

The impact of the COVID-19 pandemic on adult bronchiectasis patients and the relationship between clinical parameters and bronchiectasis severity

S. GUL¹, M.A. UYSAL¹, H. ABALI¹, A. YETER¹, E.S. AKALIN KARACA¹,
N. ALAGOZ¹, D. BILICI², E.Y. OZGUN NIKSARLIOGLU¹

¹Chest Diseases Department, University of Health Sciences, Yedikule Chest Diseases and Chest Surgery Education and Research Hospital, Istanbul, Turkey

²Chest Diseases Department, Medeniyet University, Goztepe Education and Research Hospital, Istanbul, Turkey

Abstract. – OBJECTIVE: Viral infections are an important cause of exacerbation in bronchiectasis patients. We aimed to determine the influence of the COVID-19 pandemic on adult bronchiectasis patients and whether there was a relationship between the clinical parameters and the COVID-19 infection.

PATIENTS AND METHODS: In this retrospective observational study, 547 bronchiectasis patients were included. Demographic characteristics, vaccination status, Bronchiectasis Severity Index (BSI), FACED and Reiff scores, and clinical and laboratory parameters during COVID-19 infection were evaluated.

RESULTS: The median age was 56, and 49.2% of the patients were male. The COVID-19 infection rate was 27.6%. 431 (78.8%) patients had at least one dose of the COVID-19 vaccine. The patients were divided into two groups according to their COVID-19 infection status. Emergency admission was significantly higher in the COVID-19-infected group. There was no statistical difference with other clinical factors. The COVID-19-infected patients were divided into home treatment and hospital/intensive care unit (ICU) treatment groups. There was a statistically significant difference between the two groups regarding advanced age, male gender, presence of asthma, long-term oxygen therapy (LTOT) and non-invasive mechanic ventilator (NIMV) usage, sputum culture positivity, BSI and FACED scores, and multiple laboratory parameters (ferritin, C-reactive protein, eosinophil). In logistic regression analysis, BSI was found as a risk factor [OR 1.252 (1.077-1.456), $p=0.004$] and eosinophilia as a protective factor [OR 0.986 (0.973-0.999), $p=0.030$] for hospital/ICU admission.

CONCLUSIONS: Frequent emergency visits might increase the risk of COVID-19 infection in bronchiectasis patients. BSI was found to be an

independent risk factor, and blood eosinophilia could play a protective role in hospital/ICU admission for COVID-19 infection.

Key Words:

Bronchiectasis, COVID-19, Eosinophilia, Hospitalization, Severity.

Introduction

The Coronavirus-19 (COVID-19) pandemic impacted the entire world and had a particularly negative effect on individuals with chronic pulmonary disease, both socially and health-wise. A cohort study from the UK¹ determined that the risk of hospitalization and death due to COVID-19 was higher in patients with previous pulmonary disease. A review article² evaluating the impact of COVID-19 on pulmonary diseases showed that hospitalization and intensive care unit (ICU) admissions were higher in patients with obstructive sleep apnea. COVID-19 causes disruptions in both the diagnosis and treatment of patients with lung cancer, and hospitalizations and ICU stays due to COVID-19 are observed more frequently in those with lung cancer. Also, COVID-19 infection is more common in patients with chronic obstructive pulmonary disease (COPD), and hospitalization and mortality due to COVID-19 are more common in patients with interstitial lung disease than other lung diseases^{2,3}.

Bronchiectasis is a respiratory disease characterized by chronic inflammatory damage of the airways and is being diagnosed more and more as awareness increases. Viral infections are im-

portant in acute exacerbations of bronchiectasis patients and are detected at a 50% rate in the respiratory tract during the exacerbation period⁴. There are different results in studies about the effect of the COVID-19 pandemic on adult bronchiectasis patients. In a case-control study⁵ of patients with COVID-19 infection, patients with bronchiectasis had more severe COVID-19 pneumonia, needed more oxygen and ICU admission, and had a higher death rate than patients without bronchiectasis. Studies by Crichton et al⁶ and Martínez-Vergara et al⁷ indicated a significant decrease in exacerbations among bronchiectasis patients during the COVID-19 pandemic compared to the pre-pandemic period.

We hypothesized that bronchiectasis patients had a high rate of COVID-19 infection and severe illness, and this was related to the clinical severity of bronchiectasis. With this hypothesis, we aimed to determine the impact of the COVID-19 pandemic on adult bronchiectasis patients and the relationship between the clinical factors (demographics, treatments, vaccination, microbiological results), bronchiectasis severity, and the COVID-19 infection.

Patients and Methods

In this retrospective observational study, the data of bronchiectasis patients followed in our pulmonology clinic between March 11, 2020 (the date of the first COVID-19 patient in our country) and December 31, 2021, were evaluated.

The study included patients diagnosed with bronchiectasis by thorax computed tomography (CT) or high-resolution computed tomography (HRCT). Exclusion criteria were being under 18 years old and having traction bronchiectasis due to interstitial lung disease.

Demographic characteristics of patients, respiratory device treatments, influenza, and pneumococcal vaccination during the COVID-19 pandemic, pneumococcal vaccination status in the last five years, hospitalization during the pandemic, emergency admission, sputum culture positivity, respiratory function test results, Bronchiectasis Severity Index (BSI), FACED and Reiff scores, COVID-19 infection and COVID-19 vaccination status, laboratory and radiological test results during COVID-19 infection, and treatment results were recorded.

BSI was applied to determine disease severity. This index includes eight parameters: age, body

mass index (BMI), FEV₁% predicted, hospital admission in the previous year, and exacerbation frequency in the previous year. Based on the BSI score, patients are classified into mild, moderate, and high-risk groups⁸.

FACED score derived from five dichotomized variables [F: forced expiratory volume in 1 s (FEV₁); A: age; C: chronic colonization by *Pseudomonas aeruginosa*; E: radiological extension (number of pulmonary lobes affected); D: dyspnea (mMRC-Modified Medical Research Council) score]. The total score is calculated by summing the scores for each variable, and it can range from 0 to 7 points. This score classifies bronchiectasis into three severity classes: mild bronchiectasis (global score of 0-2 points), moderate bronchiectasis (global score of 3-4 points), and severe bronchiectasis (global score of 5-7 points)⁹.

The radiological severity of bronchiectasis was assessed using the modified Reiff score, which evaluates the number of lobes involved (the lingula was considered a separate lobe; tubular: 1, varicose: 2, and cystic: 3 points). The minimum score is one, and the maximum score is 18¹⁰.

For the diagnosis of COVID-19, positive real-time reverse transcription-polymerase chain reaction (RT-PCR) and/or typical radiological findings (bilateral ground-glass opacities, consolidation, vascular enlargement, etc.) were sought.

Statistical Analysis

Statistical analyses were conducted using the IBM Statistical Package for the Social Sciences (SPSS) version 22 (IBM Corp., Armonk, NY, USA). Values were presented as a median and interquartile range for continuous variables and as frequencies and percentages for categorical data. Comparisons between the two groups were performed using the unpaired *t*-test, Mann-Whitney U test, or Chi-squared test, depending on the data distribution. For multivariate analysis, the possible factors identified with the univariate analyses were entered in logistic regression analysis to determine the independent predictors for hospital/ICU admission during COVID-19 infection. $p < 0.05$ was determined as the statistical significance level.

Results

Among the 555 patients evaluated, eight patients who died before the pandemic period were excluded. The flowchart of the patients

can be seen in Figure 1. Of the remaining 547 patients, 278 (50.8%) were female. The demographics and radiological characteristics in thorax CT, Reiff, BSI, and FACED scores are shown in Table I. 83% of the patients had at least one comorbid disease, and the most common comorbidities were COPD, asthma, and heart disease. The median number of involved lobes was 2 (IQR₂₅₋₇₅: 1-4). To achieve standardization, the patients were divided into two groups: those with ≤ 3 and >4 lobe involvement. According to the BSI score, 50% of the patients had mild bronchiectasis, and according to the FACED score, 64.5% of the patients had mild bronchiectasis (Figure 2).

During the COVID-19 pandemic, 97 (17.7%) patients received influenza vaccination, 109 (19.9%) received pneumococcal vaccination, and in the past five years, 271 (49.5%) received pneumococcal vaccination. During the pandemic, 131 (23.9%) patients were hospitalized at least once, and 213 (38.9%) patients had at least one emergency admission. Of the patients,

114 (21%) had sputum culture positivity, and the most identified microorganism was *Pseudomonas aeruginosa* (63.2%).

The COVID-19 infection status of bronchiectasis patients was searched through the hospital information system, and the data of 45 patients could not be accessed. Of the remaining 502 patients, 151 (27.6%) had COVID-19 infection and had a high rate of COVID-19 PCR positivity (n: 146, 96.7%). Fifty-five (36.4%) patients had radiological involvement. One hundred thirteen (70%) patients got treatment at home, 33 (22%) at hospital, and five (3%) at ICU. All of the patients in the hospital and ICU needed oxygen. 110 (72.8%) patients got treatment for COVID-19. Favipiravir, a suitable nonspecific antibiotic, low molecular weight heparin, methylprednisolone, and dexamethasone were the most given drugs. Three (2%) patients died due to COVID-19 infection.

Forty-six patients died during the pandemic period. Three (2%) of them died due to COVID-19 infection. Eleven patients died due

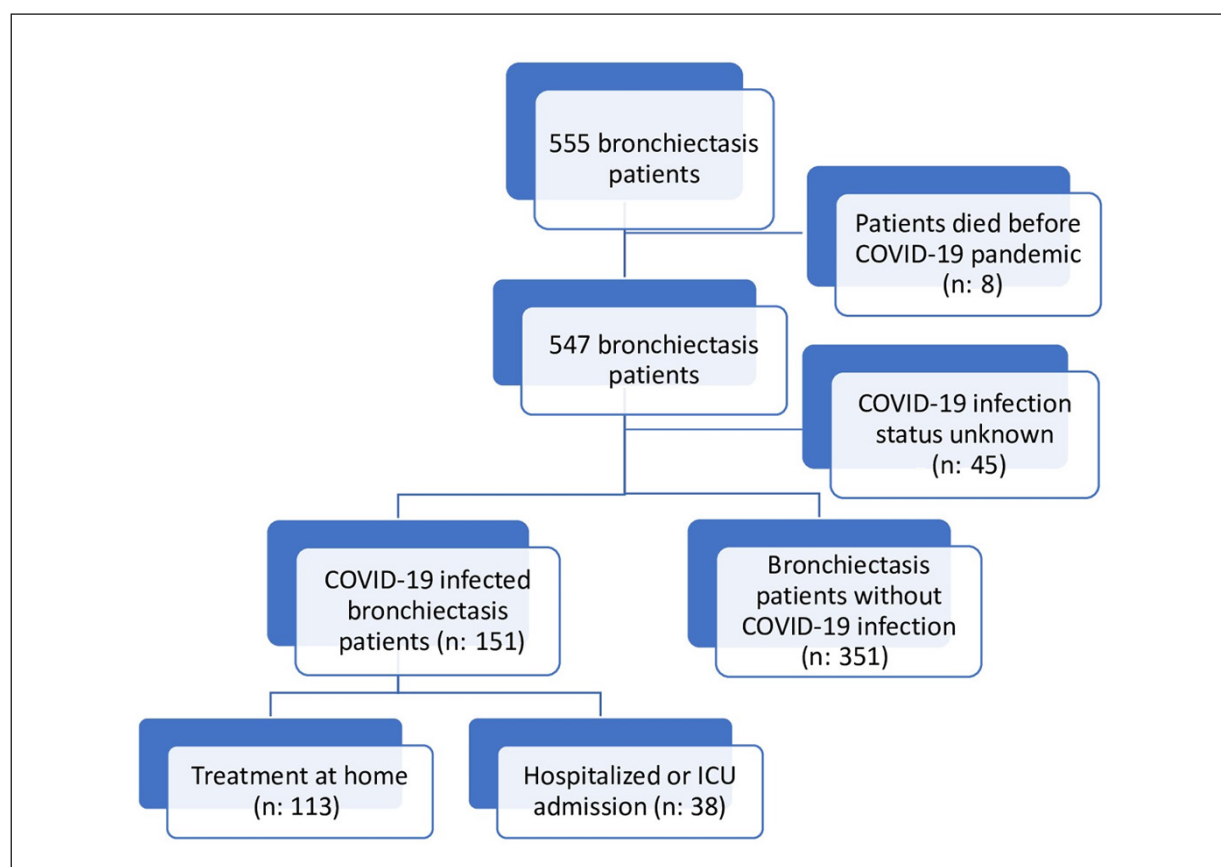


Figure 1. Flowchart of the bronchiectasis patients.

Table I. Demographics, radiological findings, and Reiff, BSI, and FACED scores of bronchiectasis patients.

Total n: 547	n (%)
Age	56 (43-66)
Comorbidity	
Yes	455 (83.2)
No	92 (16.8)
Comorbidity type	
COPD	211 (38.6)
Asthma	173 (31.6)
DM	84 (15.4)
HT+CHF	143 (26.1)
IHD	41 (7.5)
Lung cancer	5 (0.9)
Other	58 (10.6)
Smoking	
Nonsmoker	301 (55)
Ex-smoker	165 (30.2)
Smoker	81 (14.8)
Pack-years	25 (15-40)
Inhaler drug usage	
Yes	434 (79.3)
No	113 (20.7)
Inhaler steroid usage	343 (62.7)
Using respiratory device	
Nebulizer	156 (28.5)
LTOT	72 (13.2)
NIMV	27 (4.9)
Bronchiectasis type	
Cystic	199 (36.4)
Tubular	140 (25.6)
Varicose	36 (6.6)
Cystic+tubular	66 (12.1)
Cystic+varicose	61 (11.2)
Tubular+varicose	27 (4.9)
Cystic+tubular+varicose	18 (3.3)
Involved lobes	
Right upper lobe	204 (37.3)
Right middle lobe	270 (49.4)
Right lower lobe	247 (45.2)
Left upper lobe	147 (26.9)
Lingula	246 (45)
Left lower lobe	348 (63.6)
Number of lobes involved	
≤3 lobe	406 (74.2)
≥4 lobe	141 (25.8)
Reiff score	6 (3-9)
BSI (n: 456)	5 (3-8)
BSI score	
Mild	228 (50)
Moderate	117 (25.7)
High	111 (24.3)
FACED (n: 456)	1 (0-3)
FACED score	
Mild	294 (64.5)
Moderate	123 (27)
High	39 (8.6)

Continuous variables are expressed as median (interquartile range: IQR₂₅₋₇₅). BSI: bronchiectasis severity index, COPD: chronic obstructive pulmonary disease, DM: diabetes mellitus, HT: hypertension, CHF: chronic heart failure, IHD: ischemic heart disease, LTOT: long-term oxygen therapy, NIMV: non-invasive mechanic ventilator.

to non-COVID-19 reasons (respiratory failure, cardiac disease, etc.). The cause of death and COVID-19 infection status of 32 patients could not be reached.

The COVID-19 vaccination status of 59 patients could not be reached. Four hundred and thirty-one (78.8%) patients had at least one dose of the COVID-19 vaccine (Figure 3). Among the COVID-19-infected bronchiectasis patients, 127 (84%) patients had been vaccinated. Seventy-five (59%) of them were vaccinated after the disease, and 52 (41%) before the disease.

The patients were divided into two groups according to their COVID-19 infection status. Statistical analysis was performed to assess the relationship between clinical factors and COVID-19 infection (Table II). There was no difference between the two groups regarding demographic characteristics, nebulizer, long-term oxygen therapy (LTOT), and NIMV treatment. When comorbidities were divided into asthma, COPD, diabetes mellitus, ischemic heart disease, chronic heart failure, and lung cancer, no statistically significant difference was found between the two groups. Also, the rates of vaccination, hospital admission, and sputum culture positivity were similar between the two groups. Emergency admission was significantly higher in the group with COVID-19 infection ($p=0.015$). Both groups had similar BSI and FACED scores and severity levels.

COVID-19-infected bronchiectasis patients were divided into two groups: those treated at home and those treated at the hospital and ICU (Table III). In the statistical analysis evaluating risk factors for hospitalization and ICU admission, the hospitalization rate was significantly higher in patients with advanced age, male gender, and in those treated with LTOT and NIMV ($p<0.05$). Sputum culture positivity was higher in the hospitalized group, and this difference was statistically significant ($p=0.044$). The number of patients with asthma was statistically significantly higher in the group receiving home treatment. Significant results in BSI and FACED scores, as well as biochemical values, can be seen in Table III. COVID-19 vaccination rates were higher in the group treated at home, and this group was mostly vaccinated before infection, while the group treated in the hospital was mainly vaccinated after infection.

We have performed the stepwise multivariate model to predict hospital and ICU admission during COVID-19 infection in patients with

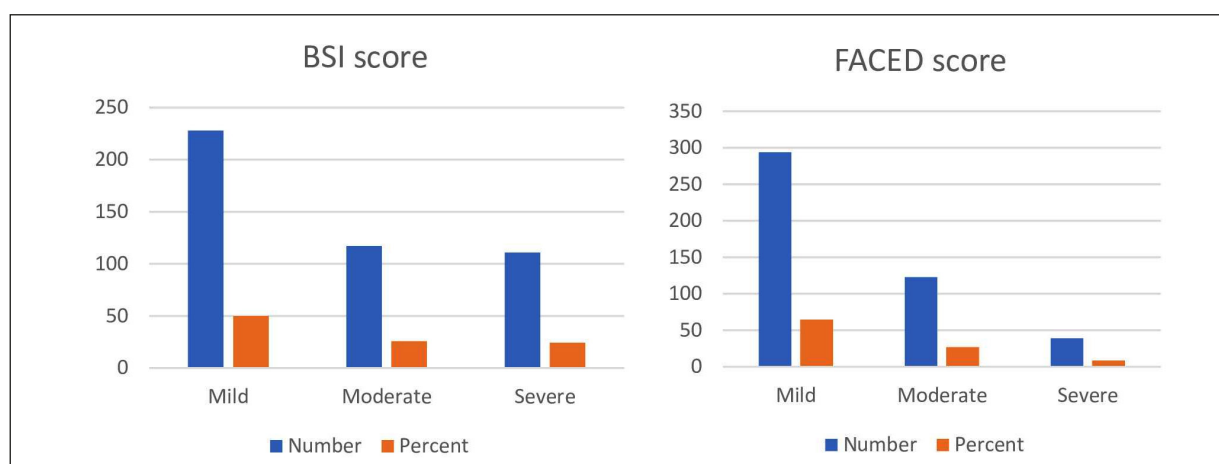


Figure 2. Bronchiectasis severity index (BSI) and FACED scores of the bronchiectasis patients.

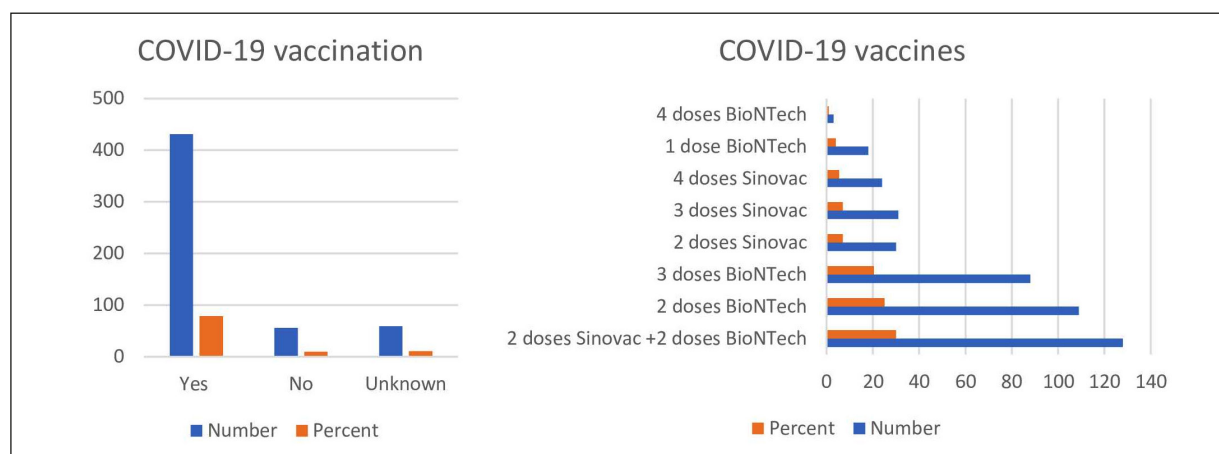


Figure 3. COVID-19 vaccination status of the bronchiectasis patients.

bronchiectasis; possible factors identified with univariate analyses were entered into multivariate logistic regression analysis. This model showed that BSI is an independent risk factor [OR 1.985 (1.020-3.864), $p=0.044$] and blood eosinophilia can be a protective factor [OR 0.921 (0.852-0.995), $p=0.037$] for hospital/ICU admission. Multivariate analysis also identified BSI as a risk factor [OR 1.252 (1.077-1.456), $p=0.004$] and blood eosinophilia as a protective factor [OR 0.986 (0.973-0.999), $p=0.030$] (Table IV). Although the presence of asthma was seen as a risk factor in univariate analysis [OR 2.962 (1.066-8.226), $p=0.037$], no statistical significance was detected in multivariate analysis ($p=0.952$).

Discussion

This study showed no significant relationship between COVID-19 infection and clinical parameters with the severity of bronchiectasis. Frequent emergency visits might increase the risk of COVID-19 infection. BSI was found to be an independent risk factor, and blood eosinophilia could play a protective role in hospital/ICU admission during COVID-19 infection. To our knowledge, this study is the first study that compares the clinical variables and disease severity of bronchiectasis patients with COVID-19 infection. 27.6% of the bronchiectasis patients had COVID-19 infections, and 78.8% of patients received at least one dose of the COVID-19 vaccine. Advanced age, male gen-

Table II. The relationship of clinical parameters with the status of COVID-19 infection in bronchiectasis patients.

	Patients with COVID-19 infection (n: 151)	Patients without COVID-19 infection (n: 351)	<i>P</i>
Age	54 (44-65)	56 (66-43)	0.602
Gender			0.402
Female	73 (48.4)	184 (52.4)	
Male	78 (51.6)	167 (47.6)	
Comorbidities			0.427
Yes	123 (81.4)	296 (84.3)	
Smoking			0.955
Nonsmoker	83 (55)	198 (56.4)	
Ex-smoker	46 (30)	103 (29.3)	
Smoker	22 (15)	50 (14.3)	
Inhaler drug usage			0.227
Yes	115 (76)	284 (81)	
No	36 (24)	67 (19)	
Inhaler steroid usage			0.424
Yes	92 (61)	227 (64.6)	
No	59 (39)	124 (35.4)	
Using respiratory device			
Nebulizer	38 (25)	101 (28.7)	0.407
LTOT	20 (13.2)	39 (11)	0.496
NIMV	7 (4.6)	14 (4)	0.745
During the pandemic			
Influenza vaccination	34 (22.5)	63 (18)	0.479
Pneumococcal vaccination	39 (25.8)	68 (19.3)	0.260
Hospitalization	42 (27.8)	74 (21)	0.101
Emergency admission	70 (46.3)	122 (34.7)	0.015
Number of lobes involved			0.821
≤3 lobe	115 (76)	264 (75)	
≥4 lobe	36 (24)	87 (25)	
BSI (n: 419)	4 (2-8)	5 (3-8)	0.635
BSI score (n: 419)	n: 122	n: 297	0.627
Mild	64 (52.4)	149 (50)	
Moderate	29 (23.8)	84 (28)	
High	29 (23.8)	64 (22)	
FACED (n: 419)	1 (0-3)	1 (0-3)	0.909
FACED score (n: 419)			0.432
Mild	84 (68.8)	192 (64.6)	
Moderate	32 (26.2)	80 (27)	
High	6 (5)	25 (8.4)	
COVID-19 vaccination			0.680
Yes	127 (84)	304 (86.5)	
No	20 (13)	37 (10.5)	
Unknown	4 (3)	10 (3)	

Continuous variables are expressed as median (interquartile range: IQR_{25,75}). Categorical variables are expressed as n (%). LTOT: long-term oxygen therapy, NIMV: non-invasive mechanic ventilator, BSI: bronchiectasis severity index.

der, using LTOT and NIMV, reproduction in sputum culture, BSI and FACED scores, and multiple laboratory parameters were found to be associated with hospital/ICU hospitalization.

Few studies^{7,11} in the literature can show the rate of COVID-19 infection in adult bronchiectasis patients. In a study⁷ including 150 bronchiectasis patients, the rate of COVID-19 infection was found to be 8.7%. In a recent study¹¹ on bron-

chiectasis patients from three countries, the incidence of COVID-19 on bronchiectasis patients was found to be approximately 4%, with variation between countries. Chiner-Vives et al² evaluated the number of bronchiectasis patients among COVID-19-infected patients, and this rate was reported as 0.5% to 1.6%. In a multicenter study¹² conducted in Spain, the rate of COVID-19 infection among cystic fibrosis patients was examined,

Table III. Comparison of COVID-19-infected bronchiectasis patients receiving home treatment and hospital or ICU treatment regarding clinical parameters.

	Treatment at home (n: 113)	Hospitalized or ICU admission (n: 38)	P
Age	52 (42-64)	61 (49-69)	0.020
Gender			0.000
Male	49 (43.4)	29 (76.3)	
Female	64 (56.6)	9 (23.6)	
Comorbidity			
Yes	92 (81.4)	31 (81.5)	0.982
Asthma diagnosed	35 (31)	5 (13.2)	0.031
Inhaler drug usage	89 (78.8)	26 (68.4)	0.196
Inhaler steroid usage	73 (64.6)	19 (50)	0.111
Using respiratory device			
LTOT	11 (10)	9 (23.6)	0.033
NIMV	3 (3)	4 (10.5)	0.040
Sputum culture positivity	16 (14)	11 (29)	0.044
Number of lobes involved			0.196
≤3 lobe	89 (78.7)	26 (68.4)	
≥4 lobe	24 (21.3)	12 (31.6)	
BSI	4 (2-7)	9 (5-12)	0.000
BSI score	n: 92	n: 30	0.000
Mild	57 (62)	7 (23)	
Moderate	21 (23)	8 (27)	
High	14 (15)	15 (50)	
FACED	1 (0-3)	2 (1-3)	0.016
FACED score			0.252
Mild	66 (72)	18 (60)	
Moderate	23 (25)	9 (30)	
High	3 (3)	3 (10)	
NLR	2.39 (1.69-5)	4.65 (3.23-6.27)	0.007
Eosinophil 10³/μL	65 (10-150)	15 (0-40)	0.020
Ferritin ng/mL	71.7 (30.1-136.5)	174 (76-412)	0.009
CRP mg/L	21.5 (6.1-50.5)	39 (18-102)	0.013
Procalcitonin ng/ml	0.04 (0.03-0.09)	0.07 (0.04-0.17)	0.116
Treatment result			0.003
Completed the treatment	113	35 (92)	
Exitus	0	3 (8)	
COVID-19 vaccination			0.031
Yes	99 (87.6)	28 (73.6)	
No	13 (11.5)	7 (18.4)	
Unknown	1 (9)	3 (8)	
Time of COVID-19 vaccination			0.173
Before infection	43 (43.4)	8 (29)	
After infection	56 (56.6)	20 (71)	

Continuous variables are expressed as median (interquartile range- IQR₂₅₋₇₅). Categorical variables are expressed as n (%). ICU: intensive care unit, LTOT: long-term oxygen therapy, NIMV: non-invasive mechanic ventilator, BSI: bronchiectasis severity index, NLR: neutrophil to lymphocyte ratio, CRP: C-reactive protein.

and this rate was found to be 32/10000, lower than the general population average. In our study, the rate of COVID-19-infected bronchiectasis patients was high compared to other studies^{7,11,12} and the country average.

There is insufficient data on the importance of vaccination in patients with bronchiectasis. Vaccine-related studies¹³ have mostly been done

on other chronic lung conditions such as COPD. However, influenza and pneumococcal vaccination are recommended to reduce the rate of lower respiratory tract infections in bronchiectasis patients¹⁴. In our study, approximately 50% of the patients received pneumococcal vaccination within the last five years; however, this rate declined during the pandemic period. A comparison

Table IV. Logistic regression analysis to predict hospital and ICU admission risk factors during COVID-19 infection in bronchiectasis patients.

	Univariate		Multivariate	
	Odds ratio (95% CI)	<i>p</i>	Odds ratio (95% CI)	<i>p</i>
Age	0.981 (0.823-1.169)	0.829		
Gender (Male)	3.126 (0.161-60.782)	0.452		
Asthma	2.962 (1.066-8.226)	0.037	1.054 (0.191-5.816)	0.952
LTOT	0.002 (0.000-5.455)	0.121		
BSI	1.985 (1.020-3.864)	0.044	1.252 (1.077-1.456)	0.004
FACED score	4.098 (0.667-25.17)	0.128		
NLR	0.924 (0.541-1.577)	0.772		
Eosinophil	0.921 (0.852-0.995)	0.037	0.986 (0.973-0.999)	0.030
Ferritin	1.010 (0.993-1.028)	0.253		
CRP	0.980 (0.920-1.044)	0.531		

ICU: Intensive care unit, LTOT: Long-term oxygen therapy, BSI: Bronchiectasis severity index, NLR: neutrophil to lymphocyte ratio, CRP: C-reactive protein.

could not be made in terms of the influenza vaccine because previous data could not be found. Nevertheless, the rate of influenza vaccination during the pandemic period was found to be as low as 17.7%. The unavailability of these vaccines under pandemic conditions and patients' neglect of other vaccines due to the COVID-19 vaccine may have caused this situation.

In this study, 78.8% of the bronchiectasis patients had at least one dose of the COVID-19 vaccine. No information was found in the literature on this subject. A noteworthy issue is that the vaccination rates were higher in the group that did not have COVID-19 infection and in those who received home treatment in the COVID-19 infected group, although it was not statistically significant. In addition, the vaccination rate was low in the hospitalized and ICU groups, and the vaccination time was mostly after hospitalization in this group. This may indicate that vaccination reduces hospitalization. In a meta-analysis¹⁵ investigating the effect of vaccination against COVID-19 infection, the vaccine prevented 68.8% of infections and 67.8% of hospitalizations. Our study's data may also support this finding, as we explained above.

Several studies^{6,16} have shown that hospital admissions and hospitalization of patients with respiratory diseases decreased during the pandemic period. In the study by Crichton et al⁶, there was a decrease in exacerbation and hospitalization due to exacerbation of bronchiectasis patients during the pandemic period compared to the pre-pandemic period. This situation has been associated with the protection of bronchiectasis

patients from other viral and bacterial agents with the use of masks, a decrease in air pollution, and a decrease in contact with the hospital. This study has no information about the severity of bronchiectasis patients. In addition, the number of exacerbations and hospitalizations were not associated with the status of COVID-19 infection. In our study, although the number of emergency admissions was significantly higher in the COVID-19-infected group, no comparison was made with previous years. The high number of emergency admissions may suggest that patients may have been infected with COVID-19 in the hospital setting.

When assessing patients for COVID-19 infection severity (treated at home/hospital/ICU), there was a statistically significant difference between the two groups regarding advanced age, male gender, LTOT and NIMV, sputum culture positivity, BSI and FACED scores. In the literature^{1,17}, the presence of COPD, asthma, bronchiectasis, and interstitial lung disease in the normal population was associated with severe COVID-19 infection, but not all of them were associated with death due to COVID-19 infection. In this study, the percentage of asthma patients was found to be statistically significantly higher in the group receiving home treatment. This may be due to the lower number of asthma patients in the hospitalized group. Some previous studies¹⁸⁻²⁰ have shown that advancing age and the male gender are poor prognostic factors in patients with COVID-19 infection, as in our study. The significantly higher positive sputum culture, LTOT and NIMV use, BSI, and FACED scores in hospitalized and ICU

admission groups warn us that patients with severe bronchiectasis may worsen when infected with COVID-19. In the study of Shteinberg et al¹¹, bronchiectasis is associated with a slightly but significantly elevated risk for moderate-to-severe COVID-19, but detailed clinical-functional and radiological characteristics of bronchiectasis patients were not evaluated in this study. So, our study is the first to present this data.

Inflammatory markers such as C-reactive protein, ferritin, and neutrophil to lymphocyte ratio were higher in the group with severe COVID-19 infection. In the literature^{21,22}, these markers are indicators of survival and mortality during COVID-19 infection. What is noteworthy here is that patients with high eosinophil levels mostly received treatment at home and had a milder COVID-19 infection. In logistic regression analysis, blood eosinophilia was a protective factor for hospitalization and ICU admission. Some publications suggest that eosinophilia may protect against severe COVID-19 infection in asthma patients. Ferstraoaru et al²³ showed that eosinophil levels of 150 cells/ μ L and above reduce hospital admissions in COVID-19 infection and mortality in hospitalized patients. Herein, decreased ACE-2 receptor expression in bronchial epithelium due to Th2 inflammation is presented as a possible mechanism. In another study²⁴, it was shown that asthma patients hospitalized due to COVID-19 infection with eosinophilia of 200 cells/ μ L and above had a milder disease and less intensive care unit admission and mortality. Unfortunately, the presence of bronchiectasis in the subgroups was not mentioned in either study.

Limitations

The most important limitation of our study is the missing data on the patients due to the study's retrospective nature. The lack of information on the causes of death in the group of patients who died has led to unclear results on mortality. Conducting the study in a single center was another limitation.

Conclusions

In conclusion, frequent emergency visits may increase the risk of COVID-19 infection in bronchiectasis patients. Other than that, no clinical risk factor has been identified for becoming infected with COVID-19. Although not

statistically significant, the protective effect of vaccination has been shown. When infected with COVID-19, patients with severe bronchiectasis with a high BSI value are at risk for hospitalization and ICU admission, while blood eosinophilia may be protective.

Conflict of Interest

The authors declare that they have no conflict of interest to disclose.

Funding

No funding is declared for this article.

Ethics Approval

Ethical approval for this study was obtained from the University of Health Sciences, Hamidiye Scientific Ethics Committee (2021-21/18).

Informed Consent

Not applicable due to the retrospective design of the study.

Acknowledgments

We want to express our sincere gratitude to all parties who generously contributed to this study.

Authors' Contributions

Conceptualization: ŞG, EYÖN. Methodology: ŞG, MAU. Software: not applicable. Validation: AY, NA. Formal analysis: ŞG, MAU. Investigation: HA, DB. Resources: NA, DB. Data curation: HA, AY, ESAK, NA, DB. Writing original draft: ŞG, MAU. Writing, review, and editing: ŞG, MAU, EYÖN. Visualization: HA, ESAK. Supervision: DB, EYÖN. Project administration: ŞG, MAU.

ORCID ID

Şule Gül: 0000-0002-7162-2611
Mehmet Atilla Uysal: 0000-0002-0430-498X
Hülya Abalı: 0000-0003-4041-7479
Ayşe Yeter: 0000-0002-1940-1248
Esmâ Seda Akalın Karaca: 0000-0002-9512-9223
Neval Alagoz: 0000-0002-4203-4562
Deniz Bilici: 0000-0003-3707-2502
Elif Yelda Özgün Niksarlıoğlu: 0000-0002-6119-6540

Data Availability

All data associated with this paper are available from the corresponding author upon reasonable request.

References

- 1) Aveyard P, Gao M, Lindson N, Hartmann-Boyce J, Watkinson P, Young D, Coupland CAC, Tan PS, Clift AK, Harrison D, Gould DW, Pavord ID, Hippisley-Cox J. Association between pre-existing respiratory disease and its treatment, and severe COVID-19: a population cohort study. *Lancet Respir Med* 2021; 9: 909-923.
- 2) Chiner-Vives E, Cordovilla-Pérez R, de la Rosa-Carrillo D, García-Clemente M, Izquierdo-Alonso JL, Otero-Candelera R, Pérez-de Llano L, Sellares-Torres J, de Granda-Orive JI. Short and Long-Term Impact of COVID-19 Infection on Previous Respiratory Diseases. *Arch Bronconeumol* 2022; 58: 39-50.
- 3) Ntatsoulis K, Karampitsakos T, Tsitoura E, Stylianaki EA, Matralis AN, Tzouvelekis A, Antoniou K, Aidinis V. Commonalities Between ARDS, Pulmonary Fibrosis and COVID-19: The Potential of Autotaxin as a Therapeutic Target. *Front Immunol* 2021; 12: 1-14.
- 4) Gao YH, Guan WJ, Xu G, Lin ZY, Tang Y, Lin ZM, Gao Y, Li HM, Zhong NS, Zhang GJ, Chen RC. The Role of Viral Infection in Pulmonary Exacerbations of Bronchiectasis in Adults: A Prospective Study. *Chest* 2015; 147: 1635-1643.
- 5) Choi H, Lee H, Lee SK, Yang B, Chung SJ, Yeo Y, Park TS, Park DW, Moon JY, Kim TH, Sohn JW, Yoon HJ, Kim SH. Impact of bronchiectasis on susceptibility to and severity of COVID-19: a nationwide cohort study. *Ther Adv Respir Dis* 2021; 15: 4-7.
- 6) Crichton ML, Shoemark A, Chalmers JD. The impact of the COVID-19 pandemic on exacerbations and symptoms in bronchiectasis: A prospective study. *Am J Respir Crit Care Med* 2021; 204: 857-859.
- 7) Martínez-Vergara A, Girón Moreno RM, Oliveira C, Victoria Girón M, Peláez A, Ancochea J, Oscullo G, Martínez-García MÁ. Impact of the SARS-CoV-2 Virus Pandemic on Patients with Bronchiectasis: A Multicenter Study. *Antibiot Artic* 2022; 11: 1096.
- 8) Chalmers JD, Goeminne P, Aliberti S, McDonnell MJ, Lonni S, Davidson J, Poppelwell L, Salih W, Pesci A, Dupont LJ, Fardon TC, De Soyza A, Hill AT. The bronchiectasis severity index: an international derivation and validation study. *Am J Respir Crit Care Med* 2014; 189: 576-585.
- 9) Costa JC, Machado JN, Ferreira C, Gama J, Rodrigues C. The Bronchiectasis Severity Index and FACED score for assessment of the severity of bronchiectasis. *Pulmonology* 2018; S2173-5115(17)30154-9. doi: 10.1016/j.rppnen.2017.08.009. Epub ahead of print.
- 10) Reiff DB, Wells AU, Carr DH, Cole PJ, Hansell DM. CT findings in bronchiectasis: Limited value in distinguishing between idiopathic and specific types. *Am J Roentgenol* 1995; 165: 261-267.
- 11) Shteinberg M, Sibila O, Stein N, Faner R, Jordan A, Olvera N, Sivapalan P, Jensen JUS, Crichton M, Marrades P, Chalmers JD, Meyer CN, Saliba W. Risk of SARS-CoV-2 Infection and Disease Severity Among People With Bronchiectasis: Analysis of Three Population Registries. *Chest* 2024; 165: 79-83.
- 12) Mondejar-Lopez P, Quintana-Gallego E, Giron-Moreno RM, Cortell-Aznar I, Ruiz de Valbuena-Maiz M, Diab-Caceres L, Prados-Sanchez C, Alvarez-Fernandez A, Garcia-Marcos PW, Peñalver-Mellado C, Pastor-Vivero MD, Oliveira C, Lopez-Neyra A, Castillo-Corullon S, Palma-Milla S, Perez-Ruiz E, Sole-Jover A, Barrio MI, Sanchez-Solis M, Asensio de la Cruz Ó; CF-COVID19-Spain Registry Group. Impact of SARS-CoV-2 infection in patients with cystic fibrosis in Spain: Incidence and results of the national CFCOVID19-Spain survey. *Respir Med* 2020; 170: 106062.
- 13) Simon S, Joean O, Welte T, Rademacher J. The role of vaccination in COPD: influenza, SARS-CoV-2, pneumococcus, pertussis, RSV and varicella zoster virus. *Eur Respir Rev* 2023; 32: 230034.
- 14) O'Grady KAF, Cripps AW, Grimwood K. Paediatric and adult bronchiectasis: Vaccination in prevention and management. *Respirology* 2019; 24: 107-114.
- 15) Zheng C, Shao W, Chen X, Zhang B, Wang G, Zhang W. Real-world effectiveness of COVID-19 vaccines: a literature review and meta-analysis. *Int J Infect Dis* 2022; 114: 252-260.
- 16) Kyriakopoulos C, Gogali A, Exarchos K, Potosinos D, Tatsis K, Apollonatos V, Loukides S, Pappiris S, Sigala I, Katsaounou P, Aggelidis M, Fouka E, Porpodis K, Kontakiotis T, Sampsonas F, Karampitsakos T, Tzouvelekis A, Bibaki E, Karagiannis K, Antoniou K, Tzanakis N, Dimeas I, Daniil Z, Gourgoulis K, Kouratzi M, Steiropoulos P, Antonakis E, Papanikolaou IC, Ntritsos G, Kostikas K. Reduction in Hospitalizations for Respiratory Diseases during the First COVID-19 Wave in Greece. *Respiration* 2021; 100: 588-593.
- 17) Guan WJ, Liang WH, Shi Y, Gan LX, Wang HB, He JX, Zhong NS. Chronic Respiratory Diseases and the Outcomes of COVID-19: A Nationwide Retrospective Cohort Study of 39,420 Cases. *J Allergy Clin Immunol Pr* 2021; 9: 2645-2655.
- 18) Girma D, Dejene H, Adugna L, Tesema M, Awol M. COVID-19 Case Fatality Rate and Factors Contributing to Mortality in Ethiopia: A Systematic Review of Current Evidence. *Infect Drug Resist* 2022; 15: 3491-3501.
- 19) Fortunato F, Martinelli D, Lo Caputo S, Santantonio T, Dattoli V, Lopalco PL, Prato R. Original research: Sex and gender differences in COVID-19: an Italian local register-based study. *BMJ Open* 2021; 11: e051506.
- 20) Ballini A, Cantore S, Serrettiello E, Troiano G, Smimmo A, Dioguardi M, Spirito F, Sasso FC, De

- Vito D, Lo Muzio L, Di Domenico M. Multiparametric correlation of laboratory biomarkers to multiorgan failure outcome in hospitalized COVID-19 patients: a retrospective observational study. *Eur Rev Med Pharmacol Sci* 2023; 27: 8962-8974.
- 21) Palladino M. Complete blood count alterations in COVID-19 patients: A narrative review. *Biochem Med* 2021; 31: 30501.
- 22) Semiz S. COVID19 biomarkers: What did we learn from systematic reviews? *Front Cell Infect Microbiol* 2022; 12: 1-15.
- 23) Ferastraoararu D, Hudes G, Jerschow E, Jariwala S, Karagic M, de Vos G, Rosenstreich D, Ramesh M. Eosinophilia in Asthma Patients Is Protective Against Severe COVID-19 Illness. *J Allergy Clin Immunol Pract* 2021; 9: 1152-1162.e3.
- 24) Ho KS, Howell D, Rogers L, Narasimhan B, Verma H, Steiger D. The relationship between asthma, eosinophilia, and outcomes in coronavirus disease 2019 infection. *Ann Allergy Asthma Immunol* 2021; 127: 42-48.