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Original Article

Inflammatory marker interleukin-6 in risk stratification of COVID-19 patients

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Abstract

The main purpose of this study is to determine the levels of interleukin-6 in COVID-19 patients and see if these inflammatory markers can speculate the extremity of COVID-19 patients. Therefore, previous work on serum ferritin levels in COVID-19 patients has been conducted by the authors as a presumptive observational study [11]. The study's inclusion criteria comprised 100 individuals who were over the age of 18 and were diagnosed with COVID-19 by real-time quantitative reverse transcriptase polymerase chain reaction method for severe acute respiratory syndrome (SARS-CoV-2). The exclusion criterion was framed according to our previous study [11]. They were bifurcated into the following categories such as: mild to moderate (Group I) and severe to critical (Group II). IL-6 was quantified and evaluated in both groups using the chemiluminescent method [11]. Group I had a mean IL 6 value of 27 pg/ml, while Group II had a value of 126 pg/ml. COVID-19 individuals with elevated IL-6 levels had more indicative predictions, extremity, and serious illness, particularly in group II ($P<0.000$), and constant in group I, IL-6 levels showed a statistically significant ($P<0.000$) association with symptomatic indications, severity, and critical illness. Interleukin-6 can be used as a prediction factor for disease severity in the early diagnosis of COVID-19.

Keywords: Interleukin-6, COVID-19, chemiluminescence assay, inflammatory marker and qRT – PCR.

Introduction

The COVID-19 pandemic is extremely pestilent and fatal; thus, prompt detection of serious forms is critical despite urgent patient triage. While the clinical condition of COVID-19 patients, particularly their peripheral oxygen levels (SpO_2) and concomitant disorders, decide the requirement for ICU admission, various laboratory measures may aid in the evaluation of disease severity [1]. It demonstrates that mortalities of COVID-19 are accompanied by cytokine release syndrome, intimating that the illness extremity is influenced by cytokine release syndrome [2]. COVID-19 – ICU inpatients were predicted to have greater levels of proinflammatory cytokines, especially C-reactive protein (CRP), ferritin, and IL-6. However, there is no reliable and practical inflammatory marker study article for predicting illness severity. ICU inpatients are those who are critically ill, whereas mildly ill or moderately ill patients are admitted to the normal isolation ward. A tiny percentage of non-severe individuals, however, will progress to severe instances. As a result, reducing mortality and improving outcomes for COVID-19 individuals requires a solution to the problem of identifying this group of patients early and aggressively monitoring and treating them [3]. As a result, the goal of this study is to calculate Interleukin-6 levels and see if inflammatory marker levels can predict the extremity of COVID-19—the current study aimed to analyze the inflammatory marker Interleukin-6 in risk stratification of COVID-19 patients.

Material and methods

This proposed – prevalence study was organized in our laboratory with approval from the institutional

ethics committee. Acquainted compliance was procured from patients over 18 years of age detected with COVID-19 positive.

Study design and patients

A group of patients (100) segregated based on COVID-19 positive serves as the inclusive part of this study. The exclusion criteria consist of the rheumatoid population, cancerous tumor and other appertaining disorders, extended oral drugs for inflammation, or those who consumed high doses of glucocorticoids in the past 14 days.

Age, temperature, pulse rate, oxygen levels, B-cell and T-cell count, and CT chest findings were used to separate the study populace into two groups: mild to moderate (Group I) and severe to critical (Group II) [4]. Blood samples from both groups were drawn in the serum separator tubes, and IL-6 was measured:

- *Group I (Mild to moderate)*: Symptomatic COVID-19-positive patients with no evidence of viral pneumonia or hypoxia were assigned to the mild illness group. In ambient environments, SpO_2 ranges from 92 to 95 percent [5].
- *Group II (Severe to critical)*: Symptomatic COVID-19-positive patients with clinical manifestation of severe pneumonia, evidence of bilateral opacities in the chest, and 90% range of SpO_2 in an ambient environment were classified as very critical and patients suffering from ARDS, sepsis, and septic shock after other causes had been excluded [5].

Laboratory data collection

The WHO's preliminary recommendation was used to diagnose COVID-19 [6]. Patient information was gathered for data analysis. Patient demographics, case history, clinical manifestations, physical examination, and laboratory findings were collected for evaluation. The study populace was classified based on disease extremities according to the ICMR guidelines.

Statistical analysis

The mean and standard deviation were used to manifest quantitative data [5]. $P<0.05$ was chosen as the criterion of significant expression. The data were statistically analyzed and attained using the SPSS version for Windows, as used for our previous investigations [5].

Results and discussion

The current study looked at the relationship between IL6 levels and COVID-19 severity. This study comprised 100 COVID patients diagnosed with SARS-CoV-2 by qRT-PCR and were separated into two groups based on the suggested criteria. The incidence of acute respiratory syndrome and COVID-19-associated mortality were closely linked to elevated IL-6 levels [7]. In the SARS-CoV-2 illness phase, IL-6 acts as an immune modulator element. It plays a major role in COVID-19-related cytokine release immune reaction, which increases microvascular permeability and organ dysfunction [5].

The study included 100 COVID-19 patients following a similar study published earlier [5], with 70 of them falling into Group I (mild to moderate) with elevated blood IL-6 levels (6.0–30.0 pg/mL) by up to five times. Thirty patients in the severe to critical range had IL-6 levels that were remarkably higher than the upper average limit (30.0–60.0 pg/mL) (Table 1 and Table 2).

The average mean value of IL-6 in group I was observed to be 27±14, while the mean IL-6 value in group II was 126±70. The Group I; IL-6 of SARS-CoV-2 infected patients (95 percent confidence interval: 23.23±7.31, standard deviation=14.69) and the Group II; IL-6 of SARS-CoV-2 infected patients (95 percent confidence interval: 100.08±52.09, standard deviation=70.17) were compared.

The current study clearly shows a link between IL-6 and the severity of the condition. IL-6 is a type of proinflammatory signaling molecule that takes part in releasing COVID-19 cytokine, which causes microvascular permeability and organ dysfunction [5]. This

Table 1: One-sample mean test.

	Total number of individuals	Sample mean	Standard deviation	Standard mean error
Group I	70	27.4684	14.69437	1.75631
Group II	30	126.2987	70.17784	12.81266

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Table 2: One-sample t-test.

	T-Value=0					
	T-value	Degree of freedom	Two-tailed P-value	Mean variation	Difference in 95% Confidence level	
					Lower	Upper
Group I	15.640	69	.000	27.46843	23.9647	30.9722
Group II	9.857	29	.000	126.29867	100.0938	152.5035

procedure necessitates IL-6 binding to its soluble IL receptor (Sil-6R). By attaching to gp130 on the cell membrane, the generated complex initiates signal transduction and the pro-inflammatory process [8–11].

The inflammatory immune response of the respiratory system and the release of IL-6 are stimulated by the replication of the SARS-CoV-2, leading to the development of ARDS or respiratory failure.

Conclusion

Owing to the enormous release of cytokines, which drives the elevated inflammatory response, COVID-19-positive cases with inclined levels of IL-6 are obviously at greater risk of extremities and deadly illness, resulting in higher mortality. Patients ailing with SARS-CoV-2 who have exceptionally significant levels of IL-6 are at risk of developing a severe and life-threatening condition that requires intense pharmacological and supportive therapy. Early in the course of the disease, IL-6 levels could be used as an indicating factor of disease extremities in COVID-19 patients, as well as a routine clinical test to anticipate imminent poor outcomes with high fidelity.

Conflict of interest

The authors declare no conflict of interest.

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