moderate and severe/critical category using the World Health Organisation (WHO) interim guidelines.⁹

Data was analysed using SPSS 22. Frequencies and percentages as well as mean and standard deviation were presented. Comparison of different groups was done using analysis of variance (ANOVA). Chi-square test for categorical data and independent t-test for continuous variables were used for comparisons. $P \leq 0.05$ was taken as statistically significant.

Results

Of the 50 patients, 29(58%) were males and 21(42%) were females ($p=0.06$). The overall mean age was 54.12 ± 21.23 years. The mean age was 62 ± 17.1 years in critical group

Table-1: Basic characteristics of the patients in different disease severity groups.

	Total Count (%)	Mild Count (%)	Moderate Count (%)	Severe/Critical Count (%)	P- value
No. of patients	50 (100%)	8 (16%)	16 (32%)	26 (52%)	
Males	29 (58%)	7	9	13	0.06
Females	21 (42%)	1	7	13	
Mean age \pm SD (years)	54.12 ± 21.23	50 ± 19.7	52 ± 15.9	62 ± 17.1	0.068
Oxygen (O ₂) saturation					
>93%	21 (58%)	12	09	0	0.01*
<93%	29 (42%)	01	18	10	
Mortality	19 (38%)	2	3	14	0.03*

*p-value ≤ 0.05 is statistically significant.

Table-2: Inflammatory markers in different disease severity groups.

Inflammatory markers	Reference values	Mild n=8	Moderate n=16	Severe n=26	p- value
CRP (mg/L)	≤ 5	7.47 ± 4.75	9.85 ± 6.23	13.14 ± 5.98	0.002*
IL-6 (pg/ml)	< 43.5	66.13 ± 23.75	178.74 ± 70.4	301.23 ± 74.3	0.007*
Serum ferritin (μ g/L)	30-400	1228.41 ± 123.56	1640.36 ± 254.98	2211.37 ± 781.65	0.034*
D-dimer (μ g/L)	< 250	654.50 ± 135.7	1303.81 ± 130.5	1670.84 ± 255.86	0.001*

CRP: C-reactive protein, IL-6: Interleukin-6. *p-value ≤ 0.05 is statistically significant.

Table-3: Mean values of inflammatory markers and patient outcomes.

Inflammatory markers	Patient outcome	Mean n=8	Standard Deviation	P- value
CRP (mg/L)	Discharged (n=31)	10.5397	7.54829	0.02*
	Expired (n=19)	12.2326	8.69474	
IL-6 (pg/ml)	Discharged	60.0671	50.44653	<0.001*
	Expired	329.1326	139.25384	
Serum ferritin (μ g/L)	Discharged	736.9206	490.42367	<0.001*
	Expired	3007.9232	1498.04967	
D-dimer (μ g/L)	Discharged	908.4194	574.04591	0.011*
	Expired	2177.7895	1993.40554	

CRP: C-reactive protein, IL-6: Interleukin-6. *p-value ≤ 0.05 is statistically significant.

compared to 50 ± 19.7 years in mild and 52 ± 15.9 years in moderate groups. There were 8(16%) patients in the mild group, 16(32%) in the moderate group and 26(52%) in the critical severity group. Oxygen (O₂) saturation level was significantly different among the groups ($p < 0.05$). Mortality was the outcome in overall 19(38%) cases, and 14(73.7%) of them were in the critical group ($p=0.03$) (Table 1).

CRP, IL-6, serum ferritin and D-dimer levels were markedly different among the groups ($p < 0.05$) (Table 2).

The mean values of the CRP, IL-6, serum ferritin and D-dimer were significantly different in 31(62%) patients who survived and the 19(38%) who expired (Table 3).

Discussion

COVID-19 causes a pneumonia-like syndrome leading to respiratory failure in severe cases.¹ In extreme cases, it has a high fatality rate, although early detection along with prompt treatment can lower mortality and morbidity rates.

In the current study, the mean age was 62 ± 17.1 years in the critical group compared to 50 ± 19.7 years in mild and 52 ± 15.9 years in moderate groups. Kantri et al. described that advanced age was associated with severe disease and increased mortality.² Zhou et al. also noted that patients aged >50 years were at

increased risk of acute respiratory distress syndrome (ARDS) and high mortality.¹⁰ Advanced age is described as an independent risk factor for increased mortality in COVID-19.^{11,12}

In the present study, 29 (58%) of the subjects were males, but the gender difference was not significant ($p>0.05$). Earlier studies also described no gender differences.^{1,13,14}

In the current study, inflammatory markers CRP, IL-6, serum ferritin and D-dimer were found to be significantly raised in patients with severe disease, which is in agreement with earlier studies.^{14,15} Bairwa et al. reported significant difference with respect to CRP, procalcitonin and lactate dehydrogenase (LDH) between COVID-19 survivors and non-survivors.⁴ Other studies have also reported IL-6 and CRP as significantly high in severe disease group.¹⁶⁻¹⁸ It has been reported that raised levels of CRP, D-dimer, serum ferritin and procalcitonin were associated with increased mortality and morbidity, and also with increased risk of superimposed infections.¹ Studies have observed that raised levels of these parameters along with other biochemical markers were associated with increased risk of complications associated with COVID-19 infection, leading to death.^{1,19-21}

In the current study, mean values of CRP, IL-6, serum ferritin and D-dimer were compared between the survivors and non-survivors, and they were found to be significantly different between the groups ($p<0.05$). This finding was in agreement with previous studies.^{4, 6, 14} An earlier study showed that cytokine storm in COVID-19 infection was associated with poor prognosis, and raised levels of IL-6, serum ferritin, CRP, and decreased level of albumin.²² Another study reported that CRP, procalcitonin and LDH were raised in COVID-19 patients who died.²³

The current study has limitations owing to its small sample size. Since data collection took place between two main COVID-19 waves in Pakistan, the frequency of positive cases were low. Besides, the relatively small sample size is also attributed to the low affordability of the community in terms of private healthcare. Also, the CPTH is located in the outskirts of Lahore, where fewer patients reported compared to other hospitals in the city centre. Another limitation of the study is that not all the inflammatory parameters could be included as they were not tested on every patient.

Conclusion

Older people were found to have experienced disease in more severe forms. Inflammatory markers CRP, IL-6, serum ferritin and D-dimer were significantly high in

patients with severe disease and were associated with high mortality.

Acknowledgement: We are grateful to friends and colleagues for their help at various stages of the study.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

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