IL-6 AS A POTENTIAL BIOMARKER FOR DISEASE SEVERITY IN COVID-19 PATIENTS

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INTRODUCTION

In December 2019, SARS-CoV-2 infection was rapidly spreading, posing a serious threat to the health of people worldwide, and the disease it caused was named coronavirus disease (COVID-19) by the International Committee on Taxonomy of Viruses, resulting in the World Health Organization officially declaring it as a pandemic on March 11, 2020.¹ COVID-19 infection has a variable clinical presentation from asymptomatic to milder symptoms, including fever, dry cough, dyspnoea, myalgia, sore throat, and headache, to more severe and emergent manifestations including confusion, chest pain, hypoxemia, pneumonia, and other complications requiring intensive care unit (ICU) admission and mechanical ventilation. Diarrhea, anosmia, and ageusia have also been reported in a few studies and neurologic manifestations.² The diagnosis of the 2019 novel coronavirus can be made by reverse-transcriptase polymerase chain reaction (RT-PCR). Computed tomography (CT) findings include peripheral ground glass densities in which multilobar, lower lobes, and posterior segments are seen and sometimes accompanied by subsegment patchy consolidations.³ The scientific community is in urgent need of reliable biomarkers related to coronavirus disease 2019 (COVID-19) disease progression, to stratify high-risk patients. Effective biomarkers would be helpful for screening, clinical management, and prevention of serious complications.⁴ Laboratory biomarkers are less expensive, faster, and easier to obtain. As such, they have been the preferred modality to monitor and predict outcomes and prognosis of disease. The SARS-CoV-2 virus enters the host cells and in turn, a cascade of immune response pathways is generated, leading to an increase in the pro-inflammatory cytokine (IL-6, IL-1β, IL-2, IL-8, IL-17, G-CSF, GM-CSF, IP-10, MCP-1, CCL3, and TNFα) population. This “cytokine storm” attracts neutrophils, lymphocytes, and...
Interleukin 6 (IL-6), a multi-functional cytokine (a protein) produced by a range of cells, plays a central role in host defense mechanisms and is involved in the induction of B (lymphocyte) cell differentiation.[6] However, excessive synthesis of IL-6 can lead to a severe acute systemic inflammatory response known as a “cytokine storm,” which confers increased risks of vascular hyperpermeability, multiorgan failure, and eventually death. This suggests that higher IL-6 levels may be an important predictor of COVID-19 severity. IL-6 is the most common cytokine reported in SARS CoV 2 infection which is reflected in clinical manifestations, radiological features, management modalities, and outcomes.[7,8]

The present study aims to assess the IL 6 levels in COVID-19 infected patients and to evaluate its association with the severity and mortality of the disease, the requirement for additional management therapies, and outcomes.

**MATERIALS AND METHODS**

Study Design: Patients with SARS-CoV-2 infection and who were RT-PCR positive for COVID-19 admitted to the tertiary care centre from March 2021 to June 2021 were enrolled in this study. All COVID-19-positive patients referred to the Central Clinical Laboratory (CCL) irrespective of age and gender were included in the study except for those patients suffering from other diseases in which IL-6 levels can be increased. A total of 112 patients were enrolled, but out of these only 100 patients were included in the study as per inclusion/exclusion criteria.

**Sample Collection:** Throat and nasal swabs samples were used for the detection of COVID-19 infection by RT-PCR in the microbiology laboratory of the institute. The laboratory has been authorized by the Indian Council of Medical Research (ICMR) to conduct the tests for COVID-19. COVID-19-positive patients referred to the Central Clinical Laboratory (CCL) for further investigations: Including quantification of IL-6.

**IL-6 assessment:** The Beckmann Coulter Access IL-6 assay was used for the quantitative determination of IL-6 levels in the serum of COVID-19-positive patients. IL-6 range between 0.00 - 7.00 pg/ml was normal as per the assay kit instructions. We divided the patients into three categories on the basis of IL-6 levels: Mild (IL-6 range: 0.00-20.00 pg/ml), moderate (IL-6 range: 21.01-80.00 pg/ml) severe (IL-6 range: > 80.01 pg/ml).

**Data analysis:** Data was analyzed by EXCEL spreadsheet; results were documented in proportions and percentages. Statistical analysis was done using SPSS v23 software. [IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.]

**RESULTS**

A retrospective & observational study was done among 100 patients who tested positive for COVID-19 by RT-PCR on nasopharyngeal swabs and were admitted to the tertiary care hospital. The mean age of patients was 58.71 ± 15.49 years. Most of the patients were males [n=70/100 (70%)]. A total of nine (9%) patients were succumbed during the study.

A detailed description of the age, gender, oxygen saturation, and IL-6 is given in Table 1. Most of the patients were older in age. There was not a significant difference between males and females in their age. Patients who succumbed during these 14 days were older in age and these patients had higher IL-6 levels which were continuously increasing even after the treatment. The oxygen saturation levels also were dipping continuously. These patients were critical and were admitted to the ICU with continuous oxygen support and monitoring. All other parameters were also fluctuating among these 9 patients.

There was a decrease in the IL-6 levels from day one to day 14 in all patients except for the nine patients who succumbed during the study. We found that on the day of admission, most of the patients belonged to the moderate (44%) IL-6 category followed by severe (40%) and mild (16%) IL-6 category. IL-6 category on day seven had mixed results which were a little bit unpredictable, while on day 14, most of the patients were under the mild (82%) IL-6 category. A detailed description is given in [Table 2 and Figure 1].

![Figure 1.: IL-6 category of COVID-19 patients Day 1, Day 7, Day 14.](image-url)
The patients recovered and declare.

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LIMITATIONS OF THE STUDY
Also, the oxygen saturation along with IL-6 levels play an important role in the severity of disease. Patients with older age and with COVID-19 infection have higher values of IL-6 along with lower oxygen saturation levels. So, IL-6 can be used as a prognostic marker among these patients to differentiate the severity of the disease. Also, the oxygen saturation along with IL-6 can help in designing a strategy to deal with the load of COVID-19 patients.

DISCUSSION
This was a single-centre study of 100 patients with COVID-19 infection who were admitted to the hospital. Serum IL-6 levels were measured and oxygen saturation was recorded in all patients at the time of admission, seven days later, and fourteen days later. Most of the patients recovered and responded to treatment, IL-6 levels in all these patients were reduced, and oxygen saturation readings returned to normal as the patients' health stabilized. Several research on IL-6 imply that proinflammatory cytokines like IL-6 are to blame for the acute lung injury seen in COVID-19. Thus, inhibiting this IL-6 route could be the key to reducing COVID-19 lung injury.[9] In our study, IL-6 is associated with the severity of the disease which is also supported by other studies.[1,2,10]

CONCLUSION
In our study, IL-6 levels play an important role in the severity of disease. Patients with older age and with COVID-19 infection have higher values of IL-6 along with lower oxygen saturation levels. So, IL-6 can be used as a prognostic marker among these patients to differentiate the severity of the disease. Also, the oxygen saturation along with IL-6 can help in designing a strategy to deal with the load of COVID-19 patients.

REFERENCES