e-ISSN: 0975-1556, p-ISSN:2820-2643
Available online on www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2024; 16(2); 568-574

Original Research Article

Hematological Profile of COVID-19 Patients in a COVID Care Hospital

Sreeram B[1], Aysha Ali[2], Priya P Kartha[3]

[1]Assistant Professor, Department of General Medicine, Government Medical College and Hospital Palakkad, Kerala.
[2]Associate Professor, Department of Pathology, Government Medical College and Hospital Palakkad, Kerala.
[3]Associate Professor, Department of Pathology, Government Medical College and Hospital Palakkad, Kerala.

Received: 25-12-2023 / Revised: 19-01-2024 / Accepted: 08-02-2024
Corresponding Author: Dr Sreeram B
Conflict of interest: Nil

Abstract:

Background: Various hematological abnormalities have been noted in SARS-CoV-2 infection, directly correlating with disease progression, clinical severity, and mortality rates. This study aimed to assess the hematological parameter abnormalities among patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a tertiary care hospital located in southern India.

Methods: This retrospective study was conducted by the Department of Pathology, Government Medical College and Hospital, Palakkad, Kerala. The hematology profile, based on CBC results collected in this study, included hemoglobin, hematocrit, red blood cell (RBC) count, red cell distribution width (RDW), white blood cell (WBC) count, absolute eosinophil count, absolute basophil count, absolute neutrophil count, absolute lymphocyte count, absolute monocyte count, and thrombocyte count obtained from Sysmex XN-1000.

Results: A total of n=350 patients' data was included in the study. Out of which n=225(64.28%) were males and n=125(35.71%) were females. The mean age of the cohort was 38.51 ± 10.2 years. The common age group was 21 – 40 years with 63% of all the cases reported in the study. The mean NLR was 5.05, which is higher than the normal range of 0.7-2.0. This suggests that the COVID-19 patients had an elevated NLR, which is a marker of inflammation and severity of illness. Table 4 shows that COVID-19 patients have several hematological abnormalities, including elevated WBC count, anemia, thrombocytopenia, neutrophilia, lymphopenia, eosinophilia, and basophilia.

Conclusion: several hematological parameters hold promise for predicting the severity of COVID-19 and for guiding timely and appropriate treatment interventions. Complete blood count (CBC), which is a readily available and cost-effective test in most medical centers, offers significant clinical value. NLR could be utilized as an alternative parameter for assessing inflammatory states in patients with confirmed COVID-19 cases.

Keywords: Covid-19, SARS-CoV-2, Hematological parameters, Neutrophil/Lymphocyte ratio (NLR)

Introduction

The COVID-19 pandemic, caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has resulted in significant global morbidity and mortality. As of 28 Jan 2024, there have been 774,469,939 Reported COVID-19 cases and 7,026,465 deaths worldwide [1]. SARS-CoV-2 enters human cells by binding its spike protein to the ACE2 receptor, expressed in various organs such as the lungs, heart, kidneys, intestines, and vascular endothelium. The clinical presentation and severity of COVID-19 vary widely, with most cases being asymptomatic or presenting with mild to moderate symptoms resembling flu-like symptoms or mild pneumonia [2-4]. However, approximately 14% of patients develop severe disease, and 5% experience critical conditions involving respiratory failure, sepsis, or multiorgan dysfunction [4, 5]. Patients with comorbidities, including hypertension, diabetes mellitus (DM), cardiovascular disease, chronic renal disease, and chronic respiratory disease, face a higher risk of severe COVID-19 [5, 6]. Various laboratory tests are routinely performed in COVID-19 patients, including complete blood count (CBC) and molecular analysis. Hematological profiles in COVID-19 patients reveal several parameters with clinical significance. Severe COVID-19 cases often exhibit leukocytosis, neutrophilia, lymphopenia, eosinopenia, and thrombocytopenia. Hemoglobin levels in severe cases are lower than in mild to moderate cases, albeit within the normal range [7-9]. The neutrophil-lymphocyte ratio (NLR) is higher in COVID-19-positive patients and is associated with a poor outcome [3, 10]. Elevated NLR is linked to increased inflammatory markers such as interleukin-

6 and tumor necrosis factor-alpha (TNF-α). Red cell distribution width (RDW), a marker of anisocytosis, is associated with recurrent hospitalizations in COVID-19 patients [11]. Specific hematological parameters are also associated with comorbidities such as DM and hypertension [12]. Certain hematological profiles may predict frailty in diabetics during COVID-19 [13]. Reverse transcription-polymerase chain reaction (RT-PCR) is another commonly used laboratory test, providing the cycle threshold (Ct) value, which negatively correlates with viral load. However, the correlation between Ct values and patient severity remains debated and understudied [14-16]. Additionally, differences in Ct values between COVID-19 patients with and without comorbidities have not been extensively reported. This study aims to analyze the clinical significance of these routinely assessed laboratory tests, describe the hematology profile of COVID-19 patients based on severity and comorbidities, and investigate the correlation between hematological profiles and Ct values in confirmed COVID-19 patients.

Material and Methods

This retrospective study was conducted by the Department of Pathology, Government Medical College and Hospital, Palakkad, Kerala. Institutional Ethical approval was obtained for the study. The COVID-19 records were obtained from the MRD section from 07/06/2022 to 06/06/2023 and analyzed for recording the results.

Inclusion Criteria:

1. All RT PCR-positive cases,
2. Above the age of 18 years,
3. Admitted to GMC Palakkad and district hospital COVID care unit.

Exclusion Criteria :

1. pregnant females,
2. Cancer patients
3. patients on anticoagulants or antiplatelet drugs before the diagnosis of COVID-19.
4. Those with incomplete and missing hematological data records.

The records were analyzed for the demographic profile of the cases (age, sex, and comorbidities). CBC results and Ct values obtained from RT-PCR were extracted from medical records at the time of assessment in the emergency department for COVID-19 patients. The hematology profile, based on CBC results collected in this study, included hemoglobin, hematocrit, red blood cell (RBC) count, red cell distribution width (RDW), white blood cell (WBC) count, absolute eosinophil count, absolute basophil count, absolute neutrophil count, absolute lymphocyte count, absolute monocyte count, and thrombocyte count obtained from Sysmex XN-1000.

NLR was calculated as the absolute neutrophil count divided by the absolute lymphocyte count. COVID-19 severity was categorized into three groups: mild-moderate and severe. Mild-moderate cases with no signs or symptoms of severe pneumonia were hospitalized in the general infection ward, while severe cases with severe pneumonia (respiratory distress >30 breaths/minute or oxygen saturation <90%) were treated in the intensive care infection ward. COVID-19 diagnosis was confirmed based on positive SARS-CoV-2 detection from nasopharyngeal swab specimens using the RT-PCR method. Patients were categorized based on comorbidity status: COVID-19 without comorbidity if no comorbidities were present and with comorbidity if one or more comorbidities were present.

Statistical Analysis was conducted using IBM SPSS Statistics (version 22.0, IBM Corp., Armonk, NY, USA). Normality was assessed using the Kolmogorov-Smirnov test. The independent t-test was used to compare the means of two variables of hematology parameters based on severity and presence of comorbidities in cases. Results were considered significant if the p-value was <0.05.

Results

A total of n=350 patients' data was included in the study. Out of which n=225(64.28%) were males and n=125(35.71%) were females. Table 1 presents the demographic profile of COVID-19 cases included in the study, categorized by age and gender. The mean age of the cohort was 38.51 ± 10.2 years. The common age group was 21 – 40 years with 63% of all the cases reported in the study. The lowest number of cases were reported from the age group 51 – 60 years with 9.7% of cases in the study.

Table 1: Demographic profile of COVID-19 cases included in the study

Age In Years	Males	Females	Total	Percentage
18 – 20	29	12	41	11.71
21 – 30	73	36	109	31.14
31 – 40	71	40	111	31.71
41 – 50	34	21	55	15.71
51 – 60	18	16	34	09.71
Total	225	125	350	100.0

Table 2 presents the profile of COVID-19 cases included in the study, detailing the frequency and percentage of various categories. The severity of COVID-19: Mild/Moderate COVID-19: 206 cases (58.86%) Severe COVID-19: 144 cases (41.14%). Without comorbidity: 227 cases (64.86%). With comorbidities: 123 cases (35.14%) The distribution of specific Comorbidities: Hypertension: 63 cases (18.00%), Diabetes mellitus: 42 cases (12.00%), cardiovascular disease: 25 cases (7.14%), chronic kidney disease: 21 cases (6.00%), Cerebrovascular disease: 4 cases (1.14%), HIV/AIDS: 3 cases (0.85%), Others: 18 cases (5.14%) Some cases may have had more than one comorbidity.

Table 2: Profile of Covid 19 included in the study

	Frequency	Percentage
Mild/Moderate Covid-19	206	58.86
Severe Covid-19	144	41.14
Without comorbidity	227	64.86
With comorbidities	123	35.14
Hypertension	63	18.00
Diabetes mellitus	42	12.00
Cardiovascular disease	25	7.14
Chronic kidney disease	21	6.00
Cerebrovascular disease	4	1.14
HIV/AIDS	3	0.85
Others	18	5.14

Table 3 presents the hematological profile of 350 COVID-19 cases included in the study. The table shows that the mean WBC count was 9524.50 cells/µL, which is higher than the normal range of 4,500-11,000 cells/µL. This suggests that the COVID-19 patients had an elevated white blood cell count, which is a sign of inflammation. The table also shows that the average RBC count was 4.40 x 10^6/µL, which is lower than the normal range of 4.7-6.1 x 10^6/µL for men and 4.2-5.2 x 10^6/µL for women. This suggests that the COVID-19 patients had anemia, a condition in which the body does not have enough red blood cells. The mean Hb level was 16.9 g/dL, which is within the normal range of 13.5-17.5 g/dL for men and 12-15.5 g/dL for women. However, the table also shows that there was a wide range of Hb levels, with some patients having levels as low as 1.25 g/dL. This suggests that some of the COVID-19 patients had severe anemia. The mean Hct level was 38.5%, which is lower than the normal range of 41-53% for men and 36-48% for women. This suggests that the COVID-19 patients had anemia.

Table 3: Hematological profile of n= 350 Covid 19 cases included in the study

Hematology Parameters	Range		Mean	± SD
	Minimum	Maximum		
WBC cells/µL	2850	31200	952450	3950
RBC x 10^6/µL	2.51	6.01	4.40	0.85
Hb g/dL	6.2	17.8	16.9	1.25
Hct %	22	55	38.5	7.5
Platelets x 10^3/µL	45	550	290	95.2
RDW %	11.5	23.9	13.24	1.52
Neutrophils/µL	1460	26700	7250	4620.25
Lymphocyte/µL	275	6000	2150	570.25
Monocyte/µL	140	5520	640.28	260.5
Eosinophil /µL	0	1250	182.2	95.4
Basophils /µL	0	190	38.33	24.6
NLR	0.71	40.16	5.05	4.52

The average platelet count was 290 x 10^3/µL, which is within the normal range of 150-400 x 10^3/µL. However, the table also shows that there was a wide range of platelet counts, with some patients having counts as low as 95.2 x 10^3/µL. This suggests that some of the COVID-19 patients had thrombocytopenia. The mean neutrophil count was 7250/µL, which is higher than the normal range of 1,500-6,000/µL. This suggests that the COVID-19 patients had neutrophilia. the average lymphocyte count was 2150/µL, which is lower than the normal range of 1,000-3,500 /µL. This suggests that the COVID-19 patients had lymphopenia. The average monocyte count was 640.28/µL, which is within the normal range of 200-900/µL. the average eosinophil count was 182.2 /µL, which is higher than the normal

range of 0-400/µL. This suggests that the COVID-19 patients had eosinophilia. The mean basophil count was 38.33/µL, which is higher than the normal range of 0-100/µL. This suggests that the COVID-19 patients had basophilia. The mean NLR was 5.05, which is higher than the normal range of 0.7-2.0. This suggests that the COVID-19 patients had an elevated NLR, which is a marker of inflammation and severity of illness. The table shows that COVID-19 patients have a number of hematological abnormalities, including elevated WBC count, anemia, thrombocytopenia, neutrophilia, lymphopenia, eosinophilia, and basophilia. These abnormalities suggest that COVID-19 is a systemic inflammatory disease. Table 4 compares the hematological parameters of individuals with mild/moderate and severe COVID-19 cases. WBC: Severe cases had a 40% higher average WBC count compared to mild/moderate cases. RBC: Severe cases had a 17% lower average RBC count compared to mild/moderate cases. Hb: Severe cases had a 17% lower average Hb level compared to mild/moderate cases. Hct: Severe cases had a 20% lower average Hct level compared to mild/moderate cases. Platelets: Severe cases had a 12% lower average platelet count compared to mild/moderate cases. Neutrophils: Severe cases had nearly twice the average neutrophil count compared to mild/moderate cases. Lymphocytes: Severe cases had a 40% lower average lymphocyte count compared to mild/moderate cases. Monocytes: Severe cases had a 28% higher average monocyte count compared to mild/moderate cases. *NLR*: Severe cases had nearly four times the average NLR compared to mild/moderate cases.

Table 4: Comparison of hematological parameters of COVID-19 cases included in the study

Hematology Parameters	Mild/Moderate COVID 19 Mean ± SD	Severe COVID 19 Mean ± SD	p-value
WBC cells/µL	8250 ± 2452.10	11610.25 ± 5520.61	0.001
RBC x 10^6/ µL	4.79 ± 0.55	3.95 ± 0.71	0.042
Hb g/dL	13.56 ± 1.98	11.52 ± 2.41	0.019
Hct %	40.22 ± 5.33	32.28 ± 7.71	0.011
Platelets x 10^3/ µL	320.12 ± 75.64	280.33 ± 110.34	0.021
RDW %	12.25 ± 1.42	14.29 ± 1.82	0.032
Neutrophils / µL	4802.35 ± 1982.32	9210.42 ± 4925.70	0.001
Lymphocyte / µL	2395.05 ± 752.95	1440.62 ± 740.14	0.001
Monocyte / µL	609.74 ± 221.31	778.62 ± 615.37	0.002
Eosinophil / µL	185.44 ± 127.82	164.21 ± 119.08	0.337
Basophils / µL	42.57 ± 29.19	37.01 ± 22.12	0.143
NLR	2.29 ± 1.94	8.89 ± 4.54	0.001

The table shows an **Increased inflammation:** Patients with severe cases had significantly higher WBC count and Neutrophil-to-Lymphocyte Ratio (NLR) compared to mild/moderate cases, indicating greater inflammation. **Anemia:** Both groups showed signs of anemia with lower RBC counts, Hb levels, and Hct compared to normal ranges. However, these values were significantly lower in severe cases. **Thrombocytopenia:** Patients with severe cases had lower platelet counts compared to mild/moderate cases, suggesting a higher risk of bleeding. **RDW:** Both groups had elevated RDW (Red Blood Cell Distribution Width), which could indicate variation in red blood cell size and shape. However, the increase was more pronounced in severe cases. No significant differences: No significant differences were observed in Eosinophil and Basophil counts.

Table 5: Comparison of hematological parameters of Covid 19 cases with and without comorbidities included in the study

Hematology Parameters	COVID 19 without comorbidity (n=227) Mean ± SD	COVID 19 with comorbidity (n=123) Mean ± SD	p-value
WBC cells/µL	9520.32 ± 4125.92	9752.27 ± 3900.31	0.752
RBC x 10^6/ µL	4.50 ± 0.72	4.40 ± .0.63	0.321
Hb g/dL	13.50 ± 2.22	11.57 ± 2.32	0.415
Hct %	38.92 ± 7.21	36.52 ± 7.10	0.661
Platelets x 10^3/ µL	300.20 ± 90.94	301.25 ± 120.12	0.985
RDW %	13.77 ± 1.28	13.20 ± 1.57	0.654
Neutrophils / µL	6400.30 ± 3520.21	6800.25 ± 2985.13	0.647
Lymphocyte / µL	2040.22 ± 950.36	1850.22 ± 752.41	0.096
Monocyte / µL	635.32 ± 280.17	755.64 ± 254.33	0.235
Eosinophil / µL	172.12 ± 161.84	169.72 ± 162.24	0.117
Basophils / µL	41.78 ± 29.52	37.46 ± 26.70	0.224
NLR	4.92 ± 5.33	5.56 ± 6.24	0.521

Table 5 compares the hematological parameters of individuals with COVID-19 with and without comorbidities. No significant differences: Most parameters, including WBC count, RBC count, Hb level, Hct, platelets, RDW, Neutrophils, Monocytes, Eosinophils, Basophils, and NLR, showed no significant differences between the two groups. Potential trend in Lymphocytes: Individuals with comorbidities had a slightly lower average lymphocyte count compared to those without comorbidities, but the difference was not statistically significant (p=0.096). This might warrant further investigation with a larger sample size.

WBC: Both groups had elevated WBC counts compared to normal ranges, suggesting inflammation. RBC & Hb: Both groups showed signs of anemia, but again, no significant difference between them. Hct: Both groups had lower Hct compared to normal ranges, consistent with anemia. Platelets: Both groups had platelet counts within normal ranges. RDW: Both groups had elevated RDW, potentially indicating variation in red blood cell sizes and shapes. Neutrophils: Both groups had elevated neutrophil counts, indicating inflammation. Lymphocytes: As mentioned before, a potential trend for lower lymphocyte count in the comorbidity group is observed. Monocytes: Both groups had monocyte counts within normal ranges. Eosinophils & Basophils: Both groups had eosinophil and basophil counts within normal ranges. NLR: Both groups had elevated NLR, indicating inflammation.

Discussion

According to the WHO guidelines for the prevention and control of COVID-19 [17] we found Mild/moderate COVID-19 in 206(58.86%) cases and severe COVID-19 was found in n=144(41.14%). The mean age of the cohort in the study was 38.51 ± 10.2 years. N of 123 patients (35.14%) were admitted with one or more comorbidities. The commonest comorbidity was hypertension 18%, diabetes mellitus 12%, and cardiovascular diseases 7% [18]. The average counts of white blood cells (WBC), neutrophils, and monocytes were higher in severe COVID-19 patients than in those with mild to moderate symptoms, whereas the lymphocyte count was notably lower in severe cases (Table 4). The increased WBC count in patients with severe COVID-19 may be attributed to potential bacterial coinfections or a more intense immune response. These findings align with the analysis conducted by Karthabil et al. [7] which suggests that while WBC counts typically remain within normal ranges in COVID-19 patients, they tend to be elevated in severe cases compared to those with milder symptoms. Furthermore, severe COVID-19 cases exhibited lower lymphocyte counts, including instances of lymphopenia (with a mean lymphocyte count of 1440.62 cells/μL), in contrast to patients with mild-to-moderate symptoms. These observations are consistent with findings from other studies. [6, 8]. Additional insights provided by Yang et al. [19] and Qin et al. [20] indicated a reduction in regulatory T lymphocytes and memory T cell percentages, coupled with an increase in naive T lymphocytes among severe COVID-19 patients, suggesting a dysfunctional inflammatory response that exacerbates the severity of organ failure. Yang et al. [19] and Gustine et al. [21] proposed that SARS-CoV-2 directly infects the lymphocytes and macrophages. Post-mortem examinations of COVID-19 patients with lymphopenia revealed substantial lymphocyte cell death and macrophage infiltration in the lymph nodes and spleen, suggesting that activated macrophages may express inflammatory cytokines, leading to lymphocyte necrosis and apoptosis. Yang et al. [19] attributed the elevated neutrophil count in severe COVID-19 cases to compromised lymphocytes, which renders COVID-19 patients more susceptible to bacterial infections, thereby triggering the activation and recruitment of neutrophils into the bloodstream. Similarly, studies conducted by Karthabil et al. [7] and Liu et al. [8] indicated that neutrophil count serves as a prognostic indicator of disease severity [19-21]. The neutrophil-to-lymphocyte ratio (NLR) combines neutrophilia and lymphopenia to provide a more accurate assessment of systemic inflammation. Owing to its ratio-based nature, NLR is less susceptible to pre-analytical factors and can be easily derived from routine laboratory tests. NLR has been associated with various inflammatory conditions, including thyroiditis, ulcerative colitis, uncontrolled diabetes mellitus, irritable bowel disease, and, more recently, COVID-19 infection [3, 22, 23]. Moreover, NLR consistently emerged as higher in severe COVID-19 cases, with a cut-off value of ≥ 3.13 indicating a high-risk category for severe illness, in contrast with < 3.13 indicating a low-risk category. This finding corresponds with the present study, in which the mean NLR was 8.89 in severe cases and 2.29 in mild to moderate cases. Additionally, elevated NLR is associated with increased levels of inflammatory markers such as C-reactive protein (CRP), interleukin-6, TNF-α, and serum ferritin in patients with more severe COVID-19 [8, 21, 22].

In this study, severe COVID-19 cases exhibited elevated monocyte counts compared to those with mild-to-moderate symptoms. This finding contrasts with the observations of Yang et al. [19] and Karthabil et al. [7] who reported lower monocyte counts in severe cases, suggesting that an activated monocyte system can exacerbate tissue damage through the induction of inflammatory cytokines. Although not statistically significant in this study, patients with severe COVID-19 tended to have lower eosinophil and basophil counts, potentially attributable to the generally low concentrations of these cells in the blood and the absence of differentiation among critically ill COVID-19 patients with sepsis. Eosinopenia, a marker of sepsis, has been reported in

previous studies. Furthermore, patients with severe COVID-19 exhibited lower hemoglobin levels and higher red cell distribution width (RDW), indicating a more pronounced inflammatory process interfering with erythropoiesis. While the platelet count remained within the normal range overall, it was significantly lower in the severe COVID-19 cases. The presence of comorbidities did not significantly impact the hematological profile of COVID-19 patients in this study. This aligns with findings from Manson's study, which suggested that COVID-19 patients with hyperinflammatory conditions upon hospital admission had fewer comorbidities than those without hyperinflammation. However, conflicting results from studies by Zhou et al. [24] and Christensen et al. [25] suggested that more comorbidities were associated with worse outcomes, highlighting the need for further investigation of the dynamics of hematology profiles over time.

Conclusion

In conclusion, several hematological parameters hold promise for predicting the severity of COVID-19 and for guiding timely and appropriate treatment interventions. Complete blood count (CBC), which is a readily available and cost-effective test in most medical centers, offers significant clinical value. NLR could be utilized as an alternative parameter for assessing inflammatory states in patients with confirmed COVID-19 cases.

References

1. WHO Coronavirus Diseases (COVID-19) Dashboard. World Health Organization; 2024. Available from: https://data.who.int/dashboards/covid19/deaths?n=c [Accessed 3rd Feb 2024].
2. WHO. Clinical management of COVID-19: interim guidance. World Health Organization; 2020. Available from: https://www.who.int/publications/i/item/clinical-management-of-COVID-19/ [Accessed 4 Feb 2024].
3. Aktas G. Hematological predictors of novel coronavirus infection. Rev Assoc Med Bras 2021; 67:1–2.
4. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China summary of a report of 72314 cases from the Chinese Center for disease control and Prevention. JAMA 2020; 323:1239–42.
5. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical characteristic of coronavirus disease 2019 in China. N Engl J Med 2020; 382: 1708–20.
6. Guan WJ, Liang WH, Zhao Y, Liang H, Chen Z, Li Y, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. Eur Respir J 2020; 55:200 0547.
7. Khartabil TA, Russcher H, Ven AD, Rijke YB. A summary of the diagnostic and prognostic value of hemocytometry markers in COVID-19 patients. Crit Rev Clin Lab Sci 2020;57: 415–31.
8. Liu X, Zhang R, He G. Hematological findings in coronavirus diseases 2019: indications of progression of disease. Ann Hematol 2020;99 :1421–28.
9. Liao D, Zhou F, Luo L, Xu M, Wang H, Xia J, et al. Hematological characteristics and risk factors in the classification and prognostic evaluation of COVID-19: a retrospective cohort study. Lancet Haematol 2020; 7:671–78.
10. Khalid A, Jaffar MA, Khan T, Lail RA, Ali S, Aktas G, et al. Hematological and biochemical parameters as diagnostic and prognostic markers in SARS-CoV-2 infected patients of Pakistan: a retrospective comparative analysis. Hematology 2021;26: 529–42.
11. Atak Tel BM, Kahveci G, Bilgin S, Kurtkulagi O, Duman T, Demirkol M, et al. Haemoglobin and red cell distribution width levels in internal medicine patients indicate recurrent hospital admission during COVID-19. Fam Med Prim Care Rev 2022; 24:32–6.
12. Guo W, Li M, Dong Y, Zhou H, Zhang Z, Tian C, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes Metab Res Rev 2020; 36:1–9.
13. Atak Tel BM, Bilgin S, Kurkulagi O, Kahveci G, Duman T, Sagdic T, et al. Frailty in diabetic subjects during COVID-19 and its association with HbA1c, mean platelet volume, and monocyte/lymphocyte ratio. Clin Diabetology 2021; 11:119–26.
14. Huang JT, Ran RR, Lv ZH, Feng L, Ran C, Tong Y, et al. Chronological changes of viral shedding in adult inpatients with COVID-19 in Wuhan, China. Clin Infect Dis 2020; 71:2158–66.
15. Singanayagam A, Patel M, Charlett A, Bernal JL, Saliba V, Ellis J, et al. Duration of infectiousness and correlation with RT-PCR cycle threshold values in case of COVID-19, England, January to May 2020. Euro Surveill 2021; 26:210218c.
16. Rao SN, Manissero D, Steele VR, Pareja J. A narrative systematic review of the clinical utility of cycle threshold value in the context of COVID-19. Infect Dis Ther 2020; 9:573–86.
17. WHO Coronavirus Diseases (COVID-19) Dashboard. World Health Organization. Available from: https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-clinical-2023.2 [Accessed on 4th Feb 2024]
18. Sanyaolu A, Okorie C, Marinkovic A, Patidar R, Younis K, Desai P, Hosein Z, Padda I, Mangat J, Altaf M. Comorbidity and its Impact on

Patients with COVID-19. SN Compr Clin Med. 2020;2(8):1069-76.
19. Yang L, Liu S, Liu J, Zhang Z, Wan X, Huang B, et al. Review article COVID-19: immunopathogenesis and immunotherapeutics. Sig Transduct Target Ther 2020; 5:1–8.
20. Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, et al. Dysregulation of immune response in patients with coronavirus 2019 (COVID-19) in Wuhan, China. Clin Infec Dis 2020; 71:762–8.
21. Gustine JN, Jones D. Review: immunopathology of hyperinflation in COVID-19. Am J Pathol 2020; 191:4–17.
22. Aktas G, Basaran E, Duman TT, Atak BM, Kurtkulagi O, Bilgin S, et al. irritable bowel syndrome is associated with novel inflammatory markers derived from hemogram parameters. Fam Med Prim Care Rev 2020; 22:107–10.
23. Posul E, Yilmaz B, Aktas G, Kurt M. Does neutrophil-to lymphocyte ratio predict active ulcerative colitis? Wien Klin Wochenschr 2015; 127:262–65.
24. Zhou W, Qin X, Hu X, Lu Y, Pan J. Prognosis models for severe and critical COVID-19 based on the Charlson and elixhauser comorbidity indices. Int J Med Sci 2020;17: 2257–6 3.
25. Christensen DM, Strange JE. Charlson. Comorbidity index score and risk of severe outcome and death in Danish COVID-19 patients. J Gen Intern Med 2020; 35:2801–3.