Comparison of Clinical Characteristics in Adult Patients Under 65 years of age with and without Covid 19 pneumonia

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Abstract

Background: Coronavirus disease-2019 (COVID-19) can cause asymptomatic, mild upper respiratory tract symptoms, pneumonia in young persons. How the disease will progress in each patient is still unknown. Therefore, we aimed to investigate the prognostic markers of the development of pneumonia and the clinical characteristics of patients under 65 years with COVID-19 confirmed by a positive reverse transcriptase polymerase chain reaction (RT-PCR) test. Method: In this retrospective study, a total of 271 patients admitted in our unit were included. The patients were divided into two groups, those who did or did not develop pneumonia. Their clinical features, treatment protocols and laboratory parameters were recorded retrospectively. Results: Pneumonia developed in 67.9% (n = 184) of the cases. Age in the pneumonia group was higher than in the non-pneumonia group ($p < 0.001$). In the logistic regression analysis, when symptom and comorbidity status were examined according to the presence of pneumonia; HT (OR: 4,525 95% CL: 1,494–13,708) were the most important risk factor for pneumonia. When age and laboratory values were examined according to the presence of pneumonia, advanced age (OR: 1.042 95% CL: 1.01–1.073), low albumin (OR: 0.917 95% CL: 0.854–0.986) and high troponin (OR: 1.291 95% CL: 1.044–1.596) were identified as risk factors for pneumonia. Conclusion: HT, older age, low albumin, high troponin were important factors for predicting COVID-19 pneumonia in patients under 65 years of age. Young patients with these predictive factors should be more carefully evaluated by further diagnostic procedures, such as thoracic CT. Key Words: COVID-19, pneumonia, young adults

INTRODUCTION

During the pneumonia epidemic that emerged in Wuhan, China in December 2020, pneumonia due to the newly defined severe acute respiratory syndrome coronavirus 2, known as SARS-CoV-2, was defined as coronavirus disease-2019 (COVID-19). Patients presented with both asymptomatic and flu-like symptoms and showed different clinical courses, from pneumonia to respiratory failure (1, 2). Thorax computed tomography (thorax CT) is very sensitive to identifying viral pneumonia. In all age groups, patients with COVID-19 pneumonia generally have bilateral, peripheral and multifocal involvement in lung radiology, and ground-glass densities, consolidation and vascular enlargements can be seen in thorax CT (3). COVID-19 generally affects entire populations, but older people with underlying diseases are more susceptible (4). COVID-19 can cause asymptomatic or mild upper respiratory tract symptoms in young persons, and diffuse lung involvement is observed in some cases. The majority of patients who develop moderate to severe disease are over 50 years old, although there has been a substantial minority of young people requiring hospitalisation and mechanical ventilation (5). However, how the disease will progress in each patient is still unknown. Therefore, we aimed to investigate the prognostic markers of the development of pneumonia and the clinical characteristics of patients under 65 years with COVID-19 infection confirmed by a positive reverse transcriptase polymerase chain reaction (RT-PCR) test.

MATERIALS AND METHOD

Approval for the study was received from the Medical Specialty Education Board (decision no: 711/2021). We included 350 adult patients aged 18–65 years who's COVID-19 infection had been confirmed by RT-PCR positivity between August 2020 and January 2021 in our hospital's COVID-19 outpatient clinic and COVID-19 service. The patients' admission symptoms, clinical features, laboratory parameters, lung radiological imaging and treatment regimens were retrospectively obtained from the hospital information system. Patients (n = 79) who did not have a thorax CT examination and were asymptomatic or had symptoms for less than 5 days were excluded from the study. According to the thorax CT images, the patients were divided into two groups, those who developed and those who did not develop pneumonia, and their clinical features, treatment protocols and laboratory parameters; that is, D-dimer, troponin, C-reactive protein (CRP), albumin, ferritin, lymphocyte count and percentage, neutrophil count and percentage, neutrophil-to-lymphocyte ratio (NLR), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH), were recorded retrospectively. The patients' informed consent was obtained.

STATISTICS

The obtained data were evaluated using the IBM-SPSS (Version 20.0) program in the computer environment. Number, percentage and mean ± standard deviation were used for the descriptive statistics. Chi-squared tests were used to compare categorical data, and the Mann–Whitney U test was used to compare continuous data. Logistic regression models were created with variables found to be significant by bivariate analysis ($p < 0.05$). Binary logistic regression (backward stepwise method) analysis was used in the model analysis. P [?] 0.05 was accepted for statistical significance.

RESULTS

Of the study group, 45.4% were female (n = 123), and the mean age was 46.48 +- 11.99 years. Pneumonia developed in 67.9% (n = 184) of the cases, with 54.9% (n = 101) of these being men and 25.0% (n = 46) were smokers. For the pneumonia group, the hospitalisation rate was 52.2%, and 9.8% (n = 18) required intensive care. A history of smoking, the presence of dyspnea, a need for intensive care, desaturation and hospitalisation were more frequent in those with pneumonia ($p < 0.005$, respectively). The sociodemographic characteristics and COVID-19 symptoms of the study group according to the presence of pneumonia are presented in Table 1. Of those with pneumonia, 90.2% (n = 166) were using favipiravir, 53.3% (n = 98) were using hydroxychloroquine, 42.9% were using steroids and 44.6% were using non-specific antibiotics. Also, 22.3% (n = 41) of the patients with pneumonia had hypertension (HT), 21.2% (n = 39) had diabetes mellitus (DM), 10.9% had cardiac disease (n = 20), 6.5% had chronic obstructive pulmonary disease (n = 12) and 8.2% (n = 5) had asthma. Favipiravir, steroid and non-specific antibiotic use status and the presence of HT were detected more frequently in those with pneumonia ($p < 0.005$, respectively). The drug use and comorbidities of the study group according to the presence of pneumonia are presented in Table 2. Age in the pneumonia group was higher than in the non-pneumonia group ($p < 0.001$). When laboratory values were examined according to the presence of pneumonia in the study group, white blood cell count, neutrophil count, neutrophil percentage, LDH level and NLR and initial troponin, initial D-dimer, initial ferritin and initial CRP values were higher in the pneumonia group, whereas lymphocyte count, lymphocyte percentage, and albumin values were higher in the non-pneumonia group ($p < 0.005$, respectively). The study groups' ages and laboratory values according to the presence of pneumonia are presented in Table 3. In the logistic regression analysis, when symptom and comorbidity status were examined according to the presence of pneumonia, dyspnea (OR: 2,370 95% CL: 1,187–4,730), hospitalisation (OR: 3,803 95% CL: 1,877–7,705) and HT (OR: 4,525 95% CL: 1,494–13,708) were the most important risk factors for pneumonia (Table 4). In the logistic regression analysis of the study group, when age and laboratory values were examined according to the presence of pneumonia, advanced age (OR: 1.042 95% CL: 1.01–1.073), low albumin (OR: 0.917 95% CL: 0.854–0.986) and high troponin (OR: 1.291 95% CL: 1.044–1.596) were identified as risk factors for pneumonia (see Table 5).

DISCUSSION

Our study included 271 patients aged 18–65 years with positive RT-PCR tests for COVID-19 who had symptoms for longer than 5 days at the time of admission. Smoking and the presence of HT were found to be statistically significant in the group that developed pneumonia. Hospitalisation, the need for additional antibiotics, desaturation and bilateral involvement of the lung parenchyma were more common in the pneumonia group. Of the laboratory parameters, initial D-dimer, troponin, neutrophil, NLR, CRP, LDH and ferritin levels were higher in the pneumonia group, and lymphocyte, albumin and haemoglobin values were lower. Older age, presence of HT, dyspnea at hospital admission, low albumin and high troponin were found to be risk factors for the development of pneumonia. Studies have shown that the need for mechanical ventilators, intensive care hospitalisation and death rates are significantly higher in COVID-19 patients over 65 years of age compared to younger patients (6, 7). However, no specific data for the clinical features and treatment of young adult COVID-19 patients admitted to hospitals have been published. As far as we know, although studies on COVID-19 patients under the age of 65 have been published, no comparative studies between young adult patients with and without pneumonia have been published. In a study of patients under the age of 50 with a diagnosis of COVID-19, 56% of the patients were male, their mean age was 44.44 years, and 92.1% had CT lung involvement (3). Our study found that pneumonia developed at a rate of 67.9%, with a mean age of 46.48 +- 11.99 years. In another study, where a median age of 50 years (IQR; 40–68) was found in a pneumonia group, it was stated that older age was a significant risk factor for the development of pneumonia (8). In Jung et al.'s (9) study, the mean age of a group of patients who initially developed pneumonia or during a follow-up was significantly higher (51.5 and 54.9 years, respectively) compared to a group without pneumonia (38.5 years). In our study, in accordance with the literature, the median age was 51 years (IQR; 41.5–58) in the group that developed pneumonia, and older age was statistically significant for the development of pneumonia. In the literature, it has been stated that HT, CVD, DM and smoking are associated with poor clinical outcomes of COVID-19 cases (10, 11). In our study, the most common comorbidities detected in the pneumonia group were HT, DM and CVD, and there was a significant relationship between smoking and the development of pneumonia. The most commonly reported symptoms observed in COVID-19 patients are fever, cough and myalgia (12, 13). In our study, these symptoms were common in the pneumonia group, but only dyspnea was statistically significantly associated with COVID-19 pneumonia. Fever, the most common COVID-19, was not found to be significant in our study, suggesting that it was not a predictor for pneumonia. In another study, approximately 63% of hospitalised COVID-19 patients under the age of 65 had desaturation, and the hospital stay was longer in this group (14). In our study, desaturation and hospitalisation were statistically more significant in the pneumonia group. To date, most studies on prognostic markers have shown an increase in D-dimer and LDH values and a decrease in lymphocyte levels (15, 16), and Zhang et al. (17) emphasised that D-dimer levels are an important marker for determining mortality in cases with COVID-19 pneumonia. Itelman et al. (18) emphasised that patients with severe COVID-19 have higher leukocyte and neutrophil counts and LDH levels. In our study, increased D-dimer and LDH and decreased lymphocyte levels were found to be statistically significantly higher in the pneumonia group. NLR, high CRP and low albumin have high sensitivity and specificity for demonstrating inflammation. Studies have shown that the NLR and the CRP/lymphocyte ratio are independent prognostic markers for many diseases (19, 20). In our study, while the NLR and initial CRP values were high in patients with pneumonia, albumin and lymphocyte values were lower. In a retrospective cohort study involving 191 patients with COVID-19 from Wuhan, China, high LDH and ferritin levels were associated with mortality (21), and Wang et al. (22) reported that 40% of patients with COVID-19 had high LDH values at the time of admission. In a systematic review conducted by Taneri (23), including 189 studies and 57,563 patients, compared to patients with intermediate or low risk of disease, high ferritin and low haemoglobin levels were found in patients with high risk for severe disease (23). Cobre et al. (24) also found that high ferritin and low haemoglobin levels were observed in both COVID-19 patient groups and patients with severe disease (24). In our study, while haemoglobin levels were lower in the group that developed pneumonia, ferritin and LDH levels were higher. In a systematic review of four studies, including 374 patients, troponin levels were observed to be significantly higher in patients with severe COVID-19 infection compared to non-serious patients (25). Zhu et al.'s (15) study also found that troponin values were a prognostic marker for severe disease. In our study, troponin values were higher in the group with pneumonia, and they were found to be

a statistically significant risk factor for the development of pneumonia. In various studies, increased liver function markers, particularly ALT, AST, gamma-glutamyl transferase and total bilirubin levels, have been described in COVID-19 patients (26, 27). However, no statistical difference was found in these values in our study. In one study, at the time of diagnosis, 203 patients had bilateral pneumonia, 39 patients had unilateral pneumonia, 6 patients had normal thorax CT scan results and 163 (65.7%) had radiological progression of symptoms on the 7th day in repeated radiological imaging (28). In another study, patients with or without pneumonia at the time of diagnosis had negative or positive CT findings according to the duration of symptoms; it was stated that the presence of pneumonia varied depending on the time after symptom onset, and the non-pneumonia group was characterised by younger patients, normal laboratory findings, and less comorbidity (9). In another study, it was stated that positive CT findings were associated with symptom duration, and 56% of patients showed normal CT findings in the early phase (0–2 days) after symptom onset (29). Patients with symptoms for more than 5 days were included in our study, and in accordance with the literature (30), bilateral involvement was more common in the group with pneumonia, and older age was considered a risk factor for the development of pneumonia.

CONCLUSION

The presence of dyspnea and HT, older age, low albumin, high troponin and hospitalisation, which are indicators of mortality in elderly patients, were also important factors for predicting COVID-19-related pneumonia in patients under 65 years of age. Young patients with these predictive factors should be more carefully evaluated by further diagnostic procedures, such as thoracic CT.

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Table 1. Sociodemographic characteristics and COVID-19 symptoms of the study group according to the presence of pneumonia

	PNEUMONIA No n	PNEUMONIA No %	PNEUMONIA Yes n	PNEUMONIA Yes %	p

Gender	Male	47	54,0	101	54,9	0,893
	Female	40	46,0	83	45,1	
Smoking	Nonsmoker	64	73,6	110	59,8	**0,038**
	Ex smoker	5	5,7	28	15,2	
	Smoker	18	20,7	46	25,0	
Intensive care unit need	No	87	100,0	166	90,2	**0,003**
	Yes	0	0,0	18	9,8	
Fever	No	67	77,0	123	66,8	0,088
	Yes	20	23,0	61	33,2	
Cough	No	56	64,4	111	60,3	0,523
	Yes	31	35,6	73	39,7	
Dyspnea	No	72	82,8	102	55,4	**<0,001**
	Yes	15	17,2	82	44,6	
Chest pain	No	85	97,7	177	96,2	0,518
	Yes	2	2,3	7	3,8	
Flu symptoms	No	77	88,5	165	89,7	0,771
	Yes	10	11,5	19	10,3	
Loss of taste and smell	No	80	92,0	178	96,7	0,085
	Yes	7	8,0	6	3,3	
Headache	No	78	89,7	172	93,5	0,272
	Yes	9	10,3	12	6,5	
Joint pain	No	80	92,0	174	94,6	0,408
	Yes	7	8,0	10	5,4	
Myalgia	No	76	87,4	170	92,4	0,181
	Yes	11	12,6	14	7,6	
Weakness	No	63	72,4	144	78,3	0,290
	Yes	24	27,6	40	21,7	
Diarrhea	No	78	89,7	175	95,1	0,092
	Yes	9	10,3	9	4,9	
Sırt ağrısı	No	83	95,4	172	93,5	0,530
	Yes	4	4,6	12	6,5	
Desaturation	No	76	87,4	106	57,6	**<0,001**
	Yes	11	12,6	78	42,4	
Treatment	Home	74	85,1	88	47,8	**<0,001**
	Hospital	13	14,9	96	52,2	
Final	Live	87	100,0	183	99,5	0,491
	Exitus	0	0,0	1	0,5	

p values written in bold show statistically significance.

Table 2. Drug use and comorbidity status of the study group according to the presence of pneumonia

		PNEUMONIA No n	PNEUMONIA No %	PNEUMONIA Yes n	PNEUMONIA Yes %	p
Favipiravir	No	24	27,6	18	9,8	<
	Yes	63	72,4	166	90,2	

Hydroxychloroquine	No	51	58,6	86	46,7	0,0
	Yes	36	41,4	98	53,3	
Steroid need	No	77	88,5	105	57,1	<
	Yes	10	11,5	79	42,9	
Nonspecific antibiotic	No	75	86,2	102	55,4	<
	Yes	12	13,8	82	44,6	
Use of low molecular weight heparin	No	68	78,2	117	63,6	0,0
	Yes	19	21,8	67	36,4	
COPD	No	86	98,9	172	93,5	0,0
	Yes	1	1,1	12	6,5	
Asthma	No	83	95,4	169	91,8	0,2
	Yes	4	4,6	15	8,2	
Hypertension	No	83	95,4	143	77,7	<
	Yes	4	4,6	41	22,3	
Diabetes mellitus	No	78	89,7	145	78,8	**0,**
	Yes	9	10,3	39	21,2	
Lung radiological involvement	No	87	100,0	0	0,0	<
	Tek taraflı	0	0,0	13	7,1	
	Bilateral	0	0,0	171	92,9	
Malignancy	No	85	97,7	174	94,6	0,2
	Yes	2	2,3	10	5,4	
Hypothyroidism	No	84	96,6	179	97,3	0,7
	Yes	3	3,4	5	2,7	
Cardiovascular disease	No	85	97,7	164	89,1	**0,**
	Yes	2	2,3	20	10,9	
Neurological disease	No	86	98,9	182	98,9	0,9
	Yes	1	1,1	2	1,1	
Obesity	No	86	98,9%	178	96,7	0,3
	Yes	1	1,1%	6	3,3	

COPD: chronic obstructive pulmonary disease

p values written in bold show statistically significance.

Table 3. Age and laboratory values of the study group according to the presence of pneumonia

	PNEUMONIA No Ortanca	PNEUMONIA No IQR 25	PNEUMONIA No IQR 75	PNEUMONIA Yes Ortanca	PNEUMONIA Yes IQR 25	PNEUMONIA Yes IQR 75
Age	41,0	30,0	48,0	51,0	41,5	58,0
White blood cell	5750,0	4800,0	7700,0	6500,0	5150,0	8560,0
Lymphocyte count	1640,0	1290,0	2170,0	1350,0	965,0	1915,0
Neutrophil count	3630,0	2800,0	4870,0	4295,0	3200,0	6150,0
Lymphocyte %	29,4	21,0	35,0	22,0	14,5	30,0
Neutrophil %	60,5	56,0	69,0	68,0	60,4	78,6
Hemoglobin	14,5	13,5	15,7	13,8	12,7	15,0
Albumin	42,7	38,3	45,8	38,8	34,1	41,9
ALT	23,0	15,0	40,0	27,0	19,0	40,0
AST	24,0	19,0	31,0	27,0	19,0	40,0
LDH	198,0	162,0	238,0	242,0	185,0	315,0
NLR	2,0	1,5	3,2	3,0	1,9	5,3
Platellet	228,0	198,0	270,0	234,0	189,0	286,0

Initial Troponin	2,5	2,0	2,7	3,2	2,0	6,5
Initial D-Dimer	,3	,2	,6	,6	,3	1,0
Initial Ferritin	88,1	27,0	149,8	162,0	61,0	373,9
Initial CRP	5,1	1,9	16,9	24,0	7,0	89,1

CRP: C- reactive protein, ALT: Alanine transaminase, AST: Aspartate transaminase, NLR: neutrophil lymphocyte ratio, LDH: Lactate Dehydrogenase

P values written in bold show statistically significance.

Table 4. Symptom and comorbidity status according to the presence of pneumonia in the logistic regression analysis (Step 4)

	B	S.E.	p	OR	%95 CI
Dyspnea (Reference: None)	0,863	0,353	0,014	2,370	1,187-4,730
Treatment (Reference: Home)	1,336	0,360	<0,001	3,803	1,877-7,705
Favipiravir (Referance: No)	0,805	0,375	0,032	2,236	1,071-4,668
Hypertension (Referance: No)	1,510	0,566	0,008	4,525	1,494-13,708

CI, confidence interval; OR, odd's ratio; SE, standard error. The model dependent variable was the presence of pneumonia, Model content: Smoking, Dyspnea, Treatment, Favipiravir, Steroid, Nonspecific antibiotic, Hypertension.

Table 5. Age and laboratory values according to the presence of pneumonia in the logistic regression analysis (Step 9)

	B	S.E.	p	OR	%95 CI
Age	0,041	0,015	0,008	1,042	1,011-1,073
Lymphocyte %	0,079	0,047	0,095	1,083	0,986-1,188
Neutrophil %	0,076	0,044	0,084	1,079	0,990-1,176
Albumin	-0,086	0,037	0,019	0,917	0,854-0,986
Initial Troponin	0,256	0,108	0,018	1,291	1,044-1,596

CI, confidence interval; OR, odd's ratio; SE, standard error. The model dependent variable was the presence of pneumonia,

Model content: Age, White blood cell, Lymphocyte Count, Neutrophil Count, Lymphocyte %, Neutrophil%, Albumin, LDH, NLR, Initial Trop, Initial D-Dimer, Initial Ferritin, Initial CRP.