

Altered Hematological Profile: The Forerunner of Fatalities Caused by COVID-19

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Abstract

Background: Being a systemic infection, coronavirus disease 2019 (COVID-19) affects hematologic system, along with cardiovascular, pulmonary, gastrointestinal, and neurological systems, resulting in altered hematological parameters. These altered hematological findings are thought to have a role in early risk stratification and prognostication of COVID-19 patients. However, the data on hematological abnormalities associated with the disease among Eastern Indian COVID-19 patients, particularly the Bengalis, are limited. **Aim:** The aim is to study the association, if any, between various hematological parameters and disease severity of COVID-19. **Materials and Methods:** The study was a cross-sectional study involving 145 laboratory-confirmed cases of SARS-CoV-2 infection. Based on the disease severity, the patients were divided into three groups: mild, moderate, and severe. Various hematological parameters were analyzed. **Results:** Of the 145 patients, 82.8%, 9.6%, and 7.5% of the cases were in the mild, moderate, and severe groups, respectively. The mean age was 48 years. The result of our study showed that the age of the patients is directly proportional to the severity of the illness. About 62.1% of the patients were male, whereas the rest (37.9%) were female. Our study showed an independent association of Covid severity with male gender. Although mean total leukocyte count (TLC), absolute count of neutrophil, lymphocyte, eosinophil, neutrophil–lymphocyte ratio (NLR), neutrophil–monocyte ratio (NMR), lymphocyte–monocyte ratio, platelet–lymphocyte ratio, and systemic inflammatory index among mild, moderate, and severe COVID-19 cases were statistically significant ($P < 0.05$), basophil, monocyte, and platelet count were statistically insignificant among the three groups. Nearly all of the hematological parameters could be used as potential diagnostic biomarkers for subsequent analysis because their area under the curve was higher than 0.50. **Conclusion:** Severity of COVID-19 is associated with older age, male sex, higher TLC, neutrophilia, lymphopenia, eosinopenia, high NLR, and high NMR. As complete blood count is an inexpensive routine blood investigation, it can be very useful in a resource-poor healthcare facility, which is unable to provide high-end investigations.

Keywords: Covid severity, hematological profile, predictive markers

INTRODUCTION

The most discussed health issue of the recent times, without any doubt, is COVID-19. COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) created the recent pandemic shattering the whole world. Though primarily a respiratory disease, it can cause various non-respiratory manifestations, such as gastrointestinal, neurological, renal, and cardiovascular symptoms.^[1] Mostly the patients with SARS-CoV-2 infection have mild symptoms (such as fever, dry cough, dyspnea), but the disease can rapidly progress into acute respiratory distress syndrome, bleeding, coagulation dysfunction, metabolic acidosis, septic shock, and death in severe cases.^[2] The older patients and those with

underlying medical conditions are mainly prone to develop severe respiratory distress syndrome.^[3] Considering the short time of onset of acute respiratory distress syndrome after admission to hospital and the high mortality rates in COVID-19, early diagnosis and predicting the prognosis are vital.^[4] Laboratory findings and their association with disease outcomes can provide valuable knowledge during the emergence of a novel infectious disease like

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COVID-19.^[5] Despite being the gold standard, real-time polymerase chain reaction (RT-PCR) test for the detection of COVID-19 in nasal and throat swabs has its own limitations, especially in resource-limited settings. Use of RT-PCR in mass screening in a situation in which the virus is rapidly spreading is limited by testing capacity, high false negativity, the requirement of qualified personnel, high cost, and delayed results.^[6] So, many studies investigating the hematological and chemical parameters in patients with COVID-19 are emerging nowadays in order to identify common patterns and biomarkers seen in this disease.^[7,8] The association of hematological abnormalities in severe COVID-19 pneumonia is related with disease progression, severity, and mortality. Some of the well-documented features in COVID-19 patients are lymphopenia, thrombocytopenia, abnormal coagulation profile, and sepsis, leading to disseminated intravascular coagulation.^[9] Herein we performed a retrospective study of COVID-19 patients in the designated hospital in West Bengal, and the correlation between hematological parameters and different severity groups of COVID-19 was analyzed.

MATERIALS AND METHODS

This study was conducted as a retrospective, observational, single center study, including all the admitted COVID-19-positive patients only. In this study, complete medical data of 145 hospitalized cases were collected between May 23, 2021 and July 13, 2021 from the Department of Pathology, DM Medical College and Hospital, Purulia, West Bengal, India. The subjects were chosen from the population of patients by simple random sampling. Necessary approvals and consent from patients and the Institutional Ethics Committee were taken. Patients were then divided into three groups on the basis of the clinical severity. Group I included asymptomatic and mild cases (partial pressure of oxygen in artery [SpO_2] $>95\%$, respiratory rate [RR] $<24/\text{min}$), group II included moderate cases (SpO_2 $95\text{--}90\%$, RR $24\text{--}30/\text{min}$), and group III included patients suffering from severe COVID-19 (SpO_2 $<90\%$, RR $>30/\text{min}$).

Inclusion criteria

The inclusion criteria include SARS-CoV-2-infected patients using RT-PCR.

Exclusion criteria

Patients suffering from hematological malignancies and immunodeficient states not including diabetes mellitus are excluded.

Blood examinations involved measuring complete blood count. To understand the relation with disease severity, inflammatory factors, including the NLR (absolute neutrophil count/absolute lymphocyte count), NMR (absolute neutrophil count/absolute monocyte count), PLR (absolute platelet count/absolute lymphocyte count), LMR (absolute lymphocyte count/absolute monocyte count), MPV (mean platelet volume), plateletcrit, and systemic inflammatory index (SII) (platelet $\times$ neutrophil/lymphocyte), were used in this analysis.

Ethical approval

The study was conducted according to the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients' verbal and analytical approval before samples were taken. The study protocol and the subject information and the consent form were reviewed and approved by the Institutional Ethics Committee (letter no. PMC/ME/PR/1115 dated: September 15, 2021).

Statistical analysis

Categorical data were described as percentages and continuous data as means (SDs). The data were analyzed using IBM SPSS for Windows 25.0 (IBM Corp., Armonk, NY, USA). The significance between the two groups was tested by Student's *t*-test. Statistical significance was accepted as $P < 0.05$.

No funding was required for this study, and none of the authors has any conflicts of interest to declare.

RESULTS

Among 145 patients included in this study, 90 patients (62.1%) were males and 55 patients (37.9%) were females [Table 1]. Mild, moderate, and severe groups included 120 (82.8%), 14 (9.7%), and 11 (7.5%) patients, respectively. The mean age of patients in mild, moderate, and severe groups was 40.5 ± 10.3 , 48 ± 6.7 , and 60.5 ± 12.3 , respectively (P -value = 0.001). Among males, 70 (77.8%) patients suffered from mild, 12 (13.3%) patients suffered

Table 1: Demographic characteristics of the Covid patients of different severities

	Mild	Moderate	Severe	Total	P-value
Age (years) [mean $\pm$ SD]	40.5 ± 10.3	48 ± 6.7	60.5 ± 12.3		0.001
Sex					
Male	70 (77.8%)	12 (13.3%)	8 (8.9%)	90 (62.1%)	0.002
Female	50 (90.9%)	2 (3.6%)	3 (5.5%)	55 (37.9%)	
Total	120	14	11	145	

from moderate, and 8 (8.9%) patients suffered from severe COVID-19. Among females, 50 patients (90.9%) were either asymptomatic or had mild symptoms. Two (3.6%) patients presented with moderate illness, whereas only 3 (5.5%) patients developed severe COVID-19 manifestations (P -value = 0.002) [Table 1].

The statistical analysis of total leukocyte count (TLC) and differential leukocyte count has been presented in Table 2. Mean TLC in the mild group was $7.2 \times 10^9/L$, in the moderate group was $11.5 \times 10^9/L$, and in the severe group, it was $13.8 \times 10^9/L$ ($P < 0.05$). Absolute counts for neutrophil, lymphocyte, and eosinophil among the three groups suggested significant statistical differences with $P < 0.05$ for each test category. However, the basophil differential count was statistically insignificant ($P = 0.11$) [Table 2]. The mean NLR for patients in the mild group was 3.2, for the moderate group, it was 5.9, whereas for the group of severe patients, it was 9.2. The mean NMR (neutrophil/monocyte ratio) of the three groups were 16.9, 22.1, and 23.0, respectively whereas their mean LMR was 5.2, 3.7, and 2.5, and these values are statistically significant with P -value < 0.05 . Except for platelet, monocyte, and basophil count, all of the indices showed a statistically significant difference in terms of severity of the disease between the three groups. The plateletcrit was found to be significantly higher in the severe group when compared with all of the patients in the current study. Significantly higher SII values were observed in the severe disease group. Nearly all of the hematological parameters could be used as potential diagnostic biomarkers for subsequent analysis because their area under the curve was higher than 0.50.

DISCUSSION

The result of our study showed that the mean age of the patients was 48 years and the age of the patient is directly proportional to the severity of the illness. This finding is

similar to many other studies showing elderly COVID-19 patients with poorer outcome.^[10] Eight out of 11 (72.7%) severe cases were males in our study, which is also close to the result of some studies that showed an independent association of Covid severity with male gender.^[11]

One easily performed and inexpensive routine laboratory investigation is complete blood count (CBC). We, in this study, investigated the ability of CBC to predict the progression of severe disease in COVID-19 patients. We calculated certain ratios from the hemocyte counts in CBC such as NLR, PLR, NMR, LMR, and SII and tried to find out their roles as predictive markers for disease progression. Their roles as inflammatory markers were found in other studies.^[12]

In our study, increased TLC and absolute neutrophil count were more commonly seen in patients having severe COVID-19 as reported by Yuan *et al.*^[13] in their study. We found lymphopenia to be strongly associated with severe illness as found in a study by Tan *et al.*^[14] Monocyte and basophil counts in our study were unrelated to the severity of COVID-19. Our study did not show significant association of platelet count with the severity of disease, whereas Liao *et al.*^[15] found significantly lower platelet count in patients with critical and severe diseases. Fan *et al.*^[16] in one-fifth of their study cases, found mild thrombocytopenia and leukopenia (white blood cells $\leq 4 \times 10^9/L$) in almost 19% of the total cases.

We found that patients with severe symptoms had a higher NLR than patients with mild-to-moderate symptoms and our finding corroborates with the finding of Liao *et al.*^[15] Yang *et al.*^[17] also concluded that high neutrophil to lymphocyte ratio and age are the independent factors for predicting poor clinical outcomes of COVID-19 patients. Like NLR, NMR, LMR, and PLR were found to be positively correlated with COVID-19 disease severity in

Table 2: Hematological profile of the Covid patients of different severities

Hematological parameters	Mild	Moderate	Severe	P-value	AUC (area under the curve)
TLC ($\times 10^9/L$)	7.2	11.5	13.8	< 0.05	0.668
Neutrophil ($\times 10^9/L$)	7.1	7.7	9.2	< 0.05	0.712
Lymphocyte ($\times 10^9/L$)	2.2	1.3	1.0	< 0.05	0.651
Monocyte ($\times 10^9/L$)	0.42	0.35	0.40	0.40	0.455
Eosinophil ($\times 10^9/L$)	0.31	0.42	0.54	< 0.05	0.552
Basophil ($\times 10^9/L$)	0.02	0.01	0.01	0.11	0.495
NLR	3.2	5.9	9.2	< 0.05	0.757
NMR	16.9	22.1	23	< 0.05	0.657
LMR	5.2	3.7	2.5	< 0.001	0.673
Platelet count ($\times 10^9/L$)	255	200	180	0.9	0.457
PLR	115.9	153.8	180.2	< 0.001	0.662
SII	822.9	465.6	1.759	< 0.001	0.753
Plateletcrit (%)	0.22	0.20	0.25	0.02	0.556
MPV (fL)	7.5	8.2	8.8	0.03	0.584

TLC: total leukocyte count, MPV: mean platelet volume, NLR: neutrophil-lymphocyte ratio, NMR: neutrophil-monocyte ratio, PLR: platelet-lymphocyte ratio, LMR, lymphocyte-monocyte ratio, MPVLR: MPV-lymphocyte ratio, SII: systemic inflammation index

our study. Compared with non-severe patients, higher PLR levels in severe COVID-19 patients have been shown in some recent studies.^[18]

The plateletcrit was found to be significantly higher in the severe group (P -value = 0.02) when compared with all of the patients in the current study, and the result was not surprising considering the studies showing increased plateletcrit in active inflammation. A new parameter with prognostic value in COVID-19 patients, known as SII, has emerged in recent studies. SII combines three separate hematological parameters: the neutrophil, lymphocyte, and platelet counts. It was used for the prediction of recurrency and survival in many solid tumors as a systemic inflammatory indicator in some studies.^[19] We found in the current study significantly higher SII values in the severe disease group.

However, this study is not free of limitations. Ours was a retrospective single center study without external validation in large sample and multicenter studies. Some of the patients included were still hospitalized during the study period. Furthermore, the biochemical parameters and coagulation profile were not included in this study.

CONCLUSION

Early diagnosis and warning of disease progression establishes an effective treatment strategy for severe and critical patients and helps in reducing the overall mortality of patients with COVID-19. Our findings concluded that almost all the leucocyte parameters and certain ratios derived from them such as NLR, PLR, etc. may be used as an effective biomarker in predicting the fatality of COVID-19. As CBC is an inexpensive routine blood investigation, it can be very useful in a resource-poor healthcare facility unable to provide high-end investigations. However, future studies are needed to evaluate these biomarkers and optimal cutoffs as our study is retrospective and requires further data.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Vetter P, Vu DL, L'Huillier AG, Schibler M, Kaiser L, Jacquierioz F. Clinical features of Covid-19. *Br Med J* 2020;369:m1470.

- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497-506.
- Lu R, Yu X, Wang W, Duan X, Zhang L, Zhou W, *et al.* Characterization of human coronavirus etiology in Chinese adults with acute upper respiratory tract infection by real-time RT-PCR assays. *PLoS One* 2012;7:e38638.
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:496.
- Mousavi SA, Rad S, Rostami T, Rostami M, Mousavi SA, Mirhoseini SA, *et al.* Hematologic predictors of mortality in hospitalized patients with COVID-19: A comparative study. *Hematology* 2020;25:383-8.
- Antonio Russo CM, Starace M, Astorri R, Calò F, Coppola N. Current status of laboratory diagnosis for COVID-19: A narrative review. *Infect Drug Resist* 2020;13:2657-65.
- Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): A meta-analysis. *Clin Chem Lab Med* 2020;58:1021-8.
- Fan BE. Hematologic parameters in patients with COVID-19 infection: A reply. *Am J Hematol* 2020;95:E215.
- Lillicrap D. Disseminated intravascular coagulation in patients with 2019-nCoV pneumonia. *J Thromb Haemostasis* 2020;18:786.
- Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. *J Infect* 2020;80:e14-8.
- Palaodimos L, Kokkinidis DG, Li W, Karamanis D, Ognibene J, Arora S, *et al.* Severe obesity, increasing age and male sex are independently associated with worse in-hospital outcomes, and higher in-hospital mortality, in a cohort of patients with COVID-19 in the Bronx, New York. *Metabolism* 2020;108:154262.
- Liu J, Li S, Zhang S, Liu Y, Ma L, Zhu J, *et al.* Systemic immune-inflammation index, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio can predict clinical outcomes in patients with metastatic non-small-cell lung cancer treated with nivolumab. *J Clin Lab Anal* 2019;33:e22964.
- Yuan J, Zou R, Zeng L, Kou S, Lan J, Li X, *et al.* The correlation between viral clearance and biochemical outcomes of 94 COVID19 infected discharged patients. *Inflamm Res* 2020;69:599-606.
- Tan L, Wang Q, Zhang D, Ding J, Huang Q, Tang YQ, *et al.* Lymphopenia predicts disease severity of COVID-19: A descriptive and predictive study. *Signal Transduct Target Ther* 2020;5:33.
- 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:e671-8.
- Fan BE, Chong VCL, Chan SSW, Lim GH, Lim KGE, Tan GB, *et al.* Hematologic parameters in patients with COVID-19 infection. *Am J Hematol* 2020;95:E131-4.
- Yang AP, Liu JP, Tao WQ, Li HM. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. *Int Immunopharmacol* 2020;84:106504.
- Shi C, Pamer EG. Monocyte recruitment during infection and inflammation. *Nat Rev Immunol* 2011;11:762-74.
- Imamoglu GI, Eren T, Baylan B, Karacın C. May high levels of systemic immune-inflammation index and hematologic inflammation markers suggest a further stage in testicular tumours? *Urol Int* 2019;103:303-10.