Association of inflammatory markers with clinical outcome in COVID-19 patients during the second wave in 100 bedded dedicated COVID MCH Hospital, Raigarh, Chhattisgarh State

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ABSTRACT

Background: A novel coronavirus (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) was the causative agent of coronavirus disease 2019 (COVID-19) pandemic 2019. SARS-CoV-2 affects respiratory tract and damages the tissue resulting in generation of inflammatory cells such as cytokines and chemokines such as IFN that damage the lung alveoli, causing severe acute respiratory syndrome. Aims and Objectives: The aims and objectives of the study are to analyze the blood inflammatory markers of COVID-19 patients and association between clinical outcomes in COVID-19-positive patients with serum inflammatory markers during the second wave of COVID-19 pandemic in 100 bedded dedicated COVID MCH Raigarh CG. Materials and Methods: In this hospital-based cross-sectional observational study, 90 patients with COVID-19 were enrolled and categorized into three groups: mild, moderate, and severe. Blood inflammatory markers such as C-reactive protein (CRP), lactate dehydrogenase (LDH), ferritin, CK-Nac as well as hemogram total leukocyte count (TLC), differential leukocyte count, and neutrophil: lymphocyte (N:L) were determined and analyzed. Results: The results of the oxygen saturation (SpO₂) severity strength of association with multiple variables taken in the study through logistic regression analysis of COVID-19 patient’s inflammatory markers serum levels of LDH (P<0.05, odds ratio [OR] = 1.0146), ferritin (P<0.05, OR = 0.9788), N:L (P<0.05, OR = 4.1041), and other non-inflammatory parameters such as creatinine (P<0.05, OR = 17.8039) were significant. SpO₂ severity of COVID-19 patient’s with inflammatory markers LDH, ferritin, CK-Nac, and TLC associated with all severe, moderate, and mild groups. There was no significant association in the serum levels of CRP between the severe, moderate, and mild groups. Conclusion: The findings of this study suggest that the levels of LDH, ferritin, CK-Nac, and TLC could be used to predict the severity of COVID-19 disease.

Key words: COVID-19; SARS-CoV-2; Lactate dehydrogenase; C-reactive protein; CK-Nac; Total leukocyte count; Ferritin neutrophil: lymphocyte ratio

INTRODUCTION

The outbreak of coronavirus disease 2019 (COVID-19) worldwide pandemic has posed a huge threat to global public health in December 2019.¹ Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel single-strand RNA virus named as SARS-CoV-2. COVID-19 represents a variety of clinical findings from asymptomatic to symptoms such as
pneumonia, ARDS, and even death. SARS-CoV-2 infection associated with mortality case is linked with induced hyper-inflammation with innate and adaptive immune systems and the resulting cytokine cascade. Higher levels of inflammatory markers such as lactate dehydrogenase (LDH), C-reactive protein (CRP), CK-Nac, hematogram, and neutrophil-lymphocyte ratio have been shown to be related to a more severe clinical course in COVID-19 patients. Clinical, as well as, laboratory monitoring of inflammatory markers of the COVID-19 patients is helpful for early intervention and reducing mortality. Therefore, the aim of this study is to the association of inflammatory markers with clinical outcomes in COVID-19 patients during the second wave in 100 bedded dedicated COVID MCH hospital, Raigarh, Chhattisgarh state helpful for contributing to treatment and reducing mortality rate.

Aims and objectives
To study the level of inflammatory markers & its association with clinical outcome in Covid-19 patients during the second wave of COVID admitted in 100 bedded dedicated Covid MCH hospital Raigarh.

MATERIALS AND METHODS

The study was a hospital-based cross-sectional observational study conducted between March 2021 and July 2021 at a 100 bedded dedicated COVID center MCH associated with Late Shri Lakhiram Agrawal Memorial Government Medical College, Raigarh (C.G.), after obtaining the ethics approval of the Institute Ethics Committee. Detailed history was taken in a specified proforma of ninety patients who were admitted to specified wards/HDU/ICU for COVID-19 and have been enrolled in the study after obtaining their informed written consent. COVID-19 disease was diagnosed in patients based on the World Health Organization guidelines by reverse transcription polymerase chain reaction test. Patients’ demographic information was collected, including age, sex, socioeconomic status, and clinical data. Blood samples were taken from each patient. Under all aseptic conditions, 5 ml of blood sample will be collected from all subjects by phlebotomy in two vials. EDTA vial blood samples were analyzed for complete hemogram by 5-Part HORIBA ABX Pentra XL80 hematology analyzer and plain vial blood samples were analyzed for inflammatory markers such as CRP, ferritin, LDH, and CK-Nac by AGAPPE biochemistry fully Auto-analyzer. Patients’ outcome in terms of mortality and recovery was noted.

Inclusion criteria
All COVID-19-positive patients admitted in 100 bedded dedicated COVID MCH hospital during the second wave of COVID-19 pandemic (March 2021–July 2021) whose blood samples were taken from inflammatory markers testing.

Exclusion criteria
COVID-19-positive patients admitted with the second wave of COVID-19 pandemic who had not tested for inflammatory markers and any other inflammatory disease at the time of study.

According to the Health and Family Welfare Department, Government of Chhattisgarh, COVID-19 clinical management guidance protocol classification of the forms of COVID-19 was made as follows:

- Mild form: Asymptomatic or mild symptomatic but positive for COVID-19, patients with general symptoms or upper respiratory tract symptoms, with oxygen saturation (SpO₂) more than 94%.
- Medium form: Patients with dyspnea, fever, and cough with SpO₂ between 90% and 94% in room air.
- Severe form: patients with respiratory distress, hypoxemia, dyspnea, fever, and cough with SpO₂ below 90% in room air.

Statistical analysis
The data were collected and compiled on Microsoft Excel Software and presented in the form of mean, percentages, odds ratio (OR), and figures such as tables. Data were analyzed using the Statistical Package for the Social Sciences software. Correlation between these inflammatory markers and clinical outcomes of COVID-19 patients was analyzed by Chi-square test. The P<0.05 was considered statistically significant.

RESULTS

A total of 90 COVID-19 patients were included in this study; COVID-19 cases included Group III 30 patients with severe form, Group II 30 patients with moderate form, and Group I 30 patients with mild form, admitted in 100 bedded dedicated COVID hospital MCH, Raigarh.

Table 1 shows that SpO₂ severity association with the age of COVID-19 patients admitted in 100 bedded dedicated COVID hospital MCH, Raigarh. Out of 90 patients, 22 (24.4%) patients were below 30 years of age, 49 (54.4%) patients were 31–60 years of age, and 19 (21.1%) patients were above 60 years of age. Out of 90 patients, 48 (53.3%) patients were male and 42 (46.6%) were female. In Table 2 gender distribution severity association with SpO₂ of COVID-19 patient’s, out of 48 male COVID-19 patients, 26 (28.8%) patients were mild, 8 (8.8%) patients were moderate, and 14 (15.5%) patients were severe category and 42 female COVID-19 patients, 23 (25.5%) patients were mild, 2 (2.2%) patients were moderate, and 17 (18.8%)
patients were severe category. Table 3 shows that SpO₂ severity strength of association with laboratory findings of inflammatory markers in COVID-19 patients was performed by Logistic Regression Analysis. Serum ferritin, LDH, and neutrophil: lymphocyte (N:L) values were significantly higher \( P<0.05 \). Other laboratory findings, serum creatinine, were strongly associated with the severity of SpO₂ level of COVID-19 patients \( P<0.05 \) but there was no correlation of CRP with SpO₂. Tables 4-7 show that SpO₂ severity association with levels of LDH, ferritin, CK-Nac, and total leukocyte count (TLC) was also significantly increased among patients with a poor outcome. Survival analysis showed that elevated levels of LDH, ferritin, and CK-Nac were significantly associated with mortality.

### DISCUSSION

This study provided the laboratory findings of severe COVID-19 patients. Increase in the levels of inflammatory markers, were significantly higher in severe group, as compared to moderate and mild groups of COVID-19 patients. Liao et al., 2020, study demonstrated that elevated N/L ratio and decreased platelet count were useful predictors for severity and mortality in COVID-19 patients admitted to intensive care units. In our study also, hematological findings TLC and N/L ratio significantly increased in severe group, indicating the inflammatory condition of COVID-19 patients and good sensitivity markers for clinical outcomes in COVID-19 patients. In 2020, Yang et al. found that N/L ratio was an important inflammatory marker of severity and mortality in COVID-19 patients. In 2021, Alroomi et al. showed that ferritin independently inflammatory marker predicts hospitalized severity and mortality of COVID-19 patients in Kuwaiti population. In 2022, Huang et al., retrospective study using a large sample size of COVID-19 Chinese patients showed that LDH was associated with higher mortality risk. In our study also, serum ferritin and LDH were good inflammatory markers for mortality in COVID-19 patients. Ahmed et al. in 2020 showed that elevation in serum inflammatory marker CRP may be indicative of COVID-19 infection severity and mortality and these parameters may predict COVID-19 severity. In our study, also CRP level was increased in severe group as compared to mild and moderate COVID-19 groups. In this study, SpO₂ was reduced in COVID-19 patients and showed a positive correlation with LDH, ferritin, CK-Nac and TLC in severe group as compared to mild and moderate groups. Hematological parameters such as TLC, differential leukocyte count, and N/L ratio may lead to improved prediction which needs to be helpful for future studies. Inflammatory markers ferritin, LDH, and CK-Nac could be useful as a predictor for COVID-19 mortality and could help COVID-19 patients to provide early treatment.
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and D-dimer could be correlated with disease severity to predict COVID-19 mortality.

Limitations of the study
The limitations of this study were, small patient sample size and limited resources for analysis of others inflammatory markers like IL6, IL8 & TNF-α.

CONCLUSIONS
Our study finds that the increased value of inflammatory parameters was associated with both increased severity and increased mortality. Among these parameters, the value of LDH, ferritin, and CK-Nac was statistically significantly correlated with the severity of the disease and with mortality also the total leukocytes were correlated with the severity of the disease. LDH and ferritin have been contemplated as the most accurate predictor of severity and mortality in COVID-19 patients among routine investigations. The present results implicated that increased LDH, ferritin, and CK-Nac levels were significantly correlated with severity and mortality in COVID-19 patients.

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PML- conceptualization the article; VPG- contributed study design and data collection; AMM- data analysis and interpretation of results; HK- manuscript preparation; MKM- review and editing. All authors read and approved the final manuscript.

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100. Bed Dedicated COVID MCH Associated Late Shri Lakhiram, Agrawal Memorial Govt. Medical College Raigarh (C.G.), India.

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