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COVID-19 in Geriatric Patients

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ABSTRACT

Objective: Considering the ongoing pneumonia epidemic associated with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), aging is a major risk factor alone for serious illness and death. In this study, we aimed to investigate the length of stay, hospital discharge status, and prognostic factors in geriatric patients with COVID-19.

Methods: Medical files of 199 patients over the age of 65 years, who were treated as inpatients due to the diagnosis of COVID-19, were reviewed retrospectively. Demographic characteristics, comorbid diseases, laboratory values, the length of stay, and hospital discharge status of eligible patients were evaluated.

Results: Of inpatients with COVID-19, the mean age was 75.01±7.86 years and 50.8% were men. In patients, who were transferred to ICU, C-reactive protein (CRP) and ferritin levels were higher compared to patients discharged to home and the monocyte/HDL ratio (MHR) was higher compared to nonsurvivors (p=0.037, p=0.003, p=0.023). Nonsurvivors had significantly higher white blood cell (WBC) counts and erythrocyte sedimentation rates (ESR) compared to patients discharged to home. Nonsurvivors had a significantly shorter length of hospital stay compared to patients, who were transferred to ICU.

Conclusion: Geriatric patients are susceptible to adverse clinical outcomes of COVID-19. We think that WBC, ESR, CRP, ferritin, and MHR levels may inform about poor prognosis and the potential discharge status in older adult patients with COVID-19 pneumonia. Gaining insight into poor prognostic factors in older adult patients is essential to control COVID-19 and develop rapid treatment strategies in this age group.

Keywords: Geriatrics, COVID 19, İnflammation.

Geriatrik Hastalarda COVİD-19

ÖZET

Amaç: Şiddetli akut solunum yolu koronavirüsü 2 (SARS-CoV-2) ile ilişkili devam eden pnömoni salgınında yaşlanmanın kendisi, ciddi hastalık ve ölüm için önemli bir risk faktörüdür. Bu çalışmada COVID-19'lu yaşlı hastaların yatış sürelerini, çıkış durumlarını ve prognostik faktörleri araştırmayı planladık.

Hastalar ve Yöntem: COVID-19 tanısı ile takip edilen 65 yaş üstü 199 hastanın dosyası retrospektif olarak tarandı. Çalışmaya alınan hastaların demografik özellikleri, komorbid hastalıkları, labaratuvar değerleri, yatış süreleri ve çıkış durumları değerlendirildi.

Bulgular: COVID-19 tanısı ile yatan hastaların yaş ortalaması 75,01±7,86 'ıydı ve %50,8'i erkekti. Yoğun bakıma sevk edilen hastaların C-reactive protein (CRP) ve ferritin düzeyleri eve taburcu olanlardan, monosit/HDL oranı (MHR) exitus olanlardan anlamlı derecede daha yüksekti (p=0.037, p=0.003, p=0.023). Exitus olan hastaların beyaz kan hücresi (WBC) ve erythrocyte sedimentation rate (ESR) düzeyleri eve taburcu olan hastalardan anlamlı derecede daha yüksekti ve yatış süreleri yoğun bakıma sevk edilen hastalardan anlamlı derecede kısa idi (p<0.05).

Sonuç: Yaşlı hastalar, COVID-19 enfeksiyonunda olumsuz klinik sonuçlara duyarlıdır, değerlendirme ve tedavileri zordur. COVID-19 pnömonili yaşlı hastalarda WBC, ESR CRP, ferritin ve MHR gibi parametrelerin kötü prognozu gösterebileceğini ve bunların hastaların çıkış durumuyla ilişkilendirilebileceğini düşünüyoruz. Yaşlı hastalarda bu kötü prognostik faktörleri anlamak COVID-19 enfeksiyonunu kontrol etmek ve hızlı tedavi stratejileri geliştirmek için gereklidir.

Anahtar Kelimeler: Geriatri, COVID 19, İnflamasyon

The emergence of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) in China caused the pandemic to date, resulting in uncontrollable disease outbreaks, significant death rates, and long-term disability (1). Although the pathophysiology of the disease is complex and not completely understood, it is suggested that SARS-CoV-2, similar to SARS-CoV-1, primarily targets pulmonary epithelial cells and induces reductions in the production of proinflammatory cytokines and impairs T-cell response (2).

Any individual from any age group is at risk of contracting the SARS-CoV-2 infection and developing severe disease. SARS-CoV-2 infection, also known as coronavirus disease-19 (COVID-19) can be asymptomatic or may manifest itself in many clinical pictures ranging from a mild flu-like disease to more severe manifestations with life-threatening complications. SARS-CoV-2 not only acts on the respiratory airways and causes pneumonia but may affect the gastrointestinal system (GIS), nervous system, or cardiovascular system as well (3). However, compared to younger individuals, geriatric patients are more susceptible to develop severe SARS-CoV-2 infection because of compromised immune reactions, comorbidities, and underlying disorders. Management of older adult patients with COVID-19 requires extra attention compared to younger patients (4).

Real-time reverse transcription-PCR (RT-PCR) continues to be used as the most common method to identify SARS-CoV-2 (5). In addition to the identification of SARS-CoV-2; routine hematological, biochemical, and chemical laboratory test parameters can be employed as markers to monitor the patient's condition or to detect potential clues reflecting the disease state (6,7). Lymphopenia, neutropenia, and high levels of plasma inflammatory markers were associated with disease severity and the risk of death in previous studies (8). In this study, we aimed to investigate the hematological and biochemical markers that might be associated with the length of hospital stay and discharge status of patients over 65 years of age, who were admitted to our inpatient unit due to the diagnosis of COVID-19.

MATERIAL AND METHOD

This retrospective study was approved by Dışkapı Yıldırım Beyazıt Training and Research Hospital Ethics Committee (Date: 17/05/2021, No:111/07). All procedures were carried out in compliance with the principles of the Declaration of Helsinki. Medical files of 199 patients over 65 years of age, who were treated in our hospital's inpatient care unit because of COVID-19 in the period between January 2020 and January 2021, were reviewed retrospectively. The diagnosis of COVID-19 was confirmed via RT-PCR tests in the oropharyngeal swab or sputum samples of the patients. Patients included in the study were evaluated for age, gender, levels of laboratory test parameters, the length of hospital stay, and discharge status. Comorbidities were categorized as hypertension (HT), diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), and heart disease (HD). The length of stay was defined as the time from admission to death, to discharge to home, or to the transfer to the intensive care unit (ICU).

The neutrophil-to-lymphocyte ratio (NLR), the platelet-to-lymphocyte ratio (PLR), and the monocyte-to-HDL ratio (MHR) have been in use so far as inexpensive and easy-to-calculate parameters to evaluate systemic inflammation in clinical practice (9,10). It has been reported that NLR, PLR, and MHR values may guide the diagnosis and prognosis in many systemic diseases such as malignancies, chronic inflammatory diseases, acute myocardial infarction, renal artery stenosis, or diabetes mellitus (11,12). NLR is calculated by dividing the neutrophil count by the lymphocyte count. PLR is calculated by dividing the platelet count by the lymphocyte count. MHR is calculated by dividing the monocyte count by the measured value of high-density lipoprotein cholesterol (HDL). We examined NLR, PLR, and MHR values in geriatric patients, who were admitted to our inpatient service because of the diagnosis of COVID-19 at the time of admission. The study population underwent blood tests after 12-hour fasting for the measurement of HDL Cholesterol, through enzymatic colorimetric assay.

Statistical Analysis

A total of 199 patients were included in the analysis. The statistical analyses were carried out using IBM SPSS Statistics-26 package software. The study data were summarized in frequencies (number, percentage) for categorical variables. Descriptive statistics (mean, standard deviation) were used to summarize numerical variables. The normality assumptions of the numerical variables were examined by the Kolmogorov Smirnov normality test. It was observed that the variables were normally distributed. Therefore, parametric statistical methods were used for further analysis.

Differences between two independent groups were examined by the independent samples t-test. Differences between more than two independent groups were

analyzed by One-Way Analysis of Variance (ANOVA). When differences were identified between the groups based on the results of ANOVA, Tukey's multiple comparison test was used. The relationships between two independent numerical variables were interpreted by using Pearson's correlation coefficient. Relationships between two independent categorical variables were analyzed by the chi-square analysis. Statistical significance was interpreted at the 0.05 level for all statistical test results.

RESULTS

The mean age of patients, who were admitted to the inpatient unit due to the diagnosis of COVID-19, was 75.01±7.86 years. Of the patients; 49.2% were women and 50.8% were men. HT was present in 67.3% of the patients, DM in 35.7%, HD in 27.1%, and COPD was present in 15.6% of the patients. The mean length of hospital stay was 11.82±6.20 days. The discharge status of the patients was the discharge to home in 65.3%, transfer to ICU in 12.6%, and death in 22.1% (Table 1).

The length of hospital stay was statistically significantly different by the hospital discharge status of the patients ($p<0.05$). The length of hospital stay was significantly shorter in nonsurvivors and in patients, who were discharged to home compared to that of patients, who were transferred to ICU ($p<0.001$). There was a low-level but positive and statistically significant correlation between the length of stay and the WBC count (r=0.139) (Table 2).

WBC, C-reactive protein (CRP), ferritin, HDL, erythrocyte sedimentation rate (ESR), and MHR levels were statistically significantly different by the discharge status of patients ($p<0.05$). CRP and ferritin levels of the patients, who were transferred to ICU, were significantly higher than those of patients, who were discharged to home (p=0.037, p=0.003). MHR values of the patients, who were transferred to ICU, were significantly higher compared to those of nonsurvivors (p=0.023). HDL levels of nonsurvivors were significantly higher compared to those of patients, who were discharged to home or transferred to ICU ($p<0.001$). Nonsurvivors had significantly higher WBC and ESR levels than those of patients, who were discharged to home (0.002, 0.015) (Table 3).

Table 1. Demographic characteristics of patients (n=199)

	n (%)
Gender	
Women	98 (49.2)
Men	101 (50.8)
Discharge Status	
Home	130 (65.3)
ICU	25 (12.6)
Death	44 (22.1)
HT	
Yes	134 (67.3)
No	65 (32.7)
DM	
Yes	71 (35.7)
No	128 (64.3)
COPD	
Yes	31 (15.6)
No	168 (84.4)
HD	
Yes	54(27.1)
No	145(72.9)
	Mean±S.D.
Age	75.01±7.86
Length of Hospital Stay	11.82±6.20

ICU: Intensive care unit, S.D.: Standard deviation, HT: Hypertension, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, HD: Heart disease

Table 2. Relationship between the length of stay and other variables			
	Length of Stay		
	Mean± S.D.	**Test**	**p**
Gender		t: -0.246	0.806
Women	11.71±4.99		
Men	11.93±7.21		
Discharge Status		F: 23.269	<0.001*
		Difference: 2-1,3	
1.Home	10.42±4.56		
2.ICU	18.76±7.69		
3.Death	12.02±6.89		
HT		t: -0.717	0.474
Yes	11.60±6.33		
No	12.28±5.94		
DM		t: 1.255	0.211
Yes	12.56±5.92		
No	11.41±6.33		
COPD		t: 0.770	0.442
Yes	12.61±6.68		
No	11.68±6.11		
HD		t: 1.275	0.204
Yes	12.74±7.44		
No	11.48±5.66		
		r	**p**
Age		-0.109	0.127
WBC (×103 µl)		0.139*	0.049
NEU (×103 µl)		0.038	0.592
LYM (×103 µl)		0.011	0.876
PLT (×103 µl)		0.032	0.652
MON (×103 µl)		0.027	0.71
D-Dimer (µg/ml)		0.081	0.256
CRP (mg/l)		-0.045	0.532
Ferritin (ng/ml)		0.031	0.675
HDL (mg/dl)		-0.074	0.301
ESR (mm/l)		-0.032	0.652
NLR		-0.001	0.993
PLR		-0.053	0.456
MHR		0.069	0.336

*: p<0.05, t: Independent Samples T-Test, F: One-way analysis of variance (ANOVA), Difference: Tukey's multiple comparison test, r: Pearson's correlation coefficient, ICU: Intensive care unit, S.D.: Standard deviation, HT: Hypertension, DM: Diabetes mellitus, HD: Heart disease, COPD: Chronic obstructive pulmonary disease, WBC: White blood cell (×103 µl), NEU: Neutrophils (×103 µl), LYM: Lymphocytes (×103 µl), PLT: Platelets (×103 µl), MON: monocytes (×103 µl), CRP: C-reactive protein, HDL: High-density lipoprotein, ESR: Erythrocyte sedimentation rate, NLR: Neutrophil/lymphocyte ratio, PLR: Platelet/lymphocyte ratio, MHR: Monocyte/HDL ratio

Table 3. Relationship between the discharge status and other variables					
	1. Home	**2. ICU**	**3. Death**	**Chi-square**	**p**
	n (%)	n (%)	n (%)		
Gender					
Women	70(71.4)	10(10.2)	18(18.4)	3.179	0.204
Men	60(59.4)	15(14.9)	26(25.7)		
HT					
Yes	89(66.4)	15(11.2)	30(22.4)	0.701	0.704
No	41(63.1)	10(15.4)	14(21.5)		
DM					
Yes	42(59.2)	9(12.7)	20(28.2)	2.477	0.290
No	88(68.8)	16(12.5)	24(18.8)		
COPD					
Yes	20(64.5)	6(19.4)	5(16.1)	1.946	0.378
No	110(65.5)	19(11.3)	39(23.2)		
HD					
Yes	36(66.7)	6(11.1)	12(22.2)	0.145	0.930
No	94(64.8)	19(13.1)	32(22.1)		
	Mean ± S.D.	**Mean ± S.D.**	**Mean ± S.D.**	**F**	**p**
Age	74.98 ±7.51	74.36±9.87	75.45±7.76	0.155	0.856
WBC	6.46 ±2.67	7.83 ±3.22	9.33 ±8.58	6.320	**0.002* Difference: 1-3**
NEU	4.37 ±3.78	5.33 ±2.93	5.12 ±2.60	1.312	0.272
LYM	2.15 ±3.43	1.98 ±1.10	2.27 ±1.39	0.081	0.922
PLT	215.93 ±82.70	214.68±98.67	211.57±73.79	0.045	0.956
MON	0.57 ±0.38	0.70 ±0.85	0.65 ±0.44	1.021	0.362
D-Dimer	2.07 ±5.17	4.37 ±8.05	3.05 ±6.22	1.814	0.166
CRP	8.19 ±12.45	13.98 ±8.67	11.38 ±9.43	3.359	**0.037* Difference: 1-2**
Ferritin	365.98 ±374.77	657.56±513.43	526.53±481.61	6.147	**0.003* Difference: 1-2**
HDL	31.33 ±9.12	34.84 ±9.00	50.89 ±13.68	59.681	**0.000* Difference: 3-1.2**
ESR	59.93 ±19.52	59.36 ±17.54	69.30 ±17.72	4.297	**0.015* Difference: 1-3**
NLR	3.20 ±2.70	3.70 ±2.98	3.53 ±4.56	0.346	0.708
PLR	159.36 ±117.88	144.21±100.99	143.59±149.53	0.356	0.701
MHR	0.02 ±0.01	0.02 ±0.03	0.01 ±0.01	3.846	**0.023* Difference: 2-3**

*:p<0.05, F: One-way analysis of variance (ANOVA) Difference: Tukey's multiple comparison test, HT: Hypertension, DM: Diabetes mellitus, HD: Heart disease, COPD: Chronic obstructive pulmonary disease, WBC: White blood cell (×103 µl), NEU: Neutrophils (×103 µl), LYM: Lymphocytes (×103 µl), PLT: Platelets (×103 µl), MON: Monocytes (×103 µl), CRP: C-reactive protein, HDL: High-density lipoprotein, ESR: Erythrocyte sedimentation rate, NLR: Neutrophil/lymphocyte ratio, PLR: Platelet/lymphocyte ratio, MHR: Monocyte/HDL ratio

DISCUSSION

Aging is a major risk factor alone for serious disease and death from COVID-19. Age-related decline and dysregulation in immune functions and the emergence of comorbid diseases increase susceptibility in old age, leading to serious COVID-19 outcomes (13). The mean age of patients over the age of 65, who received treatment for COVID-19 in our inpatient service, was 75.01±7.86 years. Of our patients; 50.8% were men, 65.3% were discharged to home, and 22.1% died. Jihye Hwang et al. reported that, of the older adult patients that received treatment for COVID-19, 37.9% were men, 15% were nonsurvivors, and the remaining group was discharged to home (14).

Of our patients at the age of 65 years and over, who were treated as inpatients because of the diagnosis of COVID-19, the lengths of hospital stay of nonsurvivors and those patients, who were discharged to home, were significantly shorter than those, who were transferred to ICU. Compatible with our study results, Lang Wang et al. found in their study that the length of hospital stay was significantly shorter in older nonsurvivors (15). They showed that, in older nonsurvivors, the number of comorbid diseases was high, the prognosis was poor, the disease progression was rapid, and, consequently, the length of hospital stay was short. In our study, we found that the length of stay was also short in patients, who were discharged to home. We thought that this result occurred because patients were discharged to home as soon as possible after overcoming the life-threatening situation. The aim was to protect patients from hospital-related complications and avoid potential work intensity. We could not find a significant relationship between the comorbidities of the patients and the length of hospital stay but we found a low level of positive correlation between comorbidities and high WBC counts.

CRP is an acute phase protein and an important biomarker. CRP levels increase rapidly and significantly during acute inflammatory responses (16). The CRP level has been shown to be an effective parameter in predicting the intensity and the severity of COVID-19 pneumonia at an early stage (17,18). Of the patients we treated, CRP and ferritin levels of patients, who were transferred to ICU, were significantly higher than those, who were discharged to home. In a recent study, the pneumonia severity index (PSI) and CRP levels were found to be significantly higher in older adult patients compared to younger patients (19). Similarly, in another study, it was shown that serum ferritin levels were higher in patients, who had severe disease and died (20).

Peripheral blood monocytes are the basic mononuclear cells that are in charge of the appropriate fight against pathogens including viruses. It has been reported that the normal range of the monocyte count in COVID-19 patients varies according to disease stages (21,22). HDL is an antioxidant and anti-inflammatory molecule that plays a role in the regulation of cholesterol transport between tissues. HDL is involved in the modulation of inflammation and oxidative stress (23). Recent studies have shown that MHR values may be a new marker of inflammation and oxidative stress (24). In our study, HDL levels were significantly higher in patients, who died with a diagnosis of COVID-19, while MHR rates were higher in patients, who were transferred to ICU. We thought that these results were associated with the inflammatory state and poor prognosis. In previous studies, high NLR and PLR values were defined as independent factors for poor prognosis in COVID-19 but we did not obtain significant NLR and PLR values in our study (25,26).

It has been shown that high levels of laboratory parameters including WBC, ESR, and CRP indicate the extent of inflammation and tissue damage in COVID-19 pneumonia (27,28). In our study, we found that the WBC count and erythrocyte sedimentation rates were significantly higher in nonsurvivors compared to patients, who were discharged to home. In their metaanalysis, Henry et al. concluded that patients with severe and fatal diseases had significantly increased WBC counts compared to survivors (20). In another study, ESR and the severity of pneumonia were positively correlated (29).

The limitations of our study were that we did not categorize the patients according to the severity of pneumonia and that we included a limited number of patients. More detailed evaluations with larger patient groups are required to obtain definitive results.

CONCLUSION

Geriatric patients are susceptible to adverse clinical outcomes of COVID-19. The evaluation and treatment are difficult in this age group. In this study, we observed significantly high levels of WBC, ESR, and HDL and a short duration of hospital stay in nonsurvivors compared to the rest of the patients over 65 years of age, who received treatment for COVID-19 pneumonia. We found that the CRP, ferritin, and MHR levels of the patients, who were

transferred to ICU, were significantly high. In geriatric patients with COVID 19 pneumonia, these markers may be predictors of prognosis to be used during the treatment process and may predict the discharge status. In the management of COVID-19 infection in geriatric patients, it is necessary to understand such indicators of poor prognosis. Furthermore, screening procedures need to be implemented. This way, treatment can be started as soon as possible for such patients with unfavorable prognostic marker values.

DECLARATIONS

Conflict of Interest: The authors have not declared any conflicts of interest.

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