

INVESTIGATION OF THE RELATIONSHIP BETWEEN THE CLINICAL COURSE OF THE ELDERLY PATIENTS DIAGNOSED WITH COVID-19 AND PNEUMOCOCCAL IMMUNIZATION

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ABSTRACT

Introduction: Our study aims to examine the relationship between the clinical course of patients over 65 years of age diagnosed with Covid-19 and pneumococcal immunization.

Materials and methods: We enrolled 294 patients aged 65 and over who were admitted to hospital with the suspicion of COVID-19 and whose diagnosis was confirmed. The patients were divided into three groups, service patients, patients who were treated directly in the intensive care unit, and patients who transferred from the service to the intensive care unit.

Results: The mean age of the patients was 74.93 ± 6.61 . When the patients were evaluated in terms of chronic disease, most of them (62.6%) had hypertension, 36.7% had coronary artery disease, 32.0% had diabetes mellitus, and 22.1% had respiratory system diseases such as asthma, COPD and chronic bronchitis. It was determined that the number of men (71.5%) whose CT was compatible with the viral pandemic was statistically higher than women (53.8%) ($p=0.002$). We found that most of the individuals whose CT was compatible with the viral pandemic were not vaccinated against pneumococcus (88.0%) ($p=0.001$). The prognosis of COVID-19 patients of individuals with a pneumococcal vaccine was good, and these patients had fewer pulmonary CT findings compatible with the viral pandemic, which was related to a shorter hospital stay and less intensive care needs ($p=0.001$).

Conclusion: We determined that the pneumococcal vaccine, which is mainly administered in family medicine centers, has a positive effect on the course of COVID-19, and adult immunization should be given importance in every period.

Keywords: *Pneumococcus, COVID-19, Pneumococcal vaccine, Family medicine.*

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Introduction

In December 2019, several cases of pneumonia of unknown etiology were reported in Wuhan, China⁽¹⁾. The Chinese government reported that the disease then spread rapidly from Wuhan to other regions. In January 2020, it was reported by the Chinese center for disease control and prevention (CDC) that a new type of coronavirus was detected in samples taken from patients' throat swabs, and the virus was named 2019 novel coronavirus (2019-nCoV)⁽²⁾. Due to the rapid spread of the disease globally, on January 30, the World Health Organization (WHO) declared that the epidemic had international importance and should be declared as

a public health emergency. On February 11, 2020, WHO reported that the official name of the disease is "COVID-19"⁽³⁾. COVID-19 was declared a pandemic by WHO on March 11, 2020⁽³⁾.

It has been reported that the primary transmission mechanism of SARS-CoV-2 occurs by inhalation of respiratory droplets, direct or indirect contact with the conjunctival or oral mucosa. Target host receptors are primarily located in the airway epithelium, including the oropharynx and upper respiratory tract. Conjunctiva and gastrointestinal systems are also susceptible to infection and are seen as transmission routes⁽⁴⁾.

Streptococcus pneumonia (pneumococcus) is among the leading causes of community-acquired

pneumonia. The incidence of pneumococcal pneumonia is quite high in people with advanced age and comorbidities⁽⁵⁻⁷⁾. *S. pneumoniae* frequently colonizes the nasopharynx and may spread to the sinuses or middle ears, causing medical morbidity and mortality. Bacteria can also enter the epithelial cell surface and cause localized infection or bacteremia^(8,9).

Some studies have shown that pneumococcal and Hib vaccines can protect against symptomatic SARS-CoV-2 infection and death⁽⁵⁻⁷⁾. Several international studies show an inverse relationship between pneumococcal vaccination rates and SARS-CoV-2 infections and mortality rates⁽⁵⁾. For this reason, it is estimated that the clinical course of patients aged 65 and over who are hospitalized due to the diagnosis of COVID-19 may be milder with pneumococcal immunization. Our study aimed to examine the relationship between the clinical course of patients aged 65 and over with positive COVID-19 PCR test and pneumococcal immunization.

Materials and methods

Our study was started after getting approval from Ankara Yıldırım Beyazıt University (AYBU) Clinical Researches Local Ethics Committee (Approval no: 2020/283). Our research is a descriptive, cross-sectional and retrospective study. It was carried out in individuals aged 65 and over who applied to Ankara City Hospital with the suspicion of COVID-19 and whose diagnosis was confirmed. Our study was carried out retrospectively in 6 months between March 2020 and August 2020. Our study population was the patients who applied to Ankara City Hospital with the suspicion of COVID-19 and were positive for the COVID 19 Reverse Transcription Polymerase Chain Reaction Test (RT-PCR). The sample of our research consists of 294 people. Patient groups were included in the study, with positive COVID-19 PCR test, over 65 years of age, who have e-pulse information sharing consent, who had computed tomography (CT) of the lung and who are hospitalized due to COVID-19.

The questionnaire form was filled in by looking through the system for the patients included in the study. For pneumococcal vaccination status, the patient's vaccination record on e-pulse was checked. Patients' age, gender, marital status, chronic diseases, pneumococcal vaccination status, PCR and lung CT findings were questioned in the form. When the hospitalizations of the patients are evaluated, the

first group was the service patients, the second group was the patients treated directly in the intensive care unit, and the third group was the patients who were transferred from the service to the intensive care unit. The effects of pneumococcal immunization on the length of hospital stay and lung CT findings evaluated by radiologists in Ankara City Hospital were investigated by analyzing the differences between the groups.

Statistical analysis

The data obtained in this study were analyzed using the statistical program SPSS v.25 (SPSS, Chicago, USA). Descriptive statistics such as frequency distribution, mean and standard deviation were used to evaluate the data. The difference between the means of two independent groups was compared with the Student's t-test, and the differences between more than two groups were compared with the parametric test using analysis of variance. Mann-Whitney U and Kruskal-Wallis tests, which are non-parametric alternatives, were used when parametric test assumptions were not met. Categorical data were analyzed with Chi-square or Fisher's Exact test. $p < 0.05$ value was considered statistically significant at the 95% confidence interval.

Results

The participants' sociodemographic characteristics are shown in Table 1. All of the patients participating in the study were 65 years and older, and the mean age was 74.9 ± 6.6 . It was found that 151 (51.4%) of these participants were male, and 143 (48.6%) were female. Since there has been no pneumococcal polysaccharide vaccine (PPA23) in our country for a long time, all vaccinated individuals received a conjugated pneumococcal vaccine (KPA13). When the patients are evaluated in terms of chronic disease; Most of the participants (62.60%), including those with other diseases, had hypertension, 36.73% had coronary artery disease, 31.97% had diabetes mellitus, 22.10% had respiratory system diseases such as asthma, COPD and chronic bronchitis (Table 1).

The findings of the participants regarding the COVID-19 disease are shown in Table 2. It was determined that all of the patients participating in our study had positive SARS-CoV-2 PCR test, and all had lung CT. Chest CT findings of 185 (62.9%) patients were found to be compatible with the viral pandemic (Table 2).

Gender	Total n (%)
Female	143 (48.60)
Male	151 (51.40)
Age, Year, Mean ± SD	74.93± 6.61
Chronic Diseases	
Coronary Artery Disease	10 (3.40)
Respiratory System Diseases	5 (1.70)
Hypertension	24 (8.20)
Diabetes mellitus	3 (1.00)
Rheumatic Diseases	1 (0.30)
Cancer	1 (0.30)
Other	21 (7.20)
No Disease	3 (1.00)
Those with more than one chronic disease	
Hypertension	187 (62.60)
Coronary Artery Disease	108 (36.73)
Diabetes mellitus	94 (31.97)
Respiratory System Diseases	65 (22.10)
Cancer	11 (0.37)
Rheumatic Diseases	6 (1.52)
Pneumococcal vaccination before Covid +	
Yes	128 (43.50)
No	166 (56.50)

Table 1: Sociodemographic characteristics of the participants.

PCR test result	Total n (%)
Positive	294 (100)
Lung CT status	
Yes	294 (100)
Chest CT finding by the radiologist	
Is it compatible with the viral pandemic?	
Yes	185 (62.90)
No	109 (37.10)
Hospital Accommodation	
Service	232 (78.90)
Intensive care	7 (2.40)
Service+intensive care	55 (18.70)
Length of stay	
1-7 days	81 (27.60)
8-15 days	112 (38.10)
16-23 days	65 (22.10)
24 days and above	36 (12.20)

Table 2: Participants' results on COVID-19 disease.

The comparison of the difference between the demographic variables of the patients and their CT findings is shown in Table 3. There was no significant difference between the ages of the patients and their lung CT findings being compatible with the viral pandemic. The number of men (71.5%) whose CT was compatible with the viral pandemic was found to be higher than women (53.8%), and the

difference was statistically significant (p=0.002). It was determined that most of the individuals whose CT was compatible with the viral pandemic were not vaccinated against pneumococcus (88.0%), and the difference was statistically significant (p=0.001) (Table 3).

		Is CT compatible with the viral pandemic?		p
		Yes	No	
Age ¹		74.82±6.66	75.13±6.56	0.693
Gender	Female	n 77	66	0.002*
		% 53.8%	46.2%	
Gender	Male	n 108	43	0.002*
		% 71.5%	28.5%	
Chronic Diseases	More than one	n 144	82	0.789
		% 63.7%	36.3%	
	Coronary Artery Disease	n 6	4	
		% 60.0%	40.0%	
	Respiratory System Disease	n 3	2	
		% 60.0%	40.0%	
	Hypertension	n 14	10	
		% 58.3%	41.7%	
	DM	n 2	1	
		% 66.7%	33.3%	
Pneumococcus vaccine status	Yes	n 39	89	<0.001*
		% 30.5%	69.5%	
	No	n 146	20	
		% 88.0%	12.0%	

Table 3: Comparison of the difference between demographic variables of patients and CT findings.

1: Independent sample t-test. DM: Diabetes Mellitus

	Length of stay in hospital				p
	1-7 days	8-15 days	16-23 days	24 days and above	
Gender (n, %)					
Female	47	57	30	9	0.010*
	32.9%	39.9%	21.0%	6.3%	
Male	34	55	35	27	0.010*
	22.5%	36.4%	23.2%	17.9%	
Chronic disease					
More than one	56	83	57	30	0.369
	24.8%	36.7%	25.2%	13.3%	
Coronary artery disease	2	7	1	0	
	20.0%	70.0%	10.0%	0.0%	
Respiratory System Disease	2	1	2	0	
	40.0%	20.0%	40.0%	0.0%	
Hypertension	9	9	3	3	
	37.5%	37.5%	12.5%	12.5%	
Diabetes Mellitus	1	2	0	0	
	33.3%	66.7%	0.0%	0.0%	
Other	9	9	0	3	
	42.9%	42.9%	0.0%	14.3%	
Pneumococcus vaccine status					
Yes	73	50	5	0	<0.001*
	57.0%	39.1%	3.9%	0.0%	
No	8	62	60	36	
	4.8%	37.3%	36.1%	21.7%	

Table 4: Comparison of the difference between demographic variables of patients and CT findings.

The comparison of the difference between the demographic variables of the patients and the length of stay in the hospital is shown in Table 4. It was determined that the number of men (17.9%) with a hospital stay longer than 24 days was higher than

women (6.3%), and the difference was statistically significant ($p=0.010$). It was determined that all individuals with a hospital stay of 24 days or more were not vaccinated against pneumococcus, and the difference was statistically significant ($p=0.001$) (Table 4).

The comparison of the difference between the demographic variables of the patients and their hospitalizations is shown in Table 5. There was a statistically significant difference between hospitalizations and gender ($p=0.006$). There was a statistically significant difference between pneumococcal vaccination status and hospitalization location ($p=0.001$) (Table 5).

		Place of Hospitalization			P
		Service	Intensive care	Service + intensive care	
Gender	Female	n 123 % 86.0%	4 2.8%	16 11.2%	0.006*
	Male	n 109 % 72.2%	3 2.0%	39 25.8%	
Chronic diseases	More than one	n 171 % 75.7%	6 2.7%	49 21.7%	0.154
	Coronary artery disease	n 9	0	1	
		% 90.0%	0.0%	10.0%	
	Respiratory	n 5	0	0	
		% 100.0%	0.0%	0.0%	
	System Disease	n 20	0	4	
		% 83.3%	0.0%	16.7%	
	DM	n 2	1	0	
		% 66.7%	33.3%	0.0%	
	Rheumatic diseases	n 1	0	0	
		% 100.0%	0.0%	0.0%	
	Other	n 20	0	1	
% 95.2%		0.0%	4.8%		
No disease	n 3	0	0		
	% 100.0%	0.0%	0.0%		
Pneumococcus vaccine status	Yes	n 125	2	1	<0.001*
		% 97.7%	1.6%	0.8%	
	No	n 107	5	54	
		% 64.5%	3.0%	32.5%	

Table 5: Comparison of the difference between the demographic variables of the patients and their hospitalizations.

Discussion

Bacterial co-infection is the leading cause of death in people with viral pneumonia⁽¹⁰⁾. In a study by Zhu et al., bacterial co-infection was observed in most patients diagnosed with COVID-19, and they suggested that pneumococcal vaccines may be a practical approach to prevent co-infection during the COVID-19 pandemic⁽¹¹⁾. In a study by Joseph et al., patients aged 65 years and older with a diagnosis

of COVID-19 were hospitalized with a diagnosis of COVID-19 and a lower incidence of death was observed, with a 32% lower incidence of COVID-19 between those who received and those who did not have the conjugated pneumococcal vaccine (KPA13⁽¹²⁾).

In other studies in the literature, the incidence of COVID-19 was less in people 65 years of age and older who have received conjugated pneumococcal vaccine⁽¹³⁻¹⁵⁾. In our study, patients with conjugated pneumococcal vaccine were less hospitalized in intensive care units, and lung tomography findings were within normal limits compared to those not vaccinated.

Studies have reported that the risk of developing COVID-19 infection is higher in the elderly with chronic diseases⁽¹³⁻¹⁵⁾. When the individuals participating in our study are evaluated in terms of chronic disease, the most common three diseases in which more than half of the participants have more than one chronic disease are hypertension, coronary artery disease, and diabetes mellitus. Hypertension ranks first among the comorbidities associated with the disease in COVID-19 studies⁽¹⁶⁻¹⁷⁾. It has been stated in many studies that mortality and morbidity rates are increased in patients with COVID-19 with hypertension⁽¹⁶⁻¹⁸⁾. In another study conducted to determine the chronic diseases of patients hospitalized with the diagnosis of COVID-19, the most common chronic disease in the participants was hypertension, followed by diabetes mellitus and heart disease, respectively⁽²⁰⁾. In a study conducted by Jin et al. in patients diagnosed with COVID-19, it was reported that 47% of the participants had underlying chronic diseases, and 9% had three or more chronic diseases at the same time⁽¹³⁾. Our study revealed that 53% of the patients had hypertension, 38% had diabetes mellitus, and 11% had chronic heart disease. It has been concluded that the findings of our study are compatible with the literature.

It was found that 62.9% of the patients in our study had lung CT findings consistent with the viral pandemic. In addition, it was determined that the CT findings of most of the individuals (69.5%) who had pneumococcal vaccine were not compatible with the pandemic, and the CT findings of most of the individuals who did not have the pneumococcal vaccine (88%) were found to be compatible with the pandemic, and the difference was statistically significant. When the vaccination status of our patients and the duration of hospitalization were compared, it was determined that not all individuals

with a hospitalization period of 24 days or more were vaccinated against pneumococcus, and the difference was statistically significant. In our study, 64.5% of the individuals who were not vaccinated for pneumococcus were hospitalized in the service, 3% of them were hospitalized in the intensive care unit, 32.5% of them were transferred from the service to the intensive care unit, 97.7% of the individuals with pneumococcal vaccine were in the service, 1.6% It was determined that 0.8% of them were hospitalized in the intensive care unit and 0.8% transferred to the intensive care unit, and this difference was found to be statistically significant. In another study, 48 patients with a definite diagnosis of COVID-19 were evaluated in terms of the relationship between lung CT findings and pneumonia in patients with a mean age of 59.8 years, and it was reported that 61.5% of these patients had lung CT findings compatible with the viral pandemic (19). In our study, the rate of patients whose CT findings were compatible with the COVID-19 pandemic was found similar to the literature. It can be said that the pneumococcal vaccine is effective in the development of secondary pneumococcal infection and therefore improves the prognosis of COVID-19, since CT findings consistent with the pandemic are found to be higher in patients without pneumococcal vaccine than in patients with pneumococcal vaccine, the need for intensive care of vaccinated individuals is less and the hospitalization period is shorter.

It is stated that gender is associated with the frequency of COVID-19 disease and poor prognosis. It has been reported that this situation may be proportional to the high expression of angiotensin-converting enzyme 2 (ACE2), the receptor of SARS-CoV-2^(20, 21). A study stated that Asian men have higher ACE2 expression and therefore the prognosis is worse in this group compared to women and different ethnic groups⁽²²⁾. Our study found that the number of men (17.9%) with a hospital stay longer than 24 days was statistically higher than women (6.3%). In addition, when patients are evaluated as hospitalization places; It was determined that the majority of the individuals hospitalized in the service and intensive care unit were female, and the majority of the individuals transferred from the service to the intensive care unit were male, and this difference was found to be statistically significant. Our results support the findings in the literature in terms of the male gender's contribution to poor prognosis and, therefore an increase in hospital stay and need for intensive care.

Conclusions

Our study determined that the prognosis of COVID-19 patients aged 65 and over who received the pneumococcal vaccine was good, that these patients had fewer lung CT findings compatible with the viral pandemic, thus shortening the hospital stay and less intensive care needs.

It has been observed that the pneumococcal vaccine, which is mainly administered in family health centers in our country, has a positive effect on the course of COVID-19, so adult immunization should be given importance in every period of life. By revealing the effect of the pneumococcal vaccine on the disease process of COVID-19 and examining the effects on clinical symptoms, secondary bacterial pneumonia and mortality rates related to COVID-19 can be reduced.

References

- 1) Phelan AL, Katz R, Gostin LO. The Novel Coronavirus Originating in Wuhan, China: Challenges for Global Health Governance. *JAMA* 2020; 323: 709-10
- 2) Veerabathiran R, Ragunath B, Kaviarasan V, Mohammed V, Ahmed S. Identification of selected genes associated with the SARS-CoV-2: a therapeutic approach and disease severity. *Bull Natl Res Cent* 2021; 45: 79
- 3) Dal-Re R, Bekker LG, Glud C, Holm S, Jha V, et al. Ongoing and future COVID-19 vaccine clinical trials: challenges and opportunities. *Lancet Infect Dis* 2021; 11: e342-e7
- 4) Hui KPY, Cheung MC, Perera R, Ng KC, Bui CHT, et al. Tropism, replication competence, and innate immune responses of the coronavirus SARS-CoV-2 in human respiratory tract and conjunctiva: an analysis in ex-vivo and in-vitro cultures. *Lancet Respir Med* 2020; 8: 687-95
- 5) Zhang M, Chen H, Wu F, Li Q, Lin Q, et al. Heightened Willingness toward Pneumococcal Vaccination in the Elderly Population in Shenzhen, China: A Cross-Sectional Study during the COVID-19 Pandemic. *Vaccines (Basel)* 2021; 9
- 6) Loubet P, Sotto A, group A. Covid-19 pandemic: an opportunity to seize to increase awareness and vaccine coverage in at-risk populations. *Hum Vaccin Immunother* 2021; 1-2
- 7) Root-Bernstein R. Possible Cross-Reactivity between SARS-CoV-2 Proteins, CRM197 and Proteins in Pneumococcal Vaccines May Protect Against Symptomatic SARS-CoV-2 Disease and Death. *Vaccines (Basel)* 2020; 8
- 8) Dockrell DH, Whyte MKB, Mitchell TJ. Pneumococcal pneumonia: mechanisms of infection and resolution. *Chest* 2012; 142: 482-91
- 9) Paguio JA, Yao JS, Dee EC. Silver lining of COVID-19: Heightened global interest in pneumococcal and

- influenza vaccines, an infodemiology study. *Vaccine* 2020; 38: 5430-5
- 10) Guo L, Wei D, Zhang X, Wu Y, Li Q, et al. Clinical Features Predicting Mortality Risk in Patients With Viral Pneumonia: The MuLBSTA Score. *Front Microbiol* 2019; 10:2 752
 - 11) Zhu X, Ge Y, Wu T, Zhao K, Chen Y, et al. Co-infection with respiratory pathogens among COVID-2019 cases. *Virus Res* 2020; 285: 198005
 - 12) Leonard JA, Bruxvoort KJ, Fischer H, Hong VX, Grant LR, et al. Prevention of COVID-19 among older adults receiving pneumococcal conjugate vaccine suggests interactions between *Streptococcus pneumoniae* and SARS-CoV-2 in the respiratory tract. *J Infect Dis* 2021;
 - 13) Jin A, Yan B, Hua W, Feng D, Xu B, et al. Clinical characteristics of patients diagnosed with COVID-19 in Beijing. *Bio safe Health* 2020; 2: 104-11
 - 14) Nidadavolu LS, Walston JD. Underlying Vulnerabilities to the Cytokine Storm and Adverse COVID-19 Outcomes in the Aging Immune System. *J Gerontol A Biol Sci Med Sci* 2021; 76: e13-e8
 - 15) Carethers JM. Insights into disparities observed with COVID-19. *J Intern Med* 2021; 289: 463-73
 - 16) Salazar MR. Is hypertension without any other comorbidities an independent predictor for COVID-19 severity and mortality? *J Clin Hypertens (Greenwich)* 2021; 23: 232-4
 - 17) Gupta SK, Lakshmi PVM, Kaur M, Rastogi A. Role of self-care in COVID-19 pandemic for people living with comorbidities of diabetes and hypertension. *J Family Med Prim Care* 2020; 9: 5495-501
 - 18) Presta V, Figliuzzi I, Cioni B, Gallo G, Battistoni A, et al. ARB-Based Combination Therapy for the Clinical Management of Hypertension and Hypertension-Related Comorbidities: A Spotlight on Their Use in COVID-19 Patients. *High Blood Press Cardiovasc Prev* 2021; 28: 255-62
 - 19) Werberich GM, Marchiori E, Barreto MM, Rodrigues RS. Computed tomography findings in a Brazilian cohort of 48 patients with pneumonia due to coronavirus disease. *Rev Soc Bras Med Trop* 2020; 53: e20200405
 - 20) Gottschalk G, Knox K, Roy A. ACE2: At the crossroad of COVID-19 and lung cancer. *Gene Rep* 2021; 23: 101077
 - 21) Zhang H, Quek K, Chen R, Chen J, Chen B. Expression of the SAR2-Cov-2 receptor ACE2 reveals the susceptibility of COVID-19 in non-small cell lung cancer. *J Cancer* 2020; 11: 5289-92
 - 22) Zhao Y, Zhao Z, Wang Y, Zhou Y, Ma Y, et al. Single-Cell RNA Expression Profiling of ACE2, the Receptor of SARS-CoV-2. *Am J Respir Crit Care Med* 2020; 202: 756-9

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