



STUDY OF INFLAMMATORY MARKERS IN COVID-19 PATIENTS ATTENDING A TERTIARY CARE HOSPITAL

Biochemistry

Dr. D. Sobana*	Postgraduate, Department of Biochemistry, Sree Mookambika Institute of Medical Sciences. *Corresponding Author
Dr. S. Saravanan	Associate Professor, Department of Medicine, Thoothukudi Govt. Medical College Hospital.
Dr. R. Nagendran	Professor & HOD, Department of Biochemistry, Sree Mookambika Institute of Medical Sciences.

ABSTRACT

Background: Relationship between inflammatory markers and COVID-19 has been one of the most popular topics recently. These inflammatory markers predict the unpredictable complications in COVID-19.

Aims And Objectives: To study the impact of inflammatory markers in COVID-19 patients.

Materials And Methods: Totally 80 subjects were selected for the study which included 40 apparently normal healthy population and 40 COVID-19 patients.

Results: About 37.5% of patients have high IL-6 values above 16.8pg/ml, about 42.5% of patients have D-dimer above 500ng/ml, about 35% of patients have CRP values above 10mg/L.

Conclusion: Inflammatory markers in COVID-19 patients indicate the severity of disease.

KEYWORDS

Interleukin-6, D-dimer, C-reactive protein, Ferritin, COVID-19

INTRODUCTION:

Corona virus expanded globally from Wuhan, China in late 2019. It was declared a pandemic on March 11th, 2020 by the World Health Organization. The mortality of many patients is attributed to the rapid development of ARDS and multiorgan failure as a result of a cytokine storm. An effective suppression of the cytokine storm is a pivotal way to prevent the deterioration of patients with COVID-19 and save the patient's lives.

Inflammatory responses play a critical role in the progression of COVID-19. Inflammatory responses triggered by rapid viral replication of SARS-COV-2 and cellular destruction can recruit macrophages and monocytes and induce the release of cytokines and chemokines.

These cytokines and chemokines then attract immune cells and activate immune responses leading to cytokine storm. Several inflammatory markers have tracing and detecting accuracy for disease severity and fatality. Inflammatory markers are markers which are commonly used in primary care for diagnosis and monitoring of inflammatory conditions including infections, autoimmune conditions and cancers. Detection of inflammatory markers predicts the unpredictable complications and changes the treatment strategies that reduces the mortality rate. Hence this study was carried out to know the impact of inflammatory markers in assessing severity of COVID-19.

OBJECTIVES:

- To study the impact of inflammatory markers in COVID-19 patients.
- To know the association of inflammatory markers in severity of COVID-19 patients.

MATERIALS AND METHODOLOGY:

Cross-sectional study was carried out among those patients attending COVID outpatient department during the period July 2020 - September 2020 in Sree Mookambika Institute of Medical Sciences. 40 COVID-19 patients and 40 apparently normal healthy population were included in the study. The exclusion criteria were people suffering from other inflammatory conditions like SLE, rheumatoid arthritis, inflammatory diseases, osteomyelitis, malignancy, and people with other conditions like pregnancy, obesity, alcoholic fatty liver disease etc. After getting informed consent, using a questionnaire, detailed medical history was taken, details on COVID-19 were collected. 5 ml of venous blood sample was collected for inflammatory markers.

Statistical Analysis:

Data entry was made in the Microsoft Excel Software in codes and

analysis was done with SPSS-24 computer package. Continuous variables were expressed as mean \pm standard deviation. Relationship between continuous variables was assessed by Student's t-test. P value < 0.05 was considered as statistically significant.

RESULTS:

Totally 80 participants were studied, of which 40 were cases and 40 were controls. The baseline characters are shown in Table 1.

Table 1: Demographic Profile Of Cases And Controls

Parameter	Classification	Cases	Controls
Gender	Male	22	24
	Female	18	16
Age in years	Mean Age \pm SD	51.7 \pm 10.5	49.5 \pm 12.6

Inflammatory markers among COVID-19 patients were assessed and it was found that 37.5% of individuals have high IL-6 values above 16.8 pg/ml. About 42.5% of individuals have high D-dimer values above 500ng/ml. About 35% of individuals have CRP values above 10mg/l. About 32.5% of individuals have high ferritin values and details are shown in Table 2.

Table 2: Distribution Of Inflammatory Markers Among COVID-19 Patients

		Frequency	Percentage
IL-6	Normal 0-16.8pg/ml	25	62.5
	High >16.8pg/ml	15	37.5
D-dimer	Normal <500ng/ml	23	57.5
	High >500ng/ml	17	42.5
CRP	Normal <10mg/l	26	65
	High >10mg/l	14	35
Ferritin	Normal:	27	67.5
	Males: 30-350ng/ml		
	Females: 20-200ng/ml		
High:	Males: >350ng/ml	13	32.5
	Females: >200ng/ml		

The distribution of inflammatory markers among cases and controls were compared and is found that Mean of IL-6, D-dimer, CRP and Ferritin levels are high among cases and was statistically significant ($p < 0.05$).

Table 3: comparison Of Inflammatory Markers Among Cases And Controls

Parameter	Cases		Controls		P value
	Mean	SD	Mean	SD	
Age in years	51.7	10.5	49.5	12.6	0.39(NS)

IL-6	54.35	139.6	6.6	3.8	0.03(<0.05)
D-dimer	1556.8	2685.7	182.0	103.7	0.0018(<0.05)
CRP	38.86	46.1	4.7	2.3	0.0001(<0.05)
Ferritin	366.07	345.1	71.3	56.9	0.0001(<0.05)

DISCUSSION:

Inflammatory markers are elevated in COVID-19 patients due to cytokine storm. IL-6, CRP, D-dimer and ferritin are used as independent markers to predict the severity of COVID-19. [1-3] IL-6 is a multifunctional cytokine that transmits cell signaling and regulates immune cells. This factor has a strong proinflammatory effect with multiple biological functions and is the primary trigger for cytokine storm [4,5]. CRP is a non-specific acute phase protein and a sensitive biomarker of inflammation, infection and tissue damage. Patients with elevated CRP levels were more likely to develop severe disease. [6-8]

Patients manifesting hyperferritinemic phenotype show an abnormal pattern of activation of reticuloendothelial system and multiple organ damage. The level of serum ferritin may be used as a biomarker to determine the pathological condition of a COVID-19 infection and it can also be used as a target for various therapeutic interventions in clinical practice. [9]

D-dimer elevation was associated with both increased disease severity and mortality. D-dimers are one of the fragments produced when plasmin cleaves fibrin to breakdown clots. Any pathologic or non-pathologic process that increases fibrin production or breakdown also increases plasma D-dimer levels. Increased D-dimer levels is used as a single useful biomarker for clinical outcome in patients with COVID-19.

D-dimer >1 µg/ml is a risk for mortality. [10] Elevated D-dimer identify patients at higher risk for in-hospital mortality and inform physicians about suitable candidates for intensive care and early intervention.

In this present study, the mean value of IL-6 in cases was 54.35±139.6 which is higher than that of controls 6.6±3.8 with a p value of <0.05 which is statistically significant. Similar findings were revealed in the study by Weichen et al. The mean value of D-dimer in cases was 1556.8±2685.7 higher than that of the controls 182.0±103.7 with a p value of <0.05 which is statistically significant. The study by Yumeng Yao had shown same findings.

The mean value of CRP in cases was 38.86±46.1 which is higher than of the controls 4.7±2.3 with a p value of <0.05 that is statistically significant. Similar findings were shown in the study by Kenneth I. Zheng et al. In this present study, the mean value of ferritin in cases was 366.07±345.1 which is higher than that of the controls 71.3±56.9 with a p value of <0.05 that is statistically significant. Similar findings were shown in the study done by Jyoti Upadhyay et al.

In this present study, elevated IL-R and CRP levels in COVID-19 patients indicate the severity of infection and thereby patients were treated with steroids and tocilizumab. Steroids reduced the severity and prevented the occurrence of ARDS in COVID patients. Tocilizumab reduced patient morbidity and need for mechanical ventilation.

In this present study, elevated D-dimer levels in COVID-19 patients indicate the severity of infection and recommend for use of LMW heparin in those patients. LMW heparin prevented venous thromboembolism in those patients. Increased ferritin levels denote the severity of disease.

CONCLUSION:

Inflammatory markers should be detected in COVID-19 patients which indicate the severity of the disease. Their detection initiate vigorous management in COVID patients and help to prevent complications.

REFERENCES:

- 1) Jyoti Upadhyay, Nidhi Tiwari, Mohd N. Ansari, "Role of inflammatory markers in corona virus disease (COVID-19) patients: A review". <http://doi.org/10.1177/15353>
- 2) Furong Zeng, Yuzhao Huang, Ying Guo, Mingzhu Yin, "Association of inflammatory markers with the severity of COVID-19: A meta-analysis". <http://doi.org/10.1016/j.ijid.2020>.
- 3) Linda Brookes, "The Role of Laboratory Test Biomarkers in Diagnosis, Risk Stratification and Monitoring of COVID-19 Patients" 2020-05-28
- 4) Dr. Barnali Das, "Routine lab markers in COVID-19 patients: Chasing the storm in Indian Perspective.
- 5) Jessica J Manson, Meena Naja, Colin Crooks, Trevor Liddle, "COVID-19 associated hyperinflammation and escalation of patient care: a retrospective longitudinal cohort

study, <https://doi.org/10.1016/s2665>

- 6) Sweta Gupta, "Elevated Level of C-Reactive Protein May Predict Risk for Worsening COVID-19, May 19, 2020.
- 7) Fang Liu, Lin Li, MengDa Xu, Juan Wu, Ding Luo, "Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19, April 14, 2020
- 8) Wei Chen, Kenneth Zheng, Saidoo Liu, "Plasma CRP level is positively associated with the severity of COVID-19, Annals of clinical Microbiology, volume 19, Article number 18
- 9) Muhammed Kermali, Raveena Kaur Khalsa, Kiran Pillai, Zahra Ismail, "The role of biomarkers in diagnosis of COVID-19- A systematic review Life Sciences, volume 254, Aug 2020.
- 10) Yumeng Yao, Jiatian Cao, Qingqing Shi, Kai Liu, "D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study", Journal of Intensive Care, volume 8, Article number 49.