Assessment of Hematological Indices as Potential Prognostic Markers in COVID-19 Patients at Taleghani Hospital, Urmia, Iran

Sahar Mehranfar[1] , Ali Yekanlou[2] , Mohammad Heidari[3] , Masoud Lahouty[4*]

[1]Department of Genetics and Immunology, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran;
[2]Student Research Committee, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran; [3]Department of Epidemiology and Biostatistics, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran;
[4]Department of Microbiology and Virology, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran

ARTICLE INFO

ABSTRACT

Introduction: Rapid and accurate diagnosis of COVID-19 is critical for effective patient management, timely treatment, and mitigating disease transmission. Identifying reliable prognostic markers, such as hematological indices, can enable prompt medical intervention and improve outcomes. This study aimed to investigate the associations between mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and mean corpuscular volume (MCV), measured within the first 10 days of hospital admission, and clinical outcomes (such as survival vs. non-survival) in COVID-19 patients. **Methods:** This retrospective study included 173 patients with confirmed COVID-19 (Delta variant) admitted to Taleghani Hospital in Urmia, Iran. Complete blood count (CBC) data, including hemoglobin (Hb), mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV), and white blood cell (WBC) counts, were extracted from electronic medical records. Differences between survivor and non-survivor groups were analyzed using ANOVA with Tukey post hoc test. **Results:** The median age of all patients was 53 years (IQR: 22–88), with a significant difference between survivors (52 years; IQR: 22–88) and non-survivors (60 years; IQR: 35–85) ($P = 0.04$). No overall significantly higher prevalence of comorbidities was observed in the non-survivor group compared to the survivor group. Patients with diabetes ($P=0.327$) or hypertension ($P=0.797$) did not have a significantly higher prevalence in the non-survivor group, with no evidence of association. Moreover, no significant differences were found in Hb, MCH, and MCV between the survivor and non-survivor groups ($P>0.05$). **Conclusion:** While some hematological markers are routinely used in diagnosing various diseases, this study did not find significant differences in Hb, MCH, and MCV between survivor and non-survivor groups, suggesting these specific markers may not be reliable for early diagnosis or predicting prognosis in Delta-variant COVID-19 in this Iranian cohort. Further research with a larger sample size, including a wider range of hematological and inflammatory markers, is needed to explore the potential role of Hb, MCH, and MCV in COVID-19 diagnosis and prognosis. Investigating the interplay between these markers and clinical outcomes could provide valuable insights for patient management.

INTRODUCTION

Viruses use various mechanisms to interact with host immune cells, altering or regulating their functions [1]. The novel coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), rapidly emerged in Wuhan, China, in late 2019 and quickly spread globally, resulting in a pandemic declared by the World Health Organization (WHO) in March 2020 [2]. The pandemic has profoundly impacted global health systems and posed unparalleled challenges to healthcare professionals [3]. This situation has imposed vulnerabilities in healthcare systems worldwide, placing healthcare professionals at increased risk of infection and

highlighting the need for effective preventive measures and resources. As most frontline healthcare workers cannot perform their duties remotely, this necessitates proactive strategies, such as frequent viral testing even for asymptomatic individuals, to minimize transmission risk within healthcare settings. As of August 2023, cumulative reports indicate that over 146,000 deaths attributed to the SARS-CoV-2 virus have been recorded in Iran, with over 7.6 million cases since the beginning of the pandemic [4].

Common symptoms of COVID-19 include fever, dry cough, fatigue, shortness of breath, muscle aches, headache, anosmia (loss of smell) or ageusia (loss of taste), sore throat, congestion or runny nose, nausea or vomiting, and diarrhea. While many COVID-19 cases are mild or asymptomatic, the disease can progress to severe complications, including pneumonia, acute respiratory distress syndrome (ARDS), sepsis, myocarditis, and even death, particularly in individuals with underlying health conditions or advanced age [5]. Approximately 5-15% of individuals with COVID-19 develop severe disease, often associated with comorbidities or underlying health conditions. Risk factors for severe COVID-19 include advanced age, smoking, obesity, chronic respiratory diseases (*e.g*., asthma, COPD), cardiovascular disease, diabetes, and other metabolic disorders [3]. Early prediction of COVID-19 prognosis and timely clinical intervention necessitate close monitoring of patients' clinical status throughout hospitalization.

Hematological tests, particularly complete blood count (CBC), are widely used in clinical practice and have emerged as a potential tool for assessing and managing COVID-19 patients. CBC data have been investigated as a potential supplementary tool for early diagnosis of COVID-19, particularly given its accessibility and affordability across diverse healthcare settings [6]. Severe or critical COVID-19 illness has been associated with various hematological abnormalities, including lymphopenia, which is a decrease in the number of lymphocytes [7].

While several studies have investigated the prognostic value of hematological markers in severe COVID-19, further research is needed to establish their reliability and clinical utility. Hematological parameters are routinely assessed in COVID-19 patients, and some studies suggest they may aid in early diagnosis and risk stratification. Common hematological abnormalities observed in COVID-19 patients include lymphocytopenia [8-10], eosinopenia [11, 12], neutrophilia [13-15], and thrombocytopenia, although thrombocytosis has also been reported in some rare cases [16]. Although MCV and MCH are routinely measured in CBC, their role in COVID-19 prognosis remains understudied. Our study specifically investigates these indices to determine their potential as prognostic tools.

METHODS

Study design and population. This retrospective cohort study was conducted at Taleghani Hospital in Urmia, Iran. Patients aged 16 years or older admitted to Taleghani Hospital from March 21 to September 22, 2021, with confirmed COVID-19 diagnosis based on positive PCR test results were included in the study. This period coincided with the emergence and spread of the Delta variant in Iran. Disease severity was categorized according to the WHO COVID-19 Severity Classification [17]:

- Mild: Symptomatic without evidence of viral pneumonia or hypoxia.
- Moderate: Clinical signs of pneumonia (*e.g.,* fever, cough) but no signs of severe pneumonia, with $SpO_2 \geq$ 90% on room air.
- Severe: Pneumonia with $SpO_2 < 90\%$, respiratory rate > 30/min, or lung infiltrates > 50%.
- Critical: Respiratory failure requiring mechanical ventilation, septic shock, or multi-organ dysfunction.

Patients were excluded if they had any of the following:

1. Pre-existing hematological conditions known to significantly alter CBC parameters, such as anemia (iron deficiency, vitamin B12/folate deficiency, or hemolytic), leukemia, lymphoma, myelodysplastic syndromes, and chronic kidney disease (CKD) with associated erythropoietin deficiency.

2. Ongoing treatments or medications that could affect hematological indices, including:

- Chemotherapy or radiotherapy (which cause bone marrow suppression).
- Immunosuppressants (*e.g.,* corticosteroids, methotrexate).
- Anticoagulants (*e.g.,* warfarin, heparin) or antiplatelet agents (*e.g.,* clopidogrel) due to potential effects on platelet counts.
- Iron supplements or erythropoiesis-stimulating agents (ESAs) within the past 3 months.

The determination of conditions and medications "known to affect hematological parameters" was based on established clinical guidelines (*e.g.,* WHO, NIH) and prior literature documenting their impact on CBC indices.

Patients were categorized into two groups based on their clinical outcome: a survivor group (N=132) and a non-survivor group (N=41) (total: N=173). Non-survivors were defined as patients who died during hospitalization, regardless of severity. Survivors included patients who recovered, regardless of severity [2]. CBC was performed using a Sysmex hematology analyzer (XN-1000) on days 1, 5, and 10 after hospital admission. Patients were categorized based on their clinical presentation and disease severity according to WHO guidelines for the management of COVID-19.

Data collection and classification. Data were extracted from electronic health records of 173 patients, including demographic information, comorbidities, and laboratory results. Primary hematological parameters of interest were hemoglobin (Hb), mean corpuscular hemoglobin (MCH), and mean corpuscular volume (MCV), measured as part of the CBC. Additional markers such as C-reactive protein (CRP) and lactate dehydrogenase (LDH) were recorded for contextual analysis but were not included in the primary statistical evaluation.

Ethical considerations. This study was approved by the Ethics Committee of Urmia University of Medical Sciences (ethics approval number: IR.UMSU.REC.1398.324). Informed consent was waived due to the retrospective nature of the study, and all data were anonymized to protect patient confidentiality.

Statistical analysis. Categorical variables were presented as frequencies and percentages, while continuous variables were presented as means ± standard deviations (SD). Repeated-measures ANOVA was used to compare continuous variables including MCH, MCV, Hb, WBC, CRP, and LDH between the survivor and non-survivor groups. Post hoc pairwise comparisons were performed using the Tukey test to identify specific group differences. Statistical analyses were performed using SPSS version 19. A *P*-value < 0.05 was considered statistically significant.

RESULTS

Demographic and clinical characteristics of the study population. Table 1 presents the demographic and clinical characteristics of the patients stratified by survival outcome.

Clinical analysis. The median age of all patients was 53 years (IQR 22-88 years). The median age was significantly higher in the non-survivor group (60 years, IQR 35-85) compared to the survivor group (52 years, IQR 22-88) (P=0.04). The non-survivor group had a significantly higher proportion of females (80.5% *vs.* 47.7%, $P < 0.001$). The prevalence of diabetes (P=0.327) and hypertension (P=0.797) was not significantly higher in the non-survivor group compared to the survivor group. No significant differences were observed for other comorbidities.

No significant differences were observed in Hb, MCH, and MCV between the non-survivor and survivor groups, as shown in Table 2. However, post hoc analysis using the Tukey test revealed significant differences in mean corpuscular hemoglobin concentration (MCHC) between the non-survivor and survivor groups at both the first and third time points. Significant differences were also observed between the survivor and non-survivor groups for other hematological and clinical parameters, including LDH, oxygen saturation (SpO_2), white blood cell count (WBC), and neutrophil percentage (NEU), as well as lymphocyte percentage (LYM). These results are presented in Table 2.

Table 1. Demographic and clinical characteristics of COVID-19 patients

Characteristics	Total (N=173)	Non-survivors (N=41)	Survivors (N=132)	*P*-value
Age, Median [IQR]	53 [22-88]	60 [35-85]	52 [22-88]	0.04
Gender, n (%)				
Male	77 (44.5%)	8 (19.5%)	69 (52.3%)	<0.001
Female	96 (55.5%)	33 (80.5%)	63 (47.7%)	<0.001
Comorbidities, n (%)				
Diabetes	36 (20.8%)	11 (26.8%)	25 (18.9%)	0.327
Hypertension	54 (31.2%)	12 (29.3%)	42 (31.8%)	0.797
Cardiovascular disease	13 (7.5%)	2 (4.9%)	11 (8.3%)	0.706
CVA	1 (0.6%)	1 (2.4%)	0 (0.0%)	0.237
Chronic kidney disease	2 (1.2%)	1 (2.4%)	1 (0.8%)	0.499

Data are presented as median (interquartile range) for continuous variables and frequency (percentage) for categorical variables. *P*-values were calculated using the Mann-Whitney U test for age and the chi-square test for gender and comorbidities. $P < 0.05$ was considered statistically significant. CVA: Cerebrovascular accident.

Mehranfar et al.

Table 2. Comparison of hematological and clinical parameters between COVID-19 survivors and non-survivors at different time points

Factor	Survivors (N=132)	Non-survivors (N=41)	P-value
CRP (mg/L)			
(1)	42.34 ± 31.31	52.19 ± 32.23	NS
(2)	26.91 ± 25.81	25.88 ± 29.72	NS
(3)	10.92 ± 14.77	18.98 ± 31.88	0.03
Hb (g/dL)			
(1)	13.62 ± 1.87	13.18 ± 2.73	NS
(2)	13.25 ± 1.70	12.99 ± 2.27	NS
(3)	13.44 ± 1.82	12.84 ± 2.62	NS
LDH (U/L)			
(1)	507.79 ± 185.10	725.95 ± 316.94	<0.001
(2)	463.46 ± 214.58	952.00 ± 491.58	<0.001
(3)	403.14 ± 200.35	956.10 ± 542.38	<0.001
LYM (%)			
(1)	20.55 ± 9.42	15.56 ± 7.37	0.002
(2)	15.33 ± 9.13	7.58 ± 4.67	<0.001
(3)	15.25 ± 8.35	10.05 ± 8.20	<0.001
MCH (pg)			
(1)	29.24 ± 2.73	28.99 ± 2.29	NS
(2)	29.62 ± 2.82	29.40 ± 2.04	NS
(3)	29.72 ± 2.78	29.66 ± 2.12	NS
MCHC (g/dL)			
(1)	33.11 ± 1.69	32.33 ± 1.49	0.009
(2)	33.28 ± 1.45	32.87 ± 1.35	NS
(3)	33.62 ± 1.48	32.80 ± 1.63	0.003
MCV (fL)			
(1)	88.52 ± 6.39	89.54 ± 6.64	NS
(2)	88.80 ± 6.54	89.32 ± 5.12	NS
(3)	88.35 ± 6.70	90.27 ± 6.80	NS
NEU (%)			
(1)	75.13 ± 10.08	80.49 ± 8.51	0.002
(2)	80.44 ± 9.94	88.56 ± 5.68	<0.001
(3)	79.90 ± 9.19	85.19 ± 7.71	<0.001
SpO₂ (%)			
(1)	89.73 ± 4.39	82.47 ± 8.19	<0.001
(2)	91.67 ± 3.57	86.30 ± 7.74	<0.001
(3)	93.48 ± 2.96	83.55 ± 13.08	<0.001
WBC (×10⁹/L)			
(1)	6.05 ± 3.48	8.07 ± 4.72	0.004
(2)	8.32 ± 4.33	11.71 ± 5.05	<0.001
(3)	9.50 ± 4.39	14.51 ± 8.49	<0.001

Data are presented as mean ± standard deviation (SD). *P*-values were calculated using repeated-measures ANOVA followed by Tukey post hoc test. $P < 0.05$ was considered statistically significant. Time points represent measurements taken on day 1 (1), day 5 (2), and day 10 (3) after hospital admission. CRP, C-reactive protein; LDH, lactate dehydrogenase; LYM, lymphocyte count; SpO₂, oxygen saturation; NEU, neutrophil count; HB, hemoglobin; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; WBC, white blood cell count; NS, not significant ($P > 0.05$).

DISCUSSION

The rapid emergence of COVID-19 necessitates early detection to effectively predict disease severity and prognosis. COVID-19 presents with a wide spectrum of severity, ranging from asymptomatic or mild infections to severe and critical illness, including life-threatening complications [17]. Due to the lack of specific antiviral treatments for COVID-19, the primary management approach has focused on supportive care. While some effective antiviral therapies for COVID-19 are now available (*e.g.*, for early-stage disease), early diagnosis and prompt respiratory support remain crucial for mitigating severe disease and reducing mortality. The identification of biomarkers that can predict disease severity and progression in hospitalized COVID-19 patients is crucial for optimizing resource allocation and guiding treatment decisions. Furthermore, readily available blood tests, such as CBC, can provide valuable information for early diagnosis and risk stratification of COVID-19 patients, complementing other diagnostic methods and clinical assessments [18].

Numerous studies have investigated hematological abnormalities in COVID-19 patients since the start of the pandemic. These studies have largely focused on identifying hematological markers associated with different levels of COVID-19 severity [19-22]. Further research is warranted to elucidate the relationship between specific hematological markers and clinical outcomes, including mortality, in COVID-19 patients. This study comprehensively analyzed the demographic, clinical, and laboratory characteristics of COVID-19 patients with varying degrees of severity admitted to Taleghani Hospital in Urmia.

In this study, the median age was significantly higher in the non-survivor group compared to the survivor group ($P<0.05$), suggesting that older age is a risk factor for severe COVID-19 and mortality. Aging is associated with physiological and immunological changes that can increase susceptibility to respiratory infections, including COVID-19, and impair the ability to recover from severe illness. These age-related changes contribute to the higher risk of severe outcomes and mortality observed in older COVID-19 patients. This finding is consistent with previous studies demonstrating an increased risk of mortality in older COVID-19 patients [23-25].

The results of laboratory tests, particularly hematological parameters, in COVID-19 patients can be influenced by the initial severity of the disease at presentation. One potential mechanism underlying these hematological changes observed at admission and during hospitalization is the direct or indirect effect of SARS-CoV-2 on bone marrow function. The virus can infect bone marrow cells, disrupting hematopoiesis and leading to abnormal blood cell production [16]. Additionally, the immune response triggered by the infection can result in the destruction of blood cells, contributing to the observed hematological abnormalities. However, it is important to acknowledge that disease severity in COVID-19 patients can fluctuate during hospitalization, making it challenging to define clear-cut categories based on a single time point.

MCH reflects the average amount of hemoglobin per red blood cell (RBC). Consequently, low hemoglobin levels are associated with reduced MCH values. Yousif *et al*. (2020) reported that lower hemoglobin levels were associated with poorer outcomes and delayed recovery in COVID-19 patients [26]. Our study observed slightly lower hemoglobin levels in the non-survivor group compared to the survivor group, though not statistically significant ($P>0.05$). This trend aligns with prior reports but does not confirm an association with severe COVID-19. A study by Bahramikia *et al*. (2022) investigated hematological indices in COVID-19 patients admitted to Imam Khomeini Hospital. Their findings revealed that hemoglobin levels were significantly decreased in men aged 70-90 years, while no significant differences were observed in women across all age groups. Our study showed slightly lower levels of hemoglobin, MCV, and MCH in the non-survivor group, though not significant ($P>0.05$), partially aligning with Bahramikia *et al*.'s (2022) findings on hemoglobin reductions in older male COVID-19 patients [27]. This finding aligns with Jalil *et al*. (2021), who observed reduced MCV and MCH in COVID-19 patients compared to healthy controls. They suggested that this could be attributed to impaired erythropoiesis, iron dysregulation, or the effects of inflammatory cytokines [28]. Consistent with our results, Luo *et al*. (2020) also reported a reduction in MCV and MCH among COVID-19 patients [29]. This agreement between studies strengthens the evidence suggesting that

these hematological changes may be a common feature of COVID-19 infection and could potentially serve as an early diagnostic marker.

In severe COVID-19 patients, Hb synthesis can be impaired due to factors such as malnutrition or iron deficiency (*e.g.*, reduced appetite, gastrointestinal symptoms, or inflammatory cytokine effects). While prolonged hypoxia typically stimulates erythropoietin production and erythroid hyperplasia to compensate for reduced oxygen-carrying capacity, this compensatory mechanism may be insufficient in some COVID-19 patients, leading to the release of reticulocytes with low hemoglobin content [30]. Several studies have reported the presence of increased numbers of immature red blood cells (reticulocytes) in peripheral blood smears of COVID-19 patients [22, 31]. This finding highlights the significance of increased reticulocytes in COVID-19 (*e.g.*, as a bone marrow response to hypoxia, accelerated erythropoiesis due to inflammation, or a potential marker for using reticulocyte count to assess disease severity). Prior studies suggest that reticulocyte counts may increase with COVID-19 progression, potentially contributing to elevated MCV in severe cases [30]. Further research is needed to confirm this in our population. The increased number of larger reticulocytes in circulation can contribute to an elevated MCV. Additionally, the presence of a heterogeneous population of red blood cells, including reticulocytes and mature erythrocytes, may also affect the red cell distribution width (RDW). However, the relationship between reticulocytosis and RDW in COVID-19 is complex and requires further investigation. Wang *et al*. (2020) reported that patients with mild COVID-19 had higher MCV values compared to those with severe disease. However, they also observed that severe patients had reduced MCV and MCH. This apparent contradiction in MCV values may reflect the complex interplay of factors, such as inflammation and nutritional deficiencies, affecting red blood cell indices in COVID-19. While increased reticulocyte counts can contribute to higher MCV, other factors, such as nutritional deficiencies and inflammation, may also play a role [30]. Wang *et al*. (2020) proposed that reticulocytes are not the sole determinant of RDW elevation in patients with severe COVID-19. They suggested that low circulating nutrients, which are often observed in critically ill patients, could lead to increased instability of the RBC membrane, contributing to greater variability in red blood cell size and thus a higher RDW [30]. Although not a primary focus, significant differences in MCHC were observed and warrant further exploration.

While primary indices (MCH, MCV) showed no significant differences, exploratory analysis revealed significant MCHC variations. Although the study primarily focused on MCH and MCV, the observed differences in MCHC between survivors and non-survivors (at admission and day 10) may reflect underlying erythrocyte dysfunction or iron metabolism

Mehranfar et al.

disturbances in severe COVID-19. Lower MCHC values in non-survivors could indicate impaired hemoglobin synthesis due to inflammation or nutritional deficits, aligning with prior reports of COVID-19-associated hematological dysregulation [30, 31]. While MCHC was not initially a primary focus, its association with outcomes suggests its potential utility as a supplementary marker for risk stratification, warranting further investigation.

This study investigated hematological indices in COVID-19 patients admitted to Taleghani Hospital in Urmia, Iran, during the Delta variant wave (March–September 2021). While prior studies have explored similar markers in diverse populations and earlier phases of the pandemic, our focus on a specific demographic (Iranian patients) and variant (Delta) adds nuance to the existing literature. The Delta variant is associated with higher virulence and altered clinical manifestations, which may influence hematological responses differently compared to earlier strains. For instance, the lack of significant differences in MCH and MCV between survivor and non-survivor groups in our study contrasts with some prior reports, possibly reflecting variant-specific pathophysiology or population-specific factors such as genetic predispositions, prevalent comorbidities (*e.g*., higher rates of diabetes and hypertension in our cohort), or regional healthcare practices.

As a retrospective, single-center study, our findings may be influenced by selection bias or local treatment protocols, limiting generalizability. The non-significant results for MCH/MCV suggest these markers may have limited prognostic value in Delta-variant patients in this context or that their utility is context-dependent. Despite these limitations, our study highlights the importance of contextualizing hematological markers by variant and population. The significant differences in MCHC, LDH, and neutrophil counts align with global trends, reinforcing their robustness as prognostic tools. However, the non-significance of MCH/MCV underscores the need for further research into how viral evolution and regional factors modulate hematological responses.

In conclusion, this study investigated the relationship between several hematological parameters, including MCH, MCHC, and COVID-19 severity in patients admitted to Taleghani Hospital. Severe COVID-19 is characterized by uncontrolled inflammation and activation of the coagulation cascade, which can significantly impact various hematological indices by affecting red blood cell production, platelet function, or leukocyte function. While MCH did not differ significantly between groups, lower MCHC levels at days 1 (P=0.009) and 10 (P=0.003) were associated with severe outcomes (P<0.01). These findings suggest MCHC may serve as a supplementary prognostic marker, warranting further investigation. Further research is needed to validate these findings in larger, diverse populations and to assess the clinical utility of incorporating these parameters into risk stratification and treatment algorithms for COVID-19.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest associated with this manuscript.

AI DISCLOSURE

No artificial intelligence (AI) tools were used in the preparation, analysis, or writing of this manuscript.

DATA AVAILABILITY

All relevant data supporting the findings of this study are contained within the manuscript itself.

AUTHORS' CONTRIBUTION

SM: Investigation; Writing – original draft; Writing – review & editing; Project administration. AY: Investigation; Writing – review & editing. MH: Investigation; Writing – review & editing. ML: Conceptualization; Supervision; Validation; Writing – review & editing.

ETHICS STATEMENT

Ethical approval for this retrospective study was obtained from the Ethics Committee of Urmia University of Medical Sciences (IR.UMSU.REC.1398.324). The committee waived the requirement for informed consent. All data used in this study were anonymized to protect patient privacy.

REFERENCES

1. Sabbaghian M, Gheitasi H, Fadaee M, Javadi Henafard H, Tavakoli A, Shekarchi AA, et al. Human cytomegalovirus microRNAs: strategies for immune evasion and viral latency. Arch Virol. 2024; 169 (8): 157.

2. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020; 8 (5): 475-81.

3. Gheitasi H, Sabbaghian M, Fadaee M, Mohammadzadeh N, Shekarchi AA, Poortahmasebi V. The relationship between autophagy and respiratory viruses. Arch Microbiol. 2024; 206 (4): 136.

4. World Health Organization. Iran (Islamic Republic of): WHO Coronavirus (COVID-19) Dashboard. Geneva: World Health Organization; 2023 [cited 2024 Dec 31]. Available from: https://www.who.int/countries/ir.

5. Struyf T, Deeks JJ, Dinnes J, Takwoingi Y, Davenport C, Leeflang MM, et al. Signs and symptoms to determine if a patient presenting in primary care or hospital outpatient settings has COVID-19. Cochrane Database Syst Rev. 2022 (5): CD013665.

6. Li X, Xu S, Yu M, Wang K, Tao Y, Zhou Y, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. J Allergy Clin Immunol. 2020; 146 (1): 110-8.

7. Zhao Q, Meng M, Kumar R, Wu Y, Huang J, Deng Y, et al. Lymphopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: a systematic review and meta-analysis. Int J Infect Dis. 2020; 96: 131-5.

8. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020; 46 (5): 846-8.

9. Wang F, Nie J, Wang H, Zhao Q, Xiong Y, Deng L, et al. Characteristics of peripheral lymphocyte subset alteration in COVID-19 pneumonia. J Infect Dis. 2020; 221 (11): 1762-9.

10. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020; 382 (18): 1708-20.

11. Liu F, Xu A, Zhang Y, Xuan W, Yan T, Pan K, et al. Patients of COVID-19 may benefit from sustained lopinavir-combined regimen and the increase of eosinophil may predict the outcome of COVID-19 progression. Int J Infect Dis. 2020; 95: 183-91.

12. Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy. 2020; 75 (7): 1730-41.

13. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020; 395 (10223): 507-13.

14. Mo P, Xing Y, Xiao Y, Deng L, Zhao Q, Wang H, et al. Clinical characteristics of refractory coronavirus disease 2019 in Wuhan, China. Clin Infect Dis. 2021; 73 (11): e4208-13.

15. Qian GQ, Yang NB, Ding F, Ma AHY, Wang ZY, Shen YF, et al. Epidemiologic and clinical characteristics of 91 hospitalized patients with COVID-19 in Zhejiang, China: a retrospective, multi-centre case series. QJM. 2020; 113 (7): 474-81.

16. 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.

17. World Health Organization. Clinical management of COVID-19: interim guidance, 27 May 2021. Geneva: World Health Organization; 2021. Report No.: WHO/2019-nCoV/clinical/2021.2.

18. World Health Organization. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). Geneva: World Health Organization; 2020 Feb 16-24 [cited 2025 Apr 01]. Available from: https://www.who.int/publications/i/item/report-of-the-who-china-joint-mission-on-coronavirus-disease-2019-(covid-19)

19. Buoro S, Di Marco F, Rizzi M, Fabretti F, Lorini FL, Cesa S, et al. Papa Giovanni XXIII Bergamo hospital at the time of the COVID-19 outbreak: letter from the warfront. Int J Lab Hematol. 2020; 42 (Suppl 1): 8-10.

20. 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 (6): E131-4.

21. 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 Infect Dis. 2020; 71 (15): 762-8.

22. Mitra A, Dwyre DM, Schivo M, Thompson GR 3rd, Cohen SH, Ku N, et al. Leukoerythroblastic reaction in a patient with COVID-19 infection. Am J Hematol. 2020; 95 (8): 999-1000.

23. Wu C, Chen X, Cai Y, Zhou X, Xu S, Huang H, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med. 2020; 180 (7): 934-43.

24. 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 (10229): 1054-62.

25. Du RH, Liang LR, Yang CQ, Wang W, Cao TZ, Li M, et al. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. Eur Respir J. 2020; 55 (5): 2000524.

26. Yousif NG, Altimimi AN, Al-Amran FG, Lee JA, Al-Fadhel SM, Hussien SR, et al. Hematological changes among coronavirus-19 patients: a longitudinal study. Syst Rev Pharm. 2020; 11 (5): 62-6.

27. Bahramikia S, Gavyar PHH, Amiri S. Evaluation of different biochemical factors in patients with coronavirus disease in Imam Khomeini hospital of Selseleh County (Lorestan Province). Jundishapur Sci Med J. 2022; 20 (6): 528-35.

28. Jalil AT, Shanshool MT, Dilfy SH, Saleh MM, Suleiman AA. Hematological and serological parameters for detection of COVID-19. J Microbiol Biotechnol Food Sci. 2021; 10 (4): e4555.

29. Luo E, Zhang D, Luo H, Liu B, Zhao K, Zhao Y, et al. Treatment efficacy analysis of traditional Chinese medicine for novel coronavirus pneumonia (COVID-19): an empirical study from Wuhan, Hubei Province, China. Chin Med. 2020; 15: 34.

30. Wang C, Zhang H, Cao X, Deng R, Ye Y, Fu Z, et al. Red cell distribution width (RDW): a prognostic indicator of severe COVID-19. Ann Transl Med. 2020; 8 (19): 1230.

31. Zini G, Bellesi S, Ramundo F, d'Onofrio G. Morphological anomalies of circulating blood cells in COVID-19. Am J Hematol. 2020; 95 (7): 870-2.