White Blood Cell Parameters in Patients Diagnosed with COVID-19

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Original Research Article

ABSTRACT

Aim: The SARS-CoV-2 virus has been a major health concern in recent times, causing a large number of deaths globally. It primarily effects the respiratory and immune system. The present study aimed at analysing the effect of this virus on the white blood cell (WBC) parameters.
Study Design: Retrospective record-based study.
Place and duration of study: The study was conducted at Lok Nayak Hospital, Delhi. It was one of the largest COVID designated hospitals in India during the COVID pandemic. A total of 200 patients admitted to Lok Nayak Hospital during the COVID wave in April-May 2021 and the COVID wave in January-February 2022 were randomly included in the study.

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Methodology: The cases were grouped into intensive care unit (ICU) patients and non-ICU patients to compare the association of severity of disease with the WBC parameters.

Results: Patients infected with COVID-19 requiring hospital admission showed leucocytosis in the present study. It was noted that the patients requiring critical care had a significantly higher total leucocyte count (TLC), absolute neutrophil count (ANC), neutrophil lymphocyte ratio (NLR) and neutrophil monocyte ratio (NMR). Though no statistically significant association was noted between absolute lymphocyte count (ALC) and the severity of infection, the ALC was markedly reduced in ICU patients as compared to non-ICU patients (p-value= 0.057).

Conclusion: WBC parameters TLC, ANC, NLR and NMR show significant correlation with severity of COVID-19 infection. These basic haematological parameters can be used to assess severity of COVID-19 infection and treatment response in resource limited conditions.

1. INTRODUCTION

The novel SARS-CoV-2 or COVID-19 is an enveloped RNA virus. Patients infected with COVID-19 present with fever, dry cough and fatigue. Patients with severe illness may require intensive care. These patients may develop acute respiratory distress syndrome and septic shock as described in a study by Zhu B et al. [1]. According to WHO, over 400,000 deaths have been reported due to COVID-19 in India till date [2]. The haematological profile of patients infected with this virus is known to change with the severity of infection. Early defence against the COVID infection commonly involves neutrophils. With increase in severity of infection, there is excessive degranulation of neutrophils leading to a cytokine storm [3]. In a study by Mardani et al, lymphopenia was noted in patients diagnosed with COVID-19 requiring critical care [4].

The present study was conducted at Lok Nayak Hospital, Delhi. The aim of the study was to evaluate the use of commonly used haematology parameters in assessing the severity of the disease in COVID infection.

2. MATERIALS AND METHODS

Patients diagnosed with COVID-19, admitted to a tertiary care hospital in Delhi during the period of study from 15 April to 15 May 2021 and from 4 January to 4 February 2022 were included in the study. Hundred cases were selected randomly from each COVID wave and were included in the two groups.

Patients were categorized into two groups, ICU and non-ICU cases. The peripheral blood samples of these patients had been sent to the Department of Clinical Pathology during their course of hospital stay. All safety precautions had been taken during phlebotomy, sample processing and proper disposal of blood samples. The white blood cell parameters of patients with severe illness requiring intensive care were compared to the patients admitted in the ward with moderate illness. White blood cell parameters included from automated haematology analyser Mindray BC-6200 and Sysmex XT-2000i were total leucocyte count, percentage and absolute counts of neutrophils, lymphocytes, eosinophils, and basophils. The highest absolute neutrophil count was considered for each patient during their period of hospital admission. Neutrophil lymphocyte ratio (NLR) and neutrophil monocyte ratio (NMR) were calculated from the data collected. Data was compiled in Excel and analysed in SPSS version 25 software. The nominal variables were expressed as mean and the continuous variable were expressed as percentage and proportions. Categorical variables were compared using Chi-square test. Statistical analysis of quantitative variables was done using student's t-test. p values < 0.05 were considered statistically significant.

3. RESULTS

A total of 200 patients diagnosed with COVID were randomly selected and included in the study. The total cases included in the present study were divided into ICU and non-ICU groups (Table 1).

Out of a total of 200 cases included in the study, it was found that 119 patients (59.5%) were males and 81 were females (40.5%). Of the 103 patients in the ward, 56 (54%) were males. However, among the patients requiring critical care, 63 patients (65%) were males. Thus, a higher percentage of patients requiring critical care were males.

The mean TLC was found to be higher than the normal range followed in our laboratory (4000-10,000 cells/mm^3)[5]. The TLC was compared in the two groups. It was found to be significantly higher in the ICU patients(Table 1)(Fig. 1).

The mean percentage of polymorphs was found to be higher than the normal range of percentage of neutrophils (40-80%) [5]. The mean percentage of polymorphs was compared in the two groups. It was found to be significantly higher in the ICU patients(Table 1)(Fig. 2).

The mean ANC of the two groups was analysed. It was found to be higher than the normal range of ANC (2000-7000 cells/mm^3)[5]. The ANC was compared in the two groups and was found to be significantly higher in the ICU patients (Fig. 3) (Table 1).

The mean ALC of the two groups was analysed. It was compared in the two groups. The ALC was found to be markedly reduced in ICU patients as compared to the non-ICU patients. (p-value= 0.057).

The mean NLR was found to be higher than normal range of neutrophil lymphocyte ratio (NLR) (1.6-3.5)[6]. The NLR was compared in the two groups and found to be significantly higher in the ICU patients (Table 1) (Fig. 4).

Table 1. White blood cell parameters in the ward and ICU patients

| Parameter	ICU n=97 Mean (SD)	Ward n=103 Mean (SD)	P-value
TLC	13409.814(11842.722)	10139.876(5606.651)	0.013
Polymorphs%	88.027(10.740)	82.673(10.249)	0.000
Lymphocytes%	8.885(7.602)	14.028(8.818)	0.000
Monocytes%	1.776(1.640)	2.452(1.624)	0.004
Eosinophils%	0.748(1.931)	0.794(1.931)	0.850
ANC	11989.241(10902.980)	8587.024(5223.508)	0.005
ALC	975.970(1168.565)	1264.969(958.084)	0.057
AMC	196.801(219.213)	223.535(175.838)	0.341
AEC	58.621(142.893)	60.492(97.249)	0.913
NLR	19.916(19.236)	10.253(9.724)	0.000
NMR	122.089(143.725)	57.056(57.784)	0.000
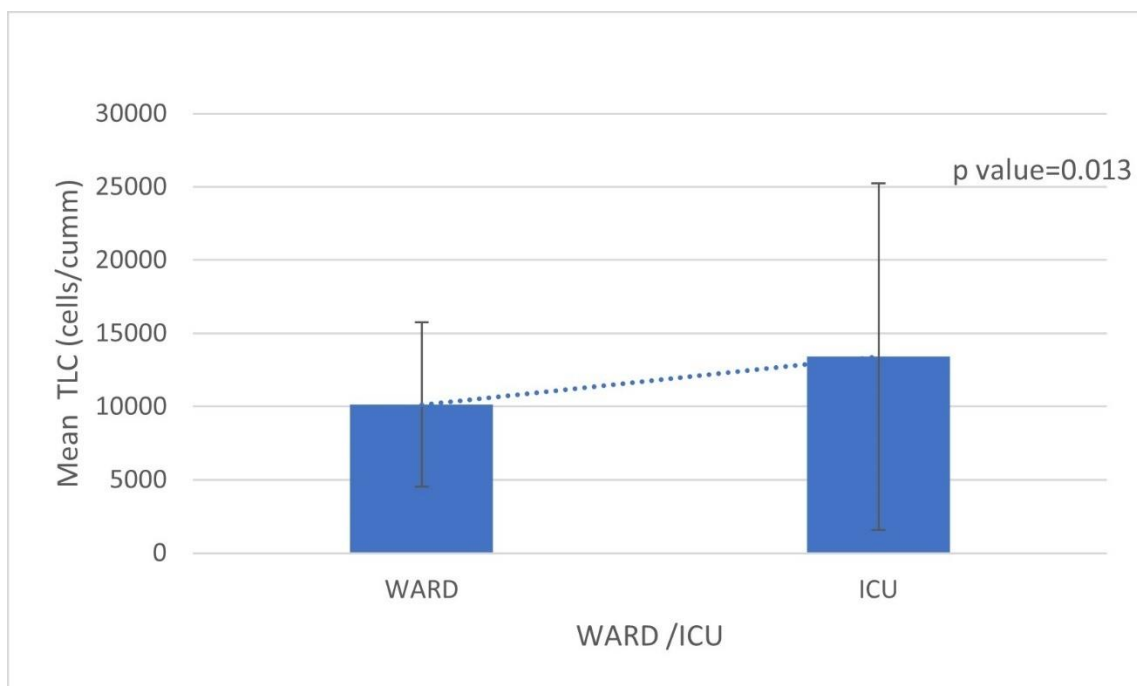
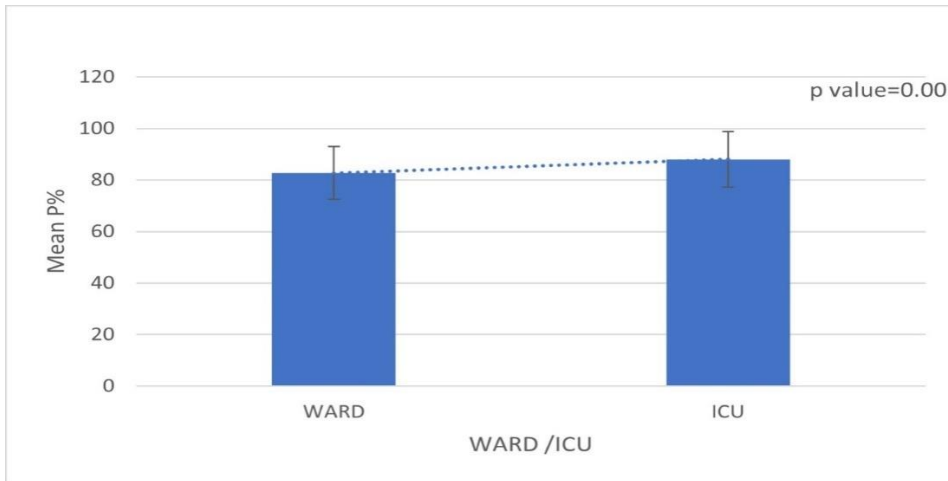**Fig. 1. Mean TLC in ward and ICU patients**

Fig. 2. Mean percentage of polymorphs in ward and ICU patients

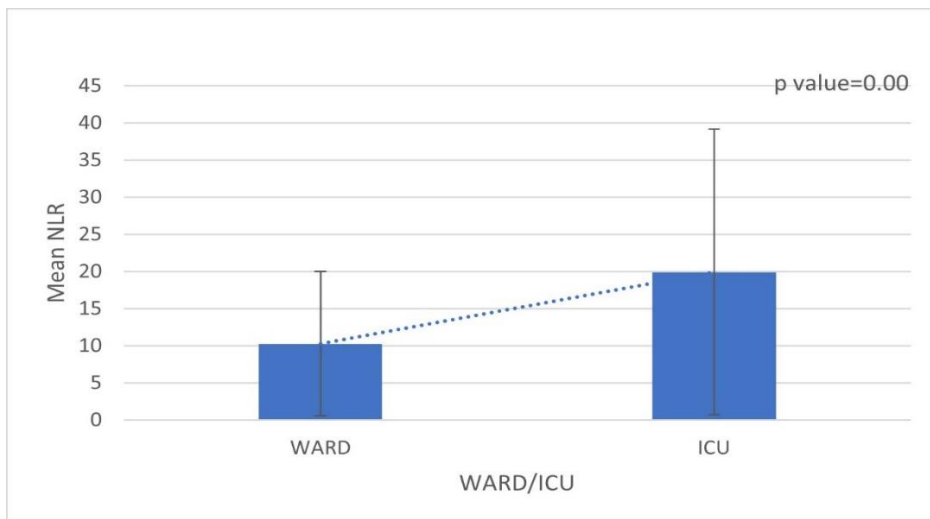**Fig. 3.Mean ANC in ward and ICU patients**
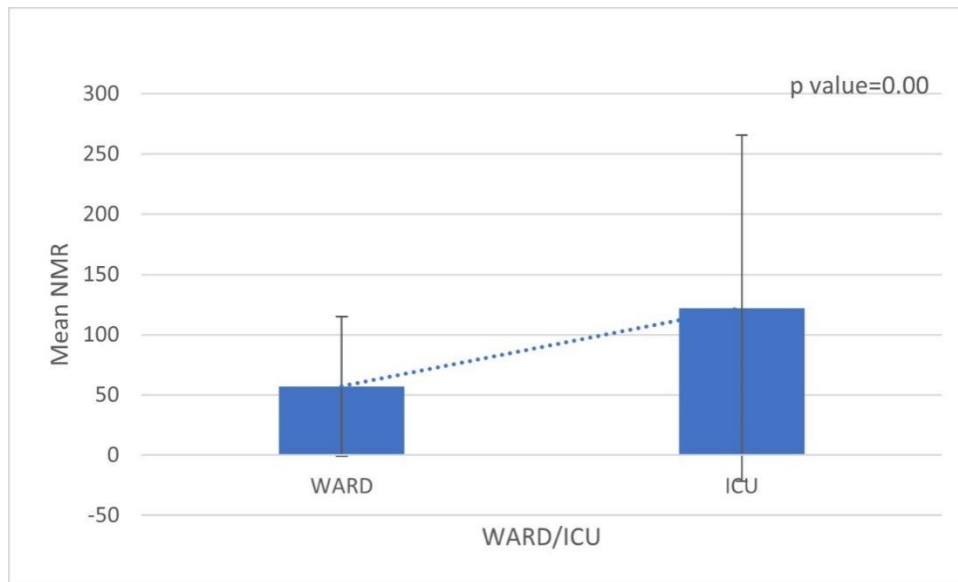

Fig. 4. Mean NLR in ward and ICU patients

Fig. 5. Mean NMR in ward and ICU patients

The mean NMR was found to be higher than normal range of neutrophil lymphocyte ratio (NMR) (NMR≥17.75) [7].The NMR was compared in the two groups and found to be significantly higher in the ICU patients (Table 1) (Fig. 5)

No other significant association was noted on comparing the WBC parameters between the ICU and non-ICU group.

4. DISCUSSION

COVID -19 had emerged in December 2019 in Wuhan, China as an outbreak of pneumonia[8]. The immune response curbs the viral replication in mild cases and limits the disease. However, uncontrolled inflammation may cause viral sepsis with immunologic impairment in severe cases [9].

In the present study, it was found that 119 (59.5%) patients were males and 81(40.5%) were females. This was similar to the findings in other studies where a higher percentage of COVID positive hospital admissions were males.In a study by Tadesse Z. et al., 57.5% of the patients were males and 42.5% were females [10].Though 52% of the patients infected with COVID-19 were females, only 33% of those who succumbed to death were females in a study by Zhu B. et al. [1]. In a study. by Tong X et al., 52.6% of the patients infected with COVID included in the study were males while 48.3% were females[9].

In the present study, on comparing the TLC, between the ICU and non-ICU patients, TLC was significantly higher in ICU patients. Tadesse Z. et al. compared the haematological parameters in patients with severe and non-severe infection. Leucocytosis was noted in 78% of the cases with severe disease while only 22% of cases with non-severe disease showed leucocytosis. Thus, severe COVID infection found to be associated with high TLC [10].

On comparing the percentage of neutrophils in the differential count and ANC between ICU and non-ICU patients, ANC was significantly higher in ICU patients. These findings were similar to the findings by Tadesse Z. et al. where neutrophilia was noted in 78% of the patients with severe COVID infection whereas only 28% of the patients with mild to moderate infection had neutrophilia [10]. Yuan et al. noted similar haematological findings in their study with higher TLC and ANC in the group of patients with severe COVID infection as compared to thegroup of patients with moderate disease[11].

COVID-19 infection causes an exaggerated inflammatory response causing a cytokine storm. Cytokine storm may be accompanied with neutrophilia (absolute neutrophil count above 7.5 $\times 10^9$ /L) [8].

The mean ALC was found to be within the normal range in the present study. The ALC was found to be markedly reduced in ICU patients as

compared to the non-ICU patients. (p-value= 0.057). In a study by Liu et al.[12], they observed that 72.3% (99/137) of the patients had lymphocytopenia[13]. Pozdnyakova O et al. in their study also noted lymphopenia in severe COVID-19 cases[13].Palladino et al. analysed the effect of COVID-19 on the lymphocyte count. The severity of lymphopenia was noted to increase with increase in severity of the disease. They found that the virus attachment or immune injuries from inflammatory mediators may be responsible for lymphocytopenia in COVID-19. Lymphocytopenia could also be due to exudation of circulating lymphocytes into inflammatory lung tissues [14].

The NLR was found to be significantly higher in the ICU patients on comparing the mean NLR of ICU and non-ICU patients (p=0.000). Liu J et al. found NLR to be an early predictor of patients with COVID-19 who are likely to develop critical illness[6]. These findings were similar to the findings by Anurag A et al. where they found increase in NLR with increase in severity of the disease[3].

The mean NMR was found to be higher than normal range of neutrophil monocyte ratio (NMR) (NMR≥17.75) [7]. The NMR was compared in the two groups. It was found to be significantly higher in the ICU patients (p=0.000). These findings were similar to the findings by Rizo-Téllez S et al. where they found a two-fold increase in NMR in non-survivors than survivors and found the NMR to be a reliable predictor of severity of COVID-19[7].

Severe COVID-19 infection has been found to be associated with a hyperinflammatory state and cytokine storm. Neutrophilia with enhanced degranulation of neutrophils plays a major role in inducing a hyperinflammatory state. Palladino et al. noted neutrophilia to be associated with poorer outcomes in COVID-19 infection [14].

Xue G et al. analysed the role of novel inflammatory markers to predict the disease severity in COVID-19. They found the neutrophil lymphocyte ratio to be elevated in the severe disease group as compared to patients with mild to moderate COVID-19 disease [15].

Myari A et al. found the WBC count, neutrophil count and neutrophil lymphocyte ratio to be the best indicators of critical disease in COVID-19 cases whereas lymphocytopenia was found to be an early predictor of severe disease [16].

The present study confirms the findings noted by other researchers in WBC parameters of patients infected with COVID-19, in a specific population at Lok Nayak Hospital, Delhi, India.

However, there were a few limitations of the present study as the health system was already overburdened during the pandemic.

1. The present study included hospitalised patients infected with COVID-19. The results of this study may not be an adequate representation of the haematological profile of all the cases infected with COVID-19 in Delhi.
2. Exposure of patients to various drugs like steroids which could have affected the WBC parameters was not taken into account as the study was retrospective.
3. There was no follow up of patients to analyse the utility of these parameters in predicting the prognosis.

5. CONCLUSION

The present study showed that the critical patients requiring ICU admission were shown to have a significantly higher TLC, ANC, NMR and NLR as compared to the non-ICU patients. Though no statistically significant difference was noted in the ALC of ICU and non-ICU patients, the ALC was found to be markedly reduced in ICU patients (p-value= 0.057). Thus, WBC parameters could help in assessing the severity of COVID-19 infection.

Various studies from across the globe have shown white blood cell count, neutrophil count, lymphocyte count and neutrophil lymphocyte ratio as important predictors of severity of COVID-19 disease[14]. The findings of the present study support the findings of previous studies.

ETHICAL APPROVAL

Ethical Clearance was taken from the institutional ethics committee (F.1/IEC/MAMC/90/02/2022/ No.127).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Zhu B, Feng X, Jiang C, Mi S, Yang L, Zhao Z et al. Correlation between white blood cell count at admission and mortality in COVID-19 patients: a retrospective study. BMC Infect Dis. 2021;21:574.
2. WHO Coronavirus (COVID-19) Pandemic. Geneva: WHO; 2022. WHO Coronavirus (COVID-19) Dashboard; updated Feb 2022.
   Accessed On: 3 Feb 2022.
   Available:https://covid19.who.int/c
3. Anurag A, Jha P, Kumar A. Differential white blood cell count in the COVID-19: A cross-sectional study of 148 patients. Diabetes Metab Syndr. 2020;14:2099-102.
4. Mardani R, Vasmehjani A, Zali F, Gholami A, Nasab S, Kaghazian H et al. Laboratory Parameters in Detection of COVID-19 Patients with Positive RT-PCR; a Diagnostic Accuracy Study. Arch Acad Emerg Med. 2020;8 e43.
5. Bain B, Bates I, Laffan M, editors. Dacie and Lewis Practical Haematology. 12th ed. Elsevier, London; 2017.
6. 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;18:206-12.
7. Rizo-Téllez S, Méndez-García L, Flores-Rebollo C, Alba-Flores F, Alcántara-Suárez R, Manjarrez-Reyna A et al. The Neutrophil-to-Monocyte Ratio and Lymphocyte-to-Neutrophil Ratio at Admission Predict In-Hospital Mortality in Mexican Patients with Severe SARS-CoV-2 Infection (Covid-19). Microorganisms. 2020;8:1560- 77.
8. Selim S. Leukocyte count in COVID-19: an important consideration. The Egyptian Journal of Bronchology. 2020;14:43-4.
9. Tong X, Cheng A, Yuan X, Zhong X, Wang H, Zhou W. Characteristics of peripheral white blood cells in COVID-19 patients revealed by a retrospective cohort study. BMC Infect Dis. 2021;21:1236-46.
10. Tadesse Z, Bayissa A, Diriba T, Chernet N, Tsegaye S, Tsega M. Neutrophil-to-lymphocyte ratio and cut-off values as predictor of severity and mortality in COVID-19 Patients in millennium COVID-19 Care Center, Addis Ababa, Ethiopia. Int J Gen Med. 2022;15:6739-55.
11. Yuan J, Zou R, Zeng L, Kou S, Lan J, Li X. The correlation between viral clearance and biochemical outcomes of 94 COVID-19 infected discharged patients. Inflamm Res. 2020:1-8.
12. Liu K, Fang Y, Deng Y, Liu W, Wang M, Ma J. et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. Chin Med J. 2020;133(9):1025–31.
13. Pozdnyakova O, Connell N, Battinelli E, Connors J, Fell G, Kim A. Clinical Significance of CBC and WBC Morphology in the Diagnosis and Clinical Course of COVID-19 Infection. Am J Clin Pathol. 2021;155:364-75.
14. Palladino M. Complete blood count alterations in COVID-19 patients: A narrative review. Biochem Med (Zagreb). 2021;15:31:030501-13.
15. Xue G, Gan X, Wu Z, Xie D, Xiong Y, Hua L et al. Novel serological biomarkers for inflammation in predicting disease severity in patients with COVID-19. Int Immunopharmacol. 2020;89:107065-74.
16. Myari A, Papapetrou E, Tsaousi C. Diagnostic value of white blood cell parameters for COVID-19: Is there a role for HFLC and IG? Int J Lab Hematol. 2022; 44:104-11.