ORIGINAL ARTICLE

Medical Journal of Western Black Sea
Batı Karadeniz Tıp Dergisi

Med J West Black Sea 2021;5(3): 391-400
DOI: 10.29058/mjwbs.984490

Abnormalities of Peripheral Blood Parameters in Hospitalized Patients with COVID-19: A Temporal Change Analysis in Relation to Survival

COVID-19 Nedeniyle Takip Edilen Hastalarda Kan Parametrelerindeki Zamansal Anormalliklerin Sağkalım Üzerine Etkisi: Retrospektif Bir Çalışma

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Cite this article as: Aslaner Ak M, et al. Abnormalities of peripheral blood parameters in hospitalized patients with COVID-19: A temporal change analysis in relation to survival. Med J West Black Sea. 2021;5(3):391-400.

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Received
19.08.2021
Revision
22.10.2021
Accepted
25.10.2021

ABSTRACT

Aim: This study aimed to investigate the abnormalities and temporal changes in peripheral blood parameters, with particular emphasis on platelet indices, in relation to survival status among hospitalized COVID-19 patients.

Material and Methods: A total of 149 patients hospitalized with the diagnosis of COVID-19 were included. Laboratory parameters were recorded on initial admission, 3rd, 7th and last day of hospitalization, and post-discharge first month and included hemoglobin (Hb, g/dL), hematocrit (%), white blood cell (WBC) (x109/L), platelet (cells/mm^3) and lymphocyte counts (cells/µL), mean platelet volume (MPV, fL), platelet distribution width (PDW, %), plateletcrit (PCT,%) and platelet-to-lymphocyte ratio (PLR), and analysed.

Results: Overall, 139 (93.9%) patients survived. Survivors vs. non-survivors had significantly higher median levels for Hb at initial admission (13.3 vs. 12.2 g/dL, p=0.023), 3rd day (12.6 vs. 11.7 g/dL, p=0.033) and 7th day of hospitalization (12.5 vs. 9.8 g/dL, p=0.014) and for lymphocyte counts at initial admission (1200 vs. 800 cells/µL, p=0.014) and 3rd day (1400 vs. 1200 cells/µL, p=0.043) of hospitalization. They also had significantly lower WBC counts at initial admission (5800 vs. 7900 x109/L, p=0.014), 3rd day (5400 vs. 6047 x109/L, p=0.007) and 7th day (6100 vs. 8400 x109/L, p=0.040) and last day (6200 vs. 17700 x109/L, p=0.018) of hospitalization and lower PLR at initial admission (165 vs. 294.5, p=0.002) and 3rd hospitalization day (150 vs. 223, p=0.003).

Conclusion: In conclusion, our findings emphasize clinical significance of dynamic monitoring of peripheral blood parameters, as combined with PLR, in assisting clinicians to identify COVID-19 patients with increased risk of worse outcomes.

Keywords: COVID-19, Hospitalization, Peripheral blood, PLR, Survival

ÖZ

Amaç: Bu çalışmada, hastanede yatarak tedavi gören Covid-19 hastalarında, özellikler trombosit parametrelerindeki değişimlerin diğer periferik kan parametreleri ve zamansal değişimle birlikte sağ kalım üzerine etkisi araştırılmıştır.

Gereç ve Yöntemler: Covid-19 tanısı ile hastaneye yatırılarak tedavi edilen 149 hasta çalışmaya dahil edildi. Başvuru anında, hastaneye yatışın üçüncü, yedinci ve son günlerinde ve taburculuk sonrası birinci ayda kaydedilen laboratuvar parametreleri, hemoglobin (Hb, g/dL), hematokrit (%), beyaz kan hücresi (lökositx109/L), trombosit (hücre/mm3) sayımı, lenfosit (hücre/µL) sayımı, ortalama trombosit hacmi (fL), trombosit dağılım genişliği (%), plateletkrit (%) ve platelet lenfosit oranı idi.

Bulgular: Toplamda, 139 hasta (%93,9) taburculuk sonrası birinci ayda hayatta idi. Hayatta kalan hastalarda, hayatta olmayanlara göre ilk başvuru (13,3 ve 12,2 g/dL, p=0,023) ve yatışın üçüncü (12,6 ve 11,7 g/dL, p=0,033) ve yedinci (12,5 ve 9,8 g/dL, p=0,014) günlerinde saptanan medyan Hb düzeyleri ile ilk başvuru (1200 ve 800 hücre/µL, p=0, 014) ve üçüncü yatış gününe (1400 ve 1200 hücre/µL, p=0,043) ait lenfosit sayıları anlamlı şekilde daha yüksekti. Hayatta kalan hastalarda, ilk başvuru (5800 ve 7900 x109/L, p=0, 014), hastaneye yatışın üçüncü (5400 ve 6047 x109/L, p=0,007), yedinci (6100 ve. 8400 x109/L, p=0, 040) ve son (6200 ve 17700 x109/L, p=0, 018) günlerinde saptanan lökosit değerleri ve ilk başvuru (165 ve 294,5, p=0,002) ve yatışın üçüncü günü (150 ve 223, p=0.003) saptanan PLR değerleri anlamlı şekilde daha düşük bulundu.

Sonuç: Sonuç olarak, bulgularımız periferik kandaki değişimlerin, özellikle de platelet/lenfosit oranının takibinin klinik önemine ve kötü prognostik seyirli COVID-19 hastaların tespitinde hekimlere öngörüde bulunma açısından yararlı olabileceğine işaret etmektedir.

Anahtar Sözcükler: COVID-19, Hospitalizasyon, Periferik kan, PLR, Sağkalım

INTRODUCTION

The coronavirus disease-2019 (COVID-19) is a systemic infection with a significant impact on the hematopoietic system and hemostasis (1), while immune system and severe inflammatory response, with particular role of cytokine storm, are the main factors that determine the progression and prognosis of COVID-19 (2-4). Hematological changes, including lymphopenia and thrombocytopenia as well as abnormal coagulation, have been reported in patients with COVID-19 (5-8). Hence, consistent with their well-known role in inflammation and immune regulation for a variety of disease, assessment of changes in lymphocyte count and platelet levels and the platelet-to-lymphocyte ratio (PLR) as a new type of inflammation index mainly reflecting both aggregation and inflammatory pathways, have been suggested to have clinical value in the management of COVID-19 (2,9-11).

Comprehensive analysis of the laboratory markers with differences in temporal changes is considered to enable predicting disease severity and progression in COVID-19 patients, allowing timely provision of a targeted treatment (12). However, the dynamic evaluation of blood routine parameters with serial measurements during the course of the disease in relation to their association with adverse COVID-19 outcome have not yet been extensively investigated (1,8,12,13).

Therefore, this study was designed to investigate the abnormalities and temporal changes in peripheral blood parameters, with particular emphasis on platelet indices, in relation to survival status among hospitalized COVID-19 patients.

MATERIAL and METHODS

Study Population

A total of 149 patients hospitalized with the diagnosed of COVID-19 were included in this retrospective study conducted between March 2020 and August 2020 at a tertiary care hospital in Turkey. Adult (≥18 years of age) patients with laboratory confirmation of SARS-CoV-2 on real-time reverse transcription-polymerase chain reaction (RT-PCR) analysis and/or SARS-CoV-2 IgG positive patients were included in this study. Presence of any hematologic disease and/or malignancy was the exclusion criterion of the study.

Assessments

Data on patient demographics, comorbid disease, need for oxygen support, requirement for intensive care stay during hospitalization, length of hospital stay (LOS, days) and laboratory parameters (on initial admission, 3rd day of hospitalization, 7th day of hospitalization, pre-discharge and post-discharge 1st month) including hemoglobin (Hb, g/dL), hematocrit (%), WBC (x10^9/L), platelet (cells/mm^3) and lymphocyte counts (cells/µL), mean platelet volume (MPV, fL), platelet distribution width (PDW, %), plateletcrit (PCT,%) and, platelet-to-lymphocyte ratio (PLR) were recorded in each patient.

Statistical Analysis

Statistical analysis was made using MedCalc Statistical Software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2013). Shapiro Wilks test was used to investigate normal distribution. Descriptive statistics were reported for categorical data. Friedman test was used to evaluate the change between more than 2 dependent continuous variables over time. Wilcoxon test with Bonferroni correction were used as Post Hoc tests. Mann-Whitney U test was used to compare two independent non-normally distributed variables (14). Data were expressed as "mean ± standard deviation (SD), median (min-max) and percent (%) where appropriate. $p<0.05$ was considered statistically significant.

RESULTS

Patient Demographics and Hospitalization Outcome

Mean±SD patient age was 55.6±16.3 years (range, 12 to 93 years) and males composed 53.0% of study population. Comorbidity was evident in 50.3% of the patients, need for oxygen support and ICU stay occurred in 23.6% and 18.2% of the patients respectively. LOS was median nine days (range, 3 - 90 days) and 139 (93.9%) patients survived (Table 1).

No significant difference was noted between survivors and non-survivors in terms gender (males: 51.1% vs. 77.8%, p=0.172), presence of comorbidity (48.2 vs. 77.8%, p=0.166) and LOS (median (min-max) 10.5 (4-90) days vs. 9 (3-65) days, p=0.697). Patient age was significantly higher among non-survivors than survivors (median 73 vs. 56 years, p=0.001).

Temporal Change in Laboratory Parameters in the Overall Study Population

A significant decrease was noted in Hb levels from initial admission to 3rd day, 7th day and the last day of hospitalization (p<0.001 for each). Post-discharge first month Hb levels were significantly higher than values obtained at hospital discharge (p<0.001) (Table 2, Figure 1).

Table 1: Patient demographics and hospitalization characteristics.

		Results
Age (year)	Mean±SD	55.6±16.3
	Median (min-max)	57 (21-93)
Gender, n (%)		
Female		70 (47.0)
Male		79 (53.0)
Comorbidity, n (%)		
Yes		75 (50.3)
No		74 (49.7)
Need for oxygen support, n (%)		
Yes		35 (23.6)
No		113 (76.4)
Need for ICU stay, n (%)		
Yes		27 (18.2)
No		121 (81.8)
Survivorship status, n (%)		
Non-survivor		9 (6.1)
Survivor		139 (93.9)
Length of hospitalization	mean±SD	12.8±11.8
	median (min-max)	9 (3-90)

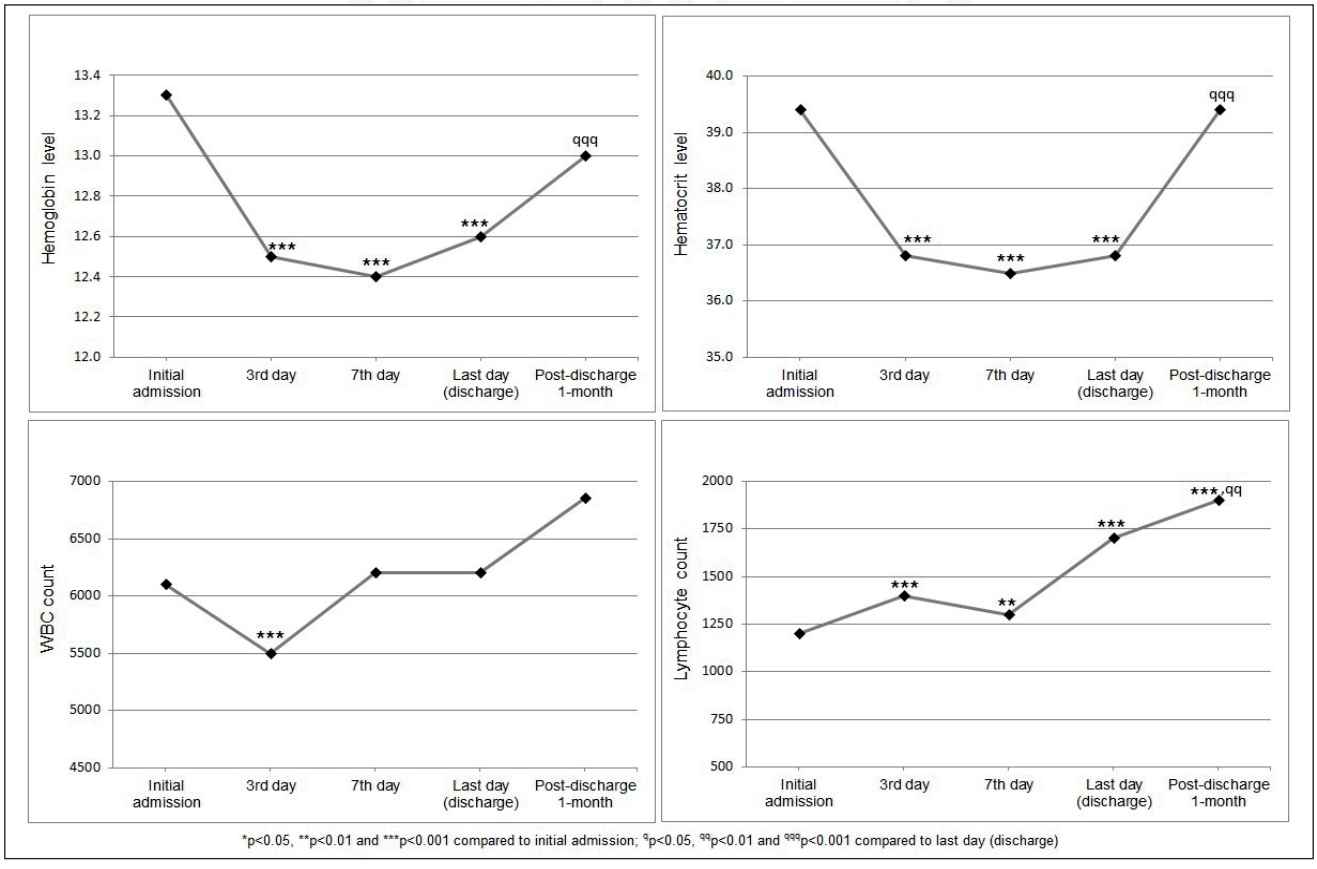

Figure 1: Temporal change in hemoglobin, hematocrit, WBC and lymphocyte values in the overall study population.

WBC counts on 3rd day of hospitalization were significantly lower than those on initial admission (p<0.001), while WBC counts at hospital discharge were significantly higher than 3rd day and 7th day values (p<0.001 for each) (Table 2, Figure 1).

Lymphocyte counts on 3rd day , 7th day and last day of hospitalization were significantly higher than those on initial admission (p<0.001 for each), while lymphocyte counts at post-discharge 1st month were significantly higher than those obtained at hospital discharge (p<0.001) (Table 2, Figure 1).

Platelet counts on 7th day and last day of hospitalization were significantly higher than those on initial admission (p<0.001 for each), while platelet counts at post-discharge first month were significantly lower than those obtained at hospital discharge (p<0.001) (Table 2, Figure 2).

MPV values at discharge were significantly lower than MPV values on initial admission (p<0.001), and on 3rd day (p<0.01) and 7th day (p<0.001) of hospitalization (Table 2, Figure 2).

PCT values on 3rd day , 7th day and last day of hospitalization were significantly higher than those on initial admission (p<0.001 for each), while PCT values at hospital discharge were also significantly higher than 3rd day (p<0.01), 7th day (p<0.001) and post-discharge first month (p<0.001) values (Table 2, Figure 2).

PLR at post-discharge first month was significantly lower than PLR on initial admission (p<0.001) and on 7th day (p<0.01) and last day (p<0.01) of hospitalization, and PLR values were significantly higher on 7th vs. 3rd day of hospitalization (p<0.01), while no significant change was noted in PLR from initial admission during hospitalization (Table 2, Figure 2).

Comparison of Laboratory Parameters According to Survivorship Status

In survivors, Hb and hematocrit levels were significantly lower but lymphocyte counts and PCT values were significantly higher on 3rd and 7th days of hospitalization compared to initial values (p<0.001 for each). WBC counts on 3rd day were significantly lower than initial values, platelet counts

Table 2: Temporal change in laboratory parameters during hospitalization and post-discharge

	Initial admission	Hospitalization			Post-discharge 1st month	p value[1]
		3rd day	7th day	Last day (discharge)		
Parameters						
Hemoglobin (g/dL) 13.3 (7.4-18.2)	13.1±1.9	12.5±1.7* 12.5 (6.5-16.8)	12.2±1.9*,w 12.4 (7.8-16.1)	12.4±1.7*,ww 12.6 (7.7-16.3)	12.8±1.8 13 (7.6-16.9)	**<0.001**
Hematocrit (%) 39.4 (23.1-55.2)	38.8±5.3	36.7±4.8* 36.8 (19.7-48.9)	36.1±5.2*,ww 36.5 (23.7-47.5)	36.8±4.8*,ww 36.8 (22.2-48.1)	39.0±5.0 39.4 (25.9-50.6)	**<0.001**
WBC ($x10^9$/L) 6100 (2000-22100)	6849±3165	6221±2785* 5500 (1800-18300)	6788±3007w 6200 (2800-19600)	6794±2913q,t 6200 (3000-26200)	6937±1961q 6850 (2700-11600)	**<0.001**
Platelet ($cells/mm^3$) 209000 (90000-503000)	222416±72380	233597±82534 219000 (85000-460000)	271162±101120*, q 250000 (81000-569000)	302436±116289*,q,w,tt 285000 (120000-710000)	259892±79377*,q 252500 (110000-628000)	**<0.001**
Lymphocyte (cells/μL) 1200 (200-3600)	1291±663	1462±643* 1400 (200-4000)	1381±631*,ww 1300 (100-3600)	1746±703*,q,w,tt 1700 (200-4700)	1875±557*,q 1900 (400-3200)	**<0.001**
MPV (fL) 8.9 (7-12.2)	9.0±1.0	9.1±1.0 9 (6.6-12.3)	8.9±0.9q,ww 8.9 (7.1-11.9)	8.8±1.0*,q,tt 8.8 (6.5-11.6)	8.7±0.9*,q 8.6 (6.3-11.2)	**<0.001**
PDW (%) 16.9 (16-18.8)	17±0.6	17±0.5 16.9 (15.9-18.6)	17.1±0.6 17 (16-19.9)	17.1±0.6 17 (15.8-19.8)	17±0.5 16.9 (15.8-18.5)	0.717
Plateletcrit (%) 0.19 (0.02-0.44)	0.2±0.07	0.21±0.07* 0.19 (0.08-0.42)	0.24±0.09*,q 0.23 (0.08-0.51)	0.26±0.09*,q,w,tt 0.24 (0.03-0.57)	0.22±0.06*,q 0.22 (0.11-0.53)	**<0.001**
PLR 175 (62-880)	223.1±153.8	194.5±139 153.7 (51-1255)	247±204.7q,w 193 (49-1840)	212.51±191.84w 164.5 (30-1990)	152.7±77.3* 135.5 (70-555)	**<0.001**

Data are shown as mean±SD and median (min-max), **WBC:** White blood cell, **MPV:** Mean platelet volume, **PDW:** Platelet distribution width, **PLR:** Platelet-to-lymphocyte ratio.

[1]Friedman test; *p<0.001 compared to values on initial admission, qp<0.001 compared to values on 3rd hospitalization day; tp<0.01 and ttp<0.001 compared to values on 7th hospitalization day; wp<0.01 and wwp<0.001 compared to values on post-discharge 1st month (Wilcoxon test with Bonferroni correction, p<0.005)

on 7th day were significantly higher than initial and 3rd day values, and 3rd day PLR was significantly lower than initial values and 7th day values (p<0.001 for each) (Table 3).

Among non-survivors no significant change was noted in any of laboratory parameters from initial admission to 3rd and 7th days of hospitalization (Table 3).

When compared to non-survivors; survivors had significantly higher Hb levels at initial admission (p=0.023), 3rd day of hospitalization (p=0.033) and 7th day of hospitalization (p=0.014) and , significantly higher lymphocyte levels at initial admission (p=0.014) and 3rd day (p=0.043) of hospitalization (Table 3, Figure 3). Survivors vs. non-survivors had significantly lower WBC counts at initial admission (p=0.014), 3rd day (p=0.007) and 7th day (p=0.040), and last day (p=0.018) of hospitalization (Table 3, Figure 3)

Survivors vs. non-survivors had significantly lower PLR at initial admission (p=0.002) and 3rd day (p=0.003) of hospitalization. No significant difference was noted in platelet, MPV and PCT values with respect to survivorship status (Table 3, Figure 4).

DISCUSSION

Our findings in a retrospective cohort of hospitalized COVID-19 patients revealed difference between survivors and non-survivors in terms of temporal changes in blood parameters over time during hospitalization. Specifically, inpatient follow up was associated with a significant decrease in Hb and hematocrit levels but increase in platelet and lymphocyte counts and PCT along with an initial decline and then increase in WBC counts and PLR until discharge, but only in survivors. Higher Hb levels and lymphocyte counts and lower PLR during early hospitalization and lower WBC counts during the entire period of hospitalization were associated with increased likelihood of survival in COVID-19 patients. No significant impact of platelet count, MPV or PCT on initial admission or during hospitalization days was noted on the survival status.

Likewise, in a study by Ouyang et al. on 94 laboratory test variables in 82 survivors and 25 non-survivors with COVID-19, authors reported significant increase in WBC count, neutrophil count, MPV and PDW, whereas significant

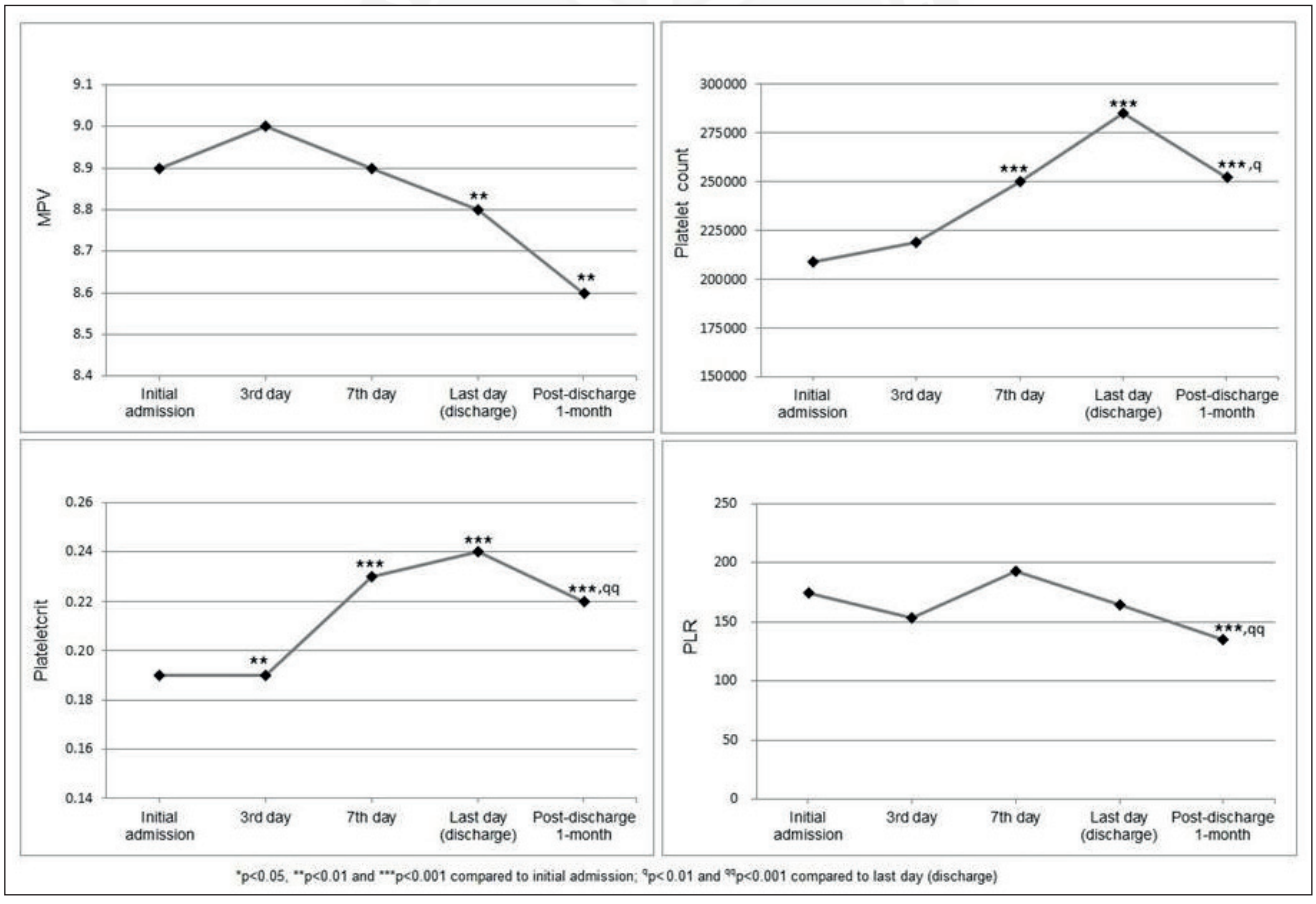

Figure 2: Temporal change in platelet, plateletcrit, MPV and PLR values in the overall study population.

decrease in lymphocyte count, hemoglobin and hematocrit in non-survivors compared with survivors (12). The authors also noted that temporal changes in lymphocyte, neutrophil and platelet counts as well as PCT to be remarkably different between survivors and non-survivors throughout the course of the disease, and thus these variables could be used as laboratory markers to identify COVID-19 patients with a high vs. low risk of mortality at any time point during their treatment course (12).

In addition, in a study by Ding et al. regarding the correlation between the time of hospitalization and hematological blood parameter follow-ups in hospitalized COVID-19 patients, the authors reported that the lymphocyte count always tended to decrease in severe patients along with an increasing tendency in the number of platelets in non-severe patients during the follow-up period (15). Other studies in COVID-19 patients also emphasized the lower counts of WBC, lymphocytes, eosinophils, platelets, and hemoglobin in COVID-19 patients vs. control subjects as well as increasing trends in WBC, neutrophil count and decreasing trends in lymphocyte count in non-survivors vs. survivors (6,13,16-18).

In this regard, significantly lower hemoglobin, hematocrit and lymphocyte counts and higher WBC and PLR values in non-survivors vs. survivors on initial admission and within the first 7 days of hospitalization in our study support the

Table 3: Comparison of laboratory parameters during hospitalization according to survivorship status

Parameters		Initial admission Median (min-max)	Hospitalization Median (min-max)		p value[1]
			3rd day	7th day	
Hemoglobin (g/dL)	Non-survivor	12.2 (7.4-14)	11.7 (6.5-13.5)	9.8 (7.8-13)	0.311
	Survivor	13.3 (7.9-18.2)	12.6 (7.6-16.8)*	12.5 (7.8-16.1)*	**<0.001**
	p value[2]	**0.023**	**0.033**	**0.014**	
Hematocrit (%)	Non-survivor	36.1 (23.1-40.9)	35 (19.7-39.9)	30.2 (23.7-39.9)	0.438
	Survivor	39.6 (24.2-55.2)	36.8 (22.6-48.9)*	36.6 (23.8-47.5)*	**<0.001**
	p value[2]	**0.015**	0.081	**0.021**	
WBC (x10^9/L)	Non-survivor	7900 (5200-17600)	7600 (4900-16600)	8400 (5500-19600)	0.738
	Survivor	5800 (2000-22100)	5400 (1800-18300)*	6100 (2800-18300)	**<0.001**
	p value[2]	**0.014**	**0.007**	**0.040**	
Platelet (cells/mm^3)	Non-survivor	238000 (147000-503000)	251000 (149000-460000)	263500 (201000-485000)	0.846
	Survivor	209000 (90000-465000)	214000 (85000-447000)	250000 (81000-569000)*,q	**<0.001**
	p value[2]	0.243	0.272	0.579	
Lymphocyte (cells/µL)	Non-survivor	800 (300-1500)	1200 (200-1600)	1000 (700-1400)	**0.042**
	Survivor	1200 (200-3600)	1400 (300-4000)*	1300 (100-3600)*	**<0.001**
	p value[2]	**0.014**	**0.043**	0.122	
MPV (fL)	Non-survivor	8.8 (7.4-10.9)	9.2 (7.9-10.6)	8.9 (7.9-10.7)	0.957
	Survivor	9.0 (7-12.2)	9.0 (6.6-12.3)	8.9 (7.1-11.9)	0.069
	p value[2]	0.782	0.822	0.932	
PDW (%)	Non-survivor	17.5 (16.3-18.1)	16.9 (16.4-17.8)	16.9 (16.5-17.5)	0.676
	Survivor	16.9 (16-18.8)	16.9 (15.9-18.6)	17.0 (16-19.9)	0.717
	p value[2]	0.604	0.850	0.374	
PCT (%)	Non-survivor	0.2 (0.14-0.44)	0.22 (0.15-0.39)	0.26 (0.16-0.41)	0.846
	Survivor	0.18 (0.02-0.41)	0.19 (0.08-0.42)*	0.23 (0.08-0.51)*,q	**<0.001**
	p value[2]	0.173	0.218	0.477	
PLR	Non-survivor	294.5 (140-718)	223.0 (151-1255)	295.2 (145-440)	0.115
	Survivor	165.0 (62-880)	150.0 (51-507)*	190.0 (49-1840)q	**<0.001**
	p value[2]	**0.002**	**0.003**	0.089	

[1]Friedman test; *p<0.001 compared to values on initial admission, qp<0.001 compared to values on 3rd hospitalization day (Wilcoxon test with Bonferroni correction, p<0.016)

[2]Mann-Whitney U test

consideration of inflammation, coagulopathy and anemia as well as cytokine storm amongst the main causes of COVID-19 death (12,19,20). Importantly, in the current study, these variables showed significant temporal changes from initial admission during the hospitalization period in survivors, whereas they remained similar with no improvement towards a better prognostic status throughout the hospitalization in non-survivors.

Association of lower WBC counts and higher lymphocyte counts on admission and during hospitalization with significantly higher likelihood of survival in the current study supports the data from a previous study by Ok et al. in Turkey, that revealed the significantly lower WBC counts and higher lymphocyte counts in COVID-19 patients with moderate vs. severe disease and the correlation of disease severity negatively with lymphocyte count and positively with WBC count (9). Indeed, several studies to date among COVID-19 patients have indicated the association of lower lymphocyte counts with increased disease severity, increased likelihood of ICU stay and mortality, while lower lymphocyte/WBC ratio on admission along with continued decrease during hospitalization was also reported to be associated with increased risk of mortality (16,21-23).

Notably, Tan et al. reported the identification of lymphocytes <20% on days 10 to 12 to signal a pre-severe disease and lymphocytes <5% on days 17 to 19 to indicate a critical illness in COVID-19 patients (24). However, Zhou et al. reported that contrary to non-survivors, survivors of COVID-19 had a nadir of lymphocytes counted on day 7 from symptom onset and a subsequent restoration (6).

Qu et al. reported increased likelihood of more severe disease and longer hospital stay among older COVID-19 patients with a lower count of lymphocyte and platelet (2). In the current study, while older patients and those with lower lymphocyte counts had lower likelihood of survival, no significant difference was noted between survivors and non-survivors in terms of platelet counts on initial admission or during hospitalization. Nonetheless, it should be noted that platelet counts on 7th day were significantly higher than initial and 3rd day values among survivors, supporting the data from a study by Liu et al. indicated the level of platelets showed an increasing trend for survivors after admission as compared with that for non-survivors (8). Significant increase in platelet counts during hospitalization in survivors in the current study seems notable in this regard, given the consideration of platelet count as an independent risk factor

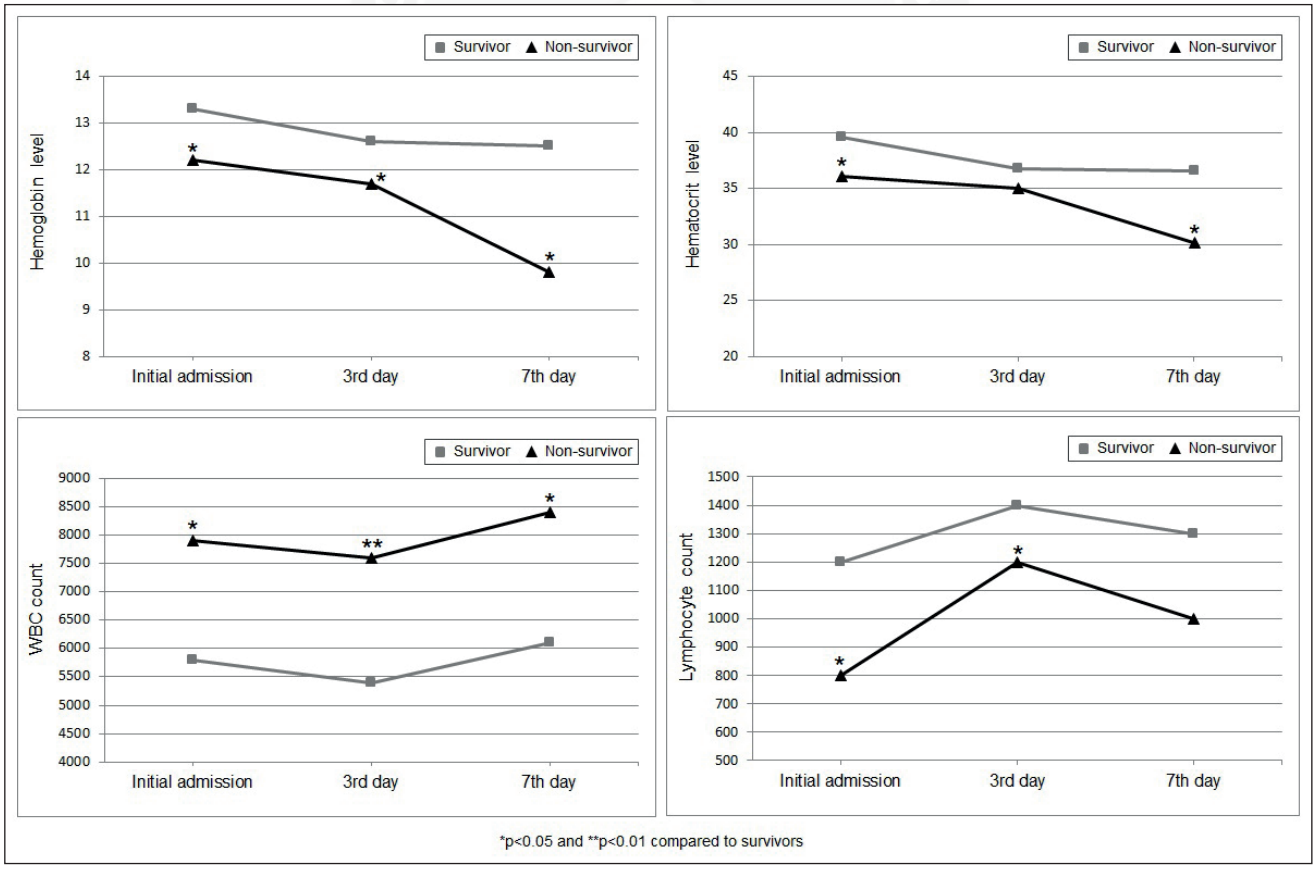

Figure 3: Temporal change in in hemoglobin, hematocrit, WBC and lymphocyte values during hospitalization in survivors vs. non-survivors.

for mortality among COVID-19 patients and association of a 50x10^9/L increase in platelet count with a 40% deceased mortality (HR 0.60, 95%CI: 0.43, 0.84) (8).

Notably, increase in lymphocyte counts over time during hospitalization was noted only in survivors, while higher lymphocyte counts and lower PLR were associated with increased likelihood of survival in the current study. These findings support the previously reported data on association of lower lymphocyte levels at the first diagnosis with increased disease severity and consideration of the progressive decline in lymphocyte proportion as well as high PLR as potential markers in the disease monitoring given their relation to a longer the hospital stay and poor prognosis in COVID-19 patients (2). In the current study, PLR in survivors, decreased from initial admission to 3rd day of hospitalization and increased again on the 7th day of hospitalization. Likewise, in a study by Sun et al. among COVID-19 patients, authors reported that the PLR in the severe ICU group fluctuated greatly, reaching a peak on the 7th day after admission (13). In a study by Qu et al. among hospitalized patients with COVID-19, using PLR was suggested to be a monitoring indicator of disease progression in COVID-19 patients (2). Indeed, Qu et al. also reported that PLR at the time of platelet peak emerged as an independent prognostic factor for prolonged hospitalization and high PLR was suggested to indicate a more pronounced cytokine storm due to enhanced platelet activation (2).

Hence, our findings indicate that routine peripheral blood parameters change differently during the course of hospitalization in survivor and non-survivor COVID-19 patients. This seems notable given the consideration of temporal changes in blood tests among patients with COVID-19 to be not consistent with the typical manifestations of common viral infection in terms of leukopenia, neutropenia and an increase in lymphocyte proportion (2). Accordingly, our findings emphasize the clinical significance of monitoring the changes in routine peripheral blood parameters, particularly the serial assessment of lymphocyte count dynamics, as combined with PLR in terms of identifying COVID-19 patients at risk of worse prognostic outcome (1,13).

Certain limitations to this study should be considered. First, potential lack of generalizability is an important limitation due to single-center retrospective study design with relatively small sample size. Second, lack of data on the group of mild patients who were followed up on an outpatient basis seems to be another limitation of the present study.

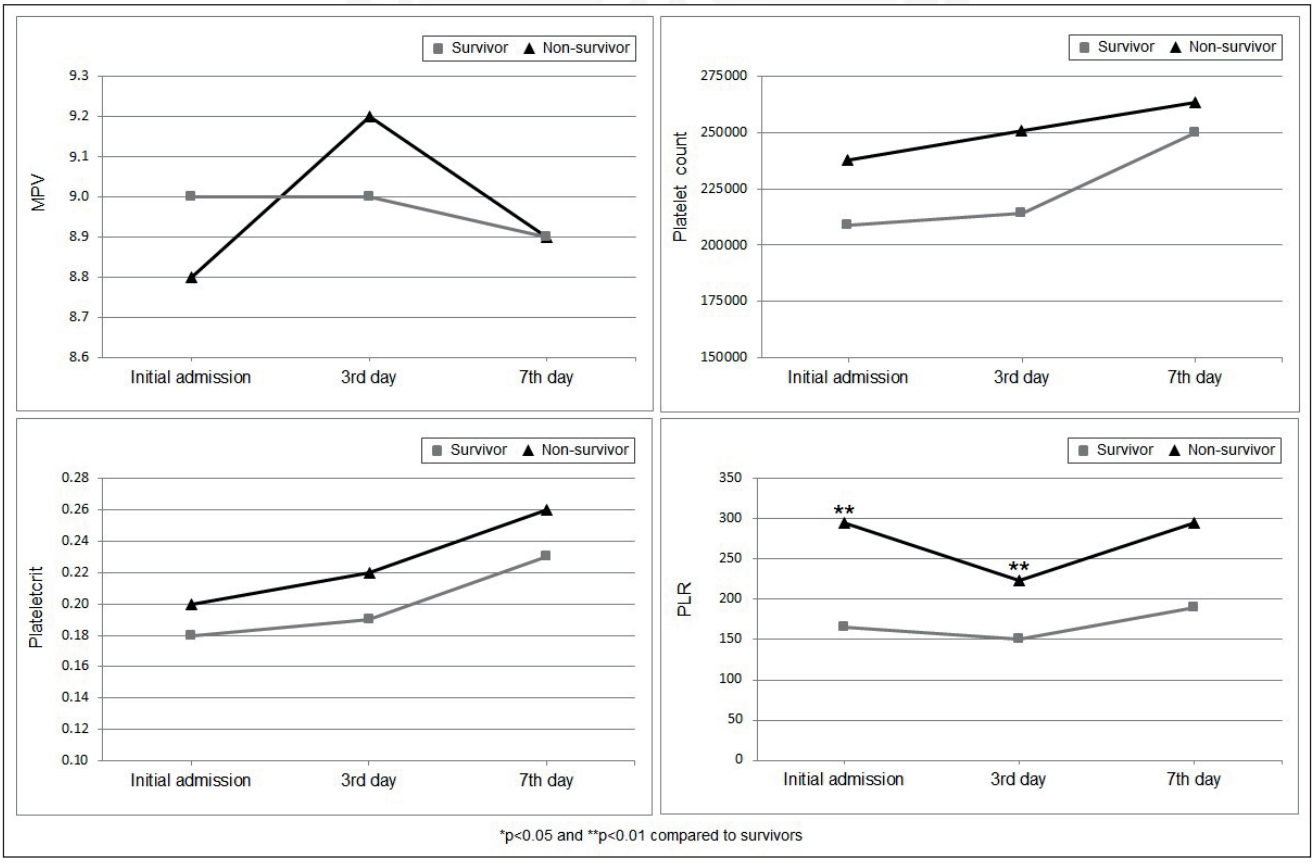

Figure 4: Temporal change in platelet, plateletcrit, MPV and PLR values during hospitalization in survivors vs. non-survivors.

In conclusion, our findings in a retrospective cohort of hospitalized COVID-19 patients revealed the association of lower hemoglobin and hematocrit levels, lower lymphocyte count and higher WBC count and PLR with increased risk of mortality. There was also a significant difference between survivors and non-survivors in terms of temporal changes in routine peripheral blood parameters over time during the hospitalization. In this regard, our findings emphasize the clinical significance of dynamic monitoring of peripheral blood parameters, as combined with PLR, in assisting clinicians to identify patients at an increased risk of worse outcomes and thus to provide timely tailored treatment in those with potentially dismal prognosis.

Acknowledgment

None.

Author Contributions

Concept: **Müzeyyen Aslaner Ak, Birsen Sahip,** Design: **Müzeyyen Aslaner Ak, Birsen Sahip,** Data Collection or Processing: **Müzeyyen Aslaner Ak, Birsen Sahip, Güven Çelebi, Emre Horuz, Şehmus Ertop,** Analysis or Interpretation: **Müzeyyen Aslaner Ak, Birsen Sahip, Güven Çelebi, Emre Horuz, Şehmus Ertop,** Literature Search: **Müzeyyen Aslaner Ak, Birsen Sahip, Güven Çelebi, Emre Horuz, Şehmus Ertop,** Writing: **Müzeyyen Aslaner Ak,** Critical revision: **Birsen Sahip, Güven Çelebi, Emre Horuz, Şehmus Ertop.**

Conflicts of Interest

The authors declare that they have no conflict of interest.

Financial Support

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical Approval

The study was approved by the Non-interventional Clinical Research Ethics Committee of Zonguldak Bulent Ecevit University along with the permission for the use of patient data for publication purposes (Date of Approval: 08/07/2020; Reference Number/Protocol No: 2020/14)

Review Process

Extremely reviewed and accepted for the publication.

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