

Impact of various hematological and biochemical parameters on mortality in coronavirus disease 2019 (COVID-19): A single-center study from North India

Tamoghna Ghosh¹, Tanima Dwivedi², Harsh Agarwal¹, Hariharan Iyer¹, Pawan Tiwari¹, Saurabh Mittal¹, Ritu Gupta², Sushma Bhatnagar³, Saurabh Vig³, Anant Mohan¹

¹Department of Pulmonary, Critical Care and Sleep Medicine, All India Institute of Medical Sciences, New Delhi, India, ²Department of Laboratory Oncology, All India Institute of Medical Sciences, New Delhi, India, ³Department of Onco-Anesthesia and Palliative Medicine, All India Institute of Medical Sciences, New Delhi, India

ABSTRACT

Background: Severe acute respiratory syndrome coronavirus 2 (SARS CoV-2), which causes coronavirus disease 2019 (COVID-19), has rapidly evolved into a pandemic, affecting more than 90 million people and more than 1.9 million deaths worldwide. Despite extensive study, the prognostic role of various hematological and biochemical parameters remains unclear. **Methods:** This study was carried out at a COVID care facility in Delhi. The demographic and clinical information, laboratory parameters (hematological, biochemical, and inflammatory), and the treatment of admitted COVID-19 patients during first wave were collected from electronic medical records and were subsequently analyzed. **Results:** Between March 2020 and November 2020, a total of 5574 patients were admitted to hospital due to COVID-19. Majority (77.2%) were male and had a mean (standard deviation [SD]) age of 38.9 (14.9) years. The mean (SD) duration of hospital stay was significantly higher in nonsurvivors. Out of the entire cohort, 8.7% of the patients had comorbidities, whereas 47.1% of the patients were asymptomatic at presentation. Compared to the survivors, the nonsurvivors had a significantly higher proportion of comorbidities and were more likely to be symptomatic. Patients who died during hospital stay had significantly higher relative neutrophil percent and neutrophil-lymphocyte ratio and lower lymphocyte percent. The patients who died had significantly higher levels of ferritin, D-dimer, and fibrinogen. **Conclusions:** Analysis of various hematological and inflammatory parameters can provide useful prognostic information among COVID-19-affected patients. It can also help in identifying patients who merit aggressive institutional care and thereby potentially mitigate the mortality.

KEY WORDS: Biochemical, biomarkers, coronavirus disease 2019, hematological, inflammatory

Address for correspondence: Dr. Anant Mohan, Department of Pulmonary, Critical Care and Sleep Medicine, All India Institute of Medical Sciences, New Delhi, India. E-mail: anantmohan@yahoo.com

Submitted: 09-Aug-2021 **Accepted:** 07-Oct-2021 **Published:** 20-Apr-2022

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), has rapidly evolved into a pandemic,

affecting more than 194 million people and more than 4.1 million deaths worldwide.^[1] Although mainly characterized as a respiratory tract infection, it is now

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Ghosh T, Dwivedi T, Agarwal H, Iyer H, Tiwari P, Mittal S, *et al.* Impact of various hematological and biochemical parameters on mortality in coronavirus disease 2019 (COVID-19): A single-center study from North India. *Lung India* 2022;39:230-3.

Access this article online	
Quick Response Code: 	Website: www.lungindia.com
	DOI: 10.4103/lungindia.lungindia_480_21

considered a systemic disease due to multiple organ involvement.^[2-4] Although older age and presence of comorbidities constitute an increased risk of death from COVID-19, younger and previously healthy individuals may also develop lethal complications such as disseminated intravascular coagulopathy and fulminant myocarditis.^[5,6]

Although several clinical parameters have been linked with COVID-related outcomes, corresponding information about biochemical parameters is lesser known. Elevation of certain inflammatory markers and cytokines has been associated with poor outcomes in critical COVID-19 disease. However, most data have emerged from relatively smaller studies in intensive care unit settings and in patients with predominantly severe disease. There is limited evidence on the discriminatory ability of initial biochemical parameters between favorable and unfavorable outcomes. This knowledge may help to establish a prediction model based on a combination of routine laboratory tests in COVID-19 patients, thereby providing a simple and feasible approach to predict the outcome of COVID-19 patients in clinical practice.

MATERIALS AND METHODS

Patients

This study was carried out between March 2020 and November 2020 at a 600-bedded dedicated COVID care facility in Delhi state. The demographic and clinical information, laboratory results, and treatment details of COVID-19 patients were collected from electronic medical records. COVID-19 was diagnosed if patients were positive for SARS-CoV-2 by the reverse transcription–polymerase chain reaction or rapid antigen testing method. As a hospital policy, initially all such patients were admitted irrespective of disease severity. The following laboratory parameters were analyzed: (1) hematological (hemoglobin, total leukocytes, neutrophil percent, lymphocyte percent, neutrophil–lymphocyte ratio [NLR], and platelets), (2) biochemical (aspartate aminotransferase, alanine aminotransferase, albumin, bilirubin, alkaline phosphatase [ALP], and creatinine), and (3) inflammatory (fibrinogen, D-dimer, ferritin, and C-reactive protein [CRP]). The laboratory values were compared between patients who recovered and those who succumbed to their illness.

Statistical analysis

The results are presented as mean (standard deviation [SD]) or median (range). Paired *t*-test or Mann–Whitney *U*-test was used to compare the difference of continuous variables. Chi-square test was used for categorical data. Statistical significance was determined as $P < 0.05$. Data were analyzed using StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX, USA: StataCorp LP.

RESULTS

During the period from March 2020 and November 2020, 5574 patients with COVID-19 were admitted with a mean (SD) age of 38.9 (14.9) years and including 77.2% of males. The mean (SD) duration of hospital stay was 10.9 (2.4) days. Among the total group, 142 (2.5%) patients died in hospital and the remaining 5432 (97.5%) were discharged. The demographic and clinical characteristics of survivors and nonsurvivors are shown in Table 1. The nonsurvivors had a significantly longer duration of hospital stay than survivors (12.2 [5.6] days vs. 10.9 [1.2] days, respectively; $P = 0.03$). Of the total cohort, 8.7% had comorbidities (10.1% diabetes and 8.3% hypertension being the most common), and 47.1% of the patients were asymptomatic at the time of admission. The patients who died had a significantly higher proportion of comorbidities and were more likely to be initially symptomatic. These are highlighted in Table 1.

Compared to patients who recovered, those who died in hospital had significant neutrophilia, lymphopenia, and higher values of NLR. No difference was found among the two groups in hemoglobin and platelet counts [Table 2].

There was no statistically significant difference in bilirubin, serum glutamic-oxaloacetic transaminase, serum glutamic-pyruvic transaminase, serum albumin, ALP, urea, and creatinine between the two groups [Table 2].

The patients who died had significantly higher baseline levels of ferritin, D-dimer, and fibrinogen. However, no significant difference was found with regard to CRP [Table 2].

DISCUSSION

In this large observational study, we found that significant differences in several clinical, hematological, and inflammatory parameters between survivors and nonsurvivors of COVID-19. Nonsurvivors were more likely to be initially symptomatic, have comorbidities, and have a longer hospital stay than the survivors. They also have a more severe inflammatory response in the form of higher total leukocyte count, neutrophil percent, NLR, ferritin, D-dimer, and fibrinogen compared to survivors.

Several previous studies have identified clinical predictors of poor outcome in COVID-19,^[7-9] although the prognostic contribution of laboratory parameters has been less reported. A few recent studies have shown that NLR is a useful parameter to distinguish severe from nonsevere cases and also to predict mortality, and an NLR value of more than 3.1 in patients aged more than 50 years predicted a higher chance of developing critical illness.^[10,11] In our study, the mean NLR among survivors and nonsurvivors was 2.13 and 3.51 and 2.13, respectively. There is also some evidence to suggest that serial measurement of NLR

Table 1: Baseline characteristics and comparison between the two groups (n=5574)

Parameters	Discharged, n (%)	Dead, n (%)	P
Number of patients	5432 (97.5)	142 (2.5)	-
Gender			
Male	4196 (77.2)	111 (72.1)	0.09
Female	1236 (22.8)	31 (27.9)	
Age, mean (SD)	38.9 (10.71)	39.6 (48.8)	0.63
Number of days of hospital stay, mean (SD)	10.9 (1.2)	12.2 (5.6)	0.03*
Patients with comorbidities	476/5432 (8.8)	11/117 (9.4)	0.03*
Asymptomatic at presentation	2593/5432 (47.7)	38/142 (26.8)	0.02*

*P<0.05; all values expressed as n (%) or mean (SD). SD: Standard deviation

Table 2: Laboratory parameters among COVID survivors and nonsurvivors

Biomarkers	Survivors, mean (SD)	Nonsurvivors, mean (SD)	P
Hematological markers			
Hemoglobin (grams per deciliter)	13.29 (3.18) n=5218	13.36 (1.69) n=142	0.47
Platelet count (platelets per microliter)	218514 (113137) n=4676	228115 (31820) n=131	0.06
Total leukocyte count (WBCs per microliter)	6252 (5315) n=4666	6625 (3758) n=131	0.04*
Relative neutrophil percent	55.6 (1.8) n=4133	58.8 (11.9) n=102	0.04*
Relative lymphocyte percent	30.9 (7.4) n=4133	28.0 (9.5) n=102	0.04*
Neutrophil-lymphocyte ratio	2.13 (0.26) n=4133	3.51 (6.60) n=102	0.03*
Biochemical markers			
Bilirubin (mg/dL)	1.1 (0.06) n=4699	0.71 (0.08) n=130	0.70
SGOT (IU/L)	45.2 (12.7) n=4690	45.8 (10.6) n=130	0.47
SGPT (IU/L)	49.8 (17.8) n=4692	47.3 (19.8) n=130	0.75
Serum albumin (grams per deciliter)	4.7 (0.6) n=4653	4.3 (0.07) n=127	0.37
Alkaline phosphatase (IU/L)	96.7 (20.1) n=4681	96.2 (24.7) n=130	0.11
Urea (mg/dL)	23.1 (9.9) n=4690	24.6 (7.6) n=130	0.26
Creatinine (mg/dL)	0.81 (0.58) n=4686	0.83 (0.36) n=128	0.07
Inflammatory markers			
Ferritin (micrograms per liter)	198.9 (205.1) n=2358	329.1 (381.2) n=53	0.01*
D-dimer (ng/mL)	165.4 (196.6) n=3050	333.3 (523.5) n=53	0.005*
C-reactive protein (milligram per liter)	1.99 (1.16) n=3096	2.72 (0.63) n=50	0.10
Fibrinogen (mg/dL)	334.3 (96.2) n=2912	371.2 (92.2) n=55	0.001*

*P<0.05; all values expressed as mean (SD). n=Number of patients whose data is available for that parameter, SD: Standard deviation, SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamic-pyruvic transaminase

could be more useful and may show a good correlation with other inflammatory markers.^[12] Similarly, lymphopenia and neutrophilia have also been correlated with adverse outcomes in COVID-19, including death and development of acute respiratory distress syndrome. Although the effects of SARS-CoV on hematopoiesis are still being explored, it has been proposed that the virus-mediated

infection leads to consumption of T-lymphocyte cells, particularly the CD4 and CD8 T-cells, thereby leading to lymphopenia.^[13] A meta-analysis has found that thrombocytopenia is significantly associated with disease severity and mortality in COVID-19. The possible reason may be that virus-mediated endothelial damage leads to platelet activation and microthrombus formation in the pulmonary vasculature thereby causing increased platelet consumption.^[14] However, we found no significant difference in the platelet count between the survivors and nonsurvivors.

We also did not find any significant difference in the liver and renal functions or other biochemical parameters between the two groups. A few studies have reported that the serum albumin level is lower in severe and critically ill patients and may be an independent factor associated with mortality.^[15,16] Among our patients, the mean albumin in the nonsurvivor group was lower than that of the other, although not statistically. A possible explanation for this fact might be the missing data. A possible explanation for this fact might be that we did not have data for 15 patients in the nonsurvivor group.

D-dimer is an indicator of activation of the coagulation cascade and the fibrinolytic system.^[17,18] This activation of coagulation cascade is postulated to be due to the viremia, accentuated cytokine levels, infection, and organ dysfunction.^[19] Elevated levels of D-dimer and fibrinogen have been associated with severity of COVID-19, higher need for critical care as well as mortality. An elevated D-dimer level above 1 µg/mL on admission was shown to have increased mortality with an odds ratio of 18.42.^[19,20] This can also possibly explain the higher incidence of venous thromboembolism seen in COVID-19 patients. These findings were replicated in our cohort as well. The mean D-dimer and fibrinogen levels on admission were significantly higher in the nonsurvivor group. Possibly, such patients with elevated D-dimer could have had a higher incidence of pulmonary thromboembolism leading to higher mortality, although this was not specifically the focus of this study.

This study has some limitations; first, it was retrospective in nature, and laboratory data were not available for many patients. Second, we collected and analyzed only a single time point laboratory data and thereby were unable to

provide information on particular trends of any parameter. Third, due to the existing hospital policy of admitting all COVID patients, the numbers in the survivor and nonsurvivor groups were vastly different, which could have been a source of bias. On the other hand, this study had a large patient number base and collected information on a comprehensive panel of hematological, biochemical, and inflammatory parameters at baseline. As a result, these findings could be potentially useful in a resource-limited setting in enabling triage of patients at baseline and thereby identify the at-risk group.

CONCLUSIONS

Various biochemical parameters measured at baseline can provide useful prognostic information among COVID-19-affected patients. It can also help in early identification of patients who merit aggressive institutional care, thereby potentially mitigating mortality.

Acknowledgments

The authors express their sincere gratitude to the Departments of Onco-Anesthesia, Hospital Administration, Laboratory Oncology, and Data Entry Staff of Pulmonary, Critical Care, and Sleep Medicine, All India Institute of Medical Sciences, New Delhi, India, for their assistance in procuring the clinical and laboratory details and preparing the raw data.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- COVID Live Update: 194,434,019 Cases and 4,168,834 Deaths from the Coronavirus – Worldometer. Available from: <https://www.worldometers.info/coronavirus/>. [Last accessed on 2021 Jul 25].
- Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, *et al.* Cardiovascular considerations for patients, health care workers, and health systems during the COVID-19 pandemic. *J Am Coll Cardiol* 2020;75:2352-71.
- Bangash MN, Patel J, Parekh D. COVID-19 and the liver: Little cause for concern. *Lancet Gastroenterol Hepatol* 2020;5:529-30.
- Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ, *et al.* COVID-19: Consider cytokine storm syndromes and immunosuppression. *Lancet* 2020;395:1033-4.
- Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Thromb Haemost* 2020;18:844-7.
- Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential effects of coronaviruses on the cardiovascular system: A review. *JAMA Cardiol* 2020;5:831-40.
- Ciceri F, Castagna A, Rovere-Querini P, De Cobelli F, Ruggeri A, Galli L, *et al.* Early predictors of clinical outcomes of COVID-19 outbreak in Milan, Italy. *Clin Immunol* 2020;217:108509.
- Mudatsir M, Fajar JK, Wulandari L, Soegiarto G, Ilmawan M, Purnamasari Y, *et al.* Predictors of COVID-19 severity: A systematic review and meta-analysis. *F1000Res* 2020;9:1107.
- Soylu K, Gedikli Ö, Ekşi A, Avcioğlu Y, Soylu Aİ, Yüksel S, *et al.* Neutrophil-to-lymphocyte ratio for the assessment of hospital mortality in patients with acute pulmonary embolism. *Arch Med Sci* 2016;12:95-100.
- Zeng ZY, Feng SD, Chen GP, Wu JN. Predictive value of the neutrophil to lymphocyte ratio for disease deterioration and serious adverse outcomes in patients with COVID-19: A prospective cohort study. *BMC Infect Dis* 2021;21:80.
- Liu J, Liu Y, Xiang P, Pu L, Xiong H, Li C, *et al.* Neutrophil-to-lymphocyte ratio predicts critical illness patients with 2019 coronavirus disease in the early stage. *J Transl Med* 2020;18:206.
- Ye W, Chen G, Li X, Lan X, Ji C, Hou M, *et al.* Dynamic changes of D-dimer and neutrophil-lymphocyte count ratio as prognostic biomarkers in COVID-19. *Respir Res* 2020;21:169.
- Liu X, Zhang R, He G. Hematological findings in coronavirus disease 2019: Indications of progression of disease. *Ann Hematol* 2020;99:1421-8.
- Lippi G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis. *Clin Chim Acta* 2020;506:145-8.
- Yuan X, Huang W, Ye B, Chen C, Huang R, Wu F, *et al.* Changes of hematological and immunological parameters in COVID-19 patients. *Int J Hematol* 2020;112:553-9.
- Salinas M, Blasco Á, Santo-Quiles A, Lopez-Garrigos M, Flores E, Leiva-Salinas C. Laboratory parameters in patients with COVID-19 on first emergency admission is different in non-survivors: Albumin and lactate dehydrogenase as risk factors. *J Clin Pathol* 2021;74:673-5.
- Wu Y. Compensation of ACE2 function for possible clinical management of 2019-nCoV-induced acute lung injury. *Virology* 2020;35:256-8.
- Gaffney PJ. Breakdown products of fibrin and fibrinogen: Molecular mechanisms and clinical implications. *J Clin Pathol Suppl (R Coll Pathol)* 1980;14:10-7.
- Wool GD, Miller JL. The impact of COVID-19 disease on platelets and coagulation. *Pathobiology* 2021;88:15-27.
- Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, *et al.* Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. *Lancet* 2020;395:1054-62.