



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

Pankaj Madhukar Luka¹, Ved Prakash Gilley², Anmol Madhur Minz³, Harish Kumar⁴, Manoj Kumar Minj⁵

¹Dean, ⁴Associate Professor, Department of Biochemistry, ⁵Professor, Department of Pathology, Late Shri Lakhi Ram, Agrawal Memorial Government Medical College, Raigarh, ²Associate Professor, Department of Medicine, ³Associate Professor, Department of Community Medicine, Government Medical College, Korba, Chhattisgarh, India

Submission: 26-11-2023

Revision: 25-01-2024

Publication: 01-03-2024

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 (SpO_2) 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. SpO_2 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

Access this article online

Website:

<http://nepjol.info/index.php/AJMS>

DOI: 10.3126/ajms.v15i3.60185

E-ISSN: 2091-0576

P-ISSN: 2467-9100

Copyright (c) 2024 Asian Journal of Medical Sciences



This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

Address for Correspondence:

Dr. Harish Kumar, Associate Professor, Department of Biochemistry, Late Shri Lakhi Ram, Agrawal Memorial Government Medical College, Raigarh, Chhattisgarh, India. **Mobile:** +91-9340729095. **E-mail:** harishuraon26@gmail.com

pneumonia, ARDS, and even death.² SARS-CoV-2 infection associated with mortality case is linked with induced hyperinflammation with innate and adaptive immune systems and the resulting cytokine cascade.^{3,4} 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.^{5,6} 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%)

Table 1: SpO₂ severity association with age

SpO ₂ level	Age			Total	Mean age	Death
	<30	31–60	>60			
Mild	16 (17.7%)	27 (30%)	6 (6.6%)	49 (54.4%)	40	0 (0%)
Moderate	3 (3.3%)	5 (5.5%)	2 (2.2%)	10 (11.1%)	42.7	3 (9.09%)
Severe	3 (3.3%)	17 (18.8%)	11 (12.2%)	31 (34.4%)	53	30 (90.9%)
Total	22 (24.4%)	49 (54.4%)	19 (21.1%)	90 (100%)		33 (100%)

SpO₂: Oxygen saturation

Table 2: SpO₂ severity association with gender

SpO ₂ level	Gender status			Total	Death
	Male	Female			
Mild	26 (28.8%)	23 (25.5%)		49 (54.4%)	0 (0%)
Moderate	8 (8.8%)	2 (2.2%)		10 (11.1%)	3 (9.09%)
Severe	14 (15.5%)	17 (18.8%)		31 (34.4%)	30 (90.9%)
Total	48 (53.3%)	42 (46.6%)		90 (100%)	33 (100%)

SpO₂: Oxygen saturation

Table 3: SpO₂ severity strength of association with multiple variables taken in the study via logistic regression analysis

Variable	Standard error	P value	Odds ratio
Creatinine	1.3665	0.0351*	17.8039
N:L ratio	0.6094	0.0205*	4.1041
CRP	0.068	0.0616	1.1355
LDH	0.0067	0.0321*	1.0146
CK-Nac	0.0067	0.2039	1.0086
Ferritin	0.0107	0.046*	0.9788
TLC	0.1661	0.4791	0.8891

SpO₂: Oxygen saturation, CRP: C-reactive protein, LDH: Lactate dehydrogenase, TLC: Total leukocyte count, N:L ratio: Neutrophil: lymphocyte ratio. *P=0.009

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.⁷ 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.⁸ In 2021, Alroomi et al. showed that ferritin independently inflammatory marker predicts hospitalized severity and mortality of COVID-19 patients in Kuwaiti population.⁹ 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.¹⁰ In our study also, serum ferritin and LDH were good inflammatory markers for mortality in COVID-19 patients. Ahmeidi 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.¹¹ 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. The current study had some limitations, this study was single tertiary healthcare center, with a relatively small sample size of only 90 patients, and unavailability of other inflammatory markers such as interleukin-6, procalcitonin,

Table 4: SpO₂ severity association with LDH level

SpO ₂ level	LDH			Mean	Death
	140–280	>280	Total		
Mild	26 (28.8%)	23 (25.5%)	49 (54.4%)	371	0 (0%)
Moderate	0 (0%)	10 (11.1%)	10 (11.1%)	435	3 (9.09%)
Severe	1 (1.1%)	30 (33.3%)	31 (34.4%)	1432	30 (90.9%)
Total	27 (30%)	63 (70%)	90 (100%)		33 (100%)

The Chi-square statistic is 24.8979. The P<0.00001. The result is significant at P<0.05. SpO₂: Oxygen saturation, LDH: Lactate dehydrogenase

Table 5: SpO₂ severity association with Ferritin level

SpO ₂ level	Ferritin			Mean	Death
	12–300	>300	Total		
Mild	29 (32.2%)	20 (22.2%)	49 (54.4%)	272	0 (0%)
Moderate	1 (1.1%)	9 (10%)	10 (11.1%)	383	3 (9.09%)
Severe	8 (8.8%)	23 (25.5%)	31 (34.4%)	574	30 (90.9%)
Total	38 (42.2%)	52 (57.7%)	90 (100%)		33 (100%)

The Chi-square statistic is 13.459. The P=0.001195. The result is significant at P<0.05. SpO₂: Oxygen saturation

Table 6: SpO₂ severity association with CK-Nac level

SpO ₂ level	CK-Nac			Mean	Death
	<200	>200	Total		
Mild	29 (32.2%)	20 (22.2%)	49 (54.4%)	243	0 (0%)
Moderate	0 (0%)	10 (11.1%)	10 (11.1%)	398	3 (9.09%)
Severe	14 (15.5%)	17 (18.8%)	31 (34.4%)	433	30 (90.9%)
Total	43 (47.7%)	47 (52.2%)	90 (100%)		33 (100%)

The Chi-square statistic is 9.2181. The P=0.009361. The result is significant at P<0.05. SpO₂: Oxygen saturation

Table 7: SpO₂ severity association with TLC level

SpO ₂ level	TLC			Total	Mean	Death
	<4	4–11	>11			
Mild	1 (1.1%)	34 (37.7%)	14 (15.5%)	49 (54.4%)	9	0 (0%)
Moderate	0 (0%)	7 (7.7%)	3 (3.3%)	10 (11.1%)	9.6	3 (9.09%)
Severe	0 (0%)	11 (12.2%)	20 (22.2%)	31 (34.4%)	12.9	30 (90.9%)
Total	1 (1.1%)	52 (57.7%)	37 (41.1%)	90 (100%)		33 (100%)

The Chi-square statistic is 11.7439. The P=0.019361. The result is significant at P<0.05. SpO₂: Oxygen saturation, TLC: Total leukocyte count

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.

ACKNOWLEDGMENT

I thanks to Dean, Dr. P. M. Luka, M.S., Dr. Manoj Kumar Minj, Assistant M.S. Dr. Shobhita K. Mane & all staff in the 100 bedded dedicated COVID MCH Raigarh for their constant support & co-operation to me.

REFERENCES

1. Grasselli G, Pesenti A and Cecconi M. Critical care utilization for the covid-19 outbreak in Lombardy, Italy: Early experience

- and forecast during an emergency response. *JAMA*. 2020;323(16):1545-1546.
<https://doi.org/10.1001/jama.2020.4031>
2. Gao Z, Xu Y, Sun C, Wang X, Guo Y, Qiu S, et al. A systematic review of asymptomatic infections with covid-19. *J Microbiol Immunol Infect*. 2021;54(1):12-16.
<https://doi.org/10.1016/j.jmii.2020.05.001>
 3. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ, et al. COVID-19: Consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020;395(10229):1033-1034.
[https://doi.org/10.1016/S0140-6736\(20\)30628-0](https://doi.org/10.1016/S0140-6736(20)30628-0)
 4. Tay MZ, Poh CM, Renia L, MacAry PA and Ng LF. The trinity of COVID-19: Immunity, inflammation and intervention. *Nat Rev Immunol*. 2020;20(6):363-374.
<https://doi.org/10.1038/s41577-020-0311-8>
 5. Ali N. Elevated level of C-reactive protein may be an early marker to predict risk for severity of covid-19. *J Med Virol*. 2020;92(11):2409-2411.
<https://doi.org/10.1002/jmv.26097>
 6. Henry BM, Aggarwal G, Wong J, Benoit S, Vikse J, Plebani M, et al. Lactate dehydrogenase levels predict coronavirus disease 2019 (covid-19) severity and mortality: A pooled analysis. *Am J Emerg Med*. 2020;38(9):1722-1726.
<https://doi.org/10.1016/j.ajem.2020.05.073>
 7. Liao D, Zhou F, Luo L, Xu M, Wang H, Xia J, et al. Haematological characteristics and risk factors in the classification and prognosis evaluation of COVID-19: A retrospective cohort study. *Lancet Haematol*. 2020;7(9):e671-e678.
[https://doi.org/10.1016/S2352-3026\(20\)30217-9](https://doi.org/10.1016/S2352-3026(20)30217-9)
 8. Yang AP, Liu JP, Tao WQ and Li HM. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. *Int Immunopharmacol*. 2020;84:106504.
<https://doi.org/10.1016/j.intimp.2020.106504>
 9. Alroomi M, Rajan R, Omar AA, Alsaber A, Pan J, Fatemi M, et al. Ferritin level: A predictor of severity and mortality in hospitalized COVID-19 patients. *Immun Infamm Dis*. 2021;9(4):1648-1655.
<https://doi.org/10.1002/iid.3517>
 10. Huang Y, Guo L, Chen J, Wu M, Zhang C, Liu Z, et al. Serum lactate dehydrogenase level as a prognostic factor for COVID-19: A retrospective study based on a large sample size. *Front Med (Lausanne)*. 2022;4(8):671667.
<https://doi.org/10.3389/fmed.2021.671667>
 11. Ahmeidi AA, Musa A, Ahmed HS, Elahmar AA, Goota RB, Ahmed IA, et al. Inflammatory markers as predictors of mortality in COVID-19 infection. *Afr J Lab Med*. 2020;9(1):1298.
<https://doi.org/10.4102/ajlm.v9i1.1298>

Authors contributions:

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.

Work attributed to:

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

Orcid ID:

Pankaj Madhukar Luka - <https://orcid.org/0009-0001-0722-8767>
Ved Prakash Gilley - <https://orcid.org/0009-0006-5590-4746>
Anmol Madhur Minz - <https://orcid.org/0009-0000-7579-2960>
Harish Kumar - <https://orcid.org/0009-0008-4284-9228>
Manoj Kumar Minj - <https://orcid.org/0009-0003-1330-3860>

Source of Support: Nil, **Conflicts of Interest:** None declared.