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Asthma and allergic diseases are not risk factors for hospitalization in children with coronavirus disease 2019

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) emerged as a pandemic toward the end of 2019, causing large numbers of people to become infected and die.
Objective: To determine whether allergic diseases are a risk factor for hospitalization in COVID-19.
Methods: We conducted a study including 107 pediatric patients after COVID-19 recovery. The International Study of Asthma and Allergies in Childhood Phase 3 questionnaires were distributed together with a detailed history of environmental factors and an allergic evaluation including skin prick tests, specific immunoglobulin E tests, and spirometry. We investigated the prevalence of allergic diseases and evaluated the factors associated with hospitalization in COVID-19.
Results: A total of 61 (57%) patients were hospitalized and 46 (43%) patients were followed closely in the outpatient clinic. The prevalences of allergic rhinitis, asthma, atopic dermatitis, and episodic wheezing were 10.3%, 6,5%, 4.7%, and 3.7%, respectively, within the whole study population. Although having asthma with or without allergic rhinitis, atopic dermatitis, and passive tobacco exposure were not found to be related to hospitalization because of COVID-19, having a pet at home was found to decrease the risk of hospitalization (odds ratio, 0.191; 95% confidence interval, 0.047-0.779; $P = .02$). Spirometry tests revealed a higher forced expiratory volume in one second to forced vital capacity ratio and a peak expiratory flow reversibility in hospitalized patients than in nonhospitalized ones ($P = .02$ and $P = .003$, respectively).
Conclusion: Asthma and allergic diseases do not seem to be risk factors for hospitalization in children because of COVID-19, and having a pet at home can be a protective effect. Pulmonary function testing seems to be important for monitoring lung damage after COVID-19.

Introduction

A novel strain of human coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in December 2019, and the disease, named coronavirus disease 2019 (COVID-19) by the World Health Organization, has infected more than 50 million people and led to the death of 1.2 million people worldwide as of November 10, 2020.[1,2] It is known that asthma is a risk factor for the severe course of viral respiratory tract infections,[3] and asthma control is inversely related to viral severity.[4]

The US Centers for Disease Control and Prevention's (CDC) published laboratory-confirmed pediatric COVID-19 cases indicate that 2572 of 149,082 (1.7%) cases of known age were under 18 years of age.[5] Among the 345 pediatric cases with information on underlying conditions, the most common underlying condition was chronic lung disease, including asthma (11.6%), followed by cardiovascular disease (7.2%), and immunosuppression (2.9%).[5] The CDC[6] and European Academy of Allergy and Clinical Immunology[7] recommend that children with asthma (especially severe and uncontrolled asthma) be included in the risk group, with a footnote that this proposal is on the basis of common sense rather than scientific evidence.[7] However, a recent systematic review in children[8] reported that out of 67 studies and 5 reviews, only 2

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studies included information on asthma as a risk factor for COVID-19—but not severity or mortality—in children. Ruano et al[9] retrospectively investigated the COVID-19 symptoms among children with asthma and did not find a difference in asthma severity, asthma control, lung functions, and allergic comorbidities between probable COVID-19 cases and non–COVID-19 cases but an increase in both reliever and controller treatment in probable COVID-19 cases, suggesting COVID-19 as a possible cause of asthma exacerbations.

The largest prevalence studies to date have been limited to a description of the number of cases by age, so it remains unclear whether childhood asthma and allergic diseases are associated with COVID-19 risk and severity. Furthermore, the allergic diseases reported in these studies were based on patient declarations or medical records. In this study, we aimed to investigate the frequency of allergic diseases in pediatric patients with COVID-19 on the basis of clinical and laboratory evaluation and evaluate whether allergic diseases are a risk factor for hospitalization.

Methods

Study Population

The study was conducted in children aged between 0 and 18 years old admitted to the hospital with COVID-19 symptoms between March 15, 2020, and May 31, 2020. Our hospital is a tertiary reference hospital in Istanbul, Turkey, and our emergency department has a COVID-19 outpatient clinic where all suspected cases (not only symptomatic but also asymptomatic individuals who have contact with a patient with COVID-19 polymerase chain reaction (PCR)–positivity) are evaluated. The study was approved by the local ethics committee (No: KAEK.2020.08.189).

The study population included the following: (1) patients admitted to the COVID-19 clinic and having a positive PCR test for SARS-CoV-2; (2) patients hospitalized for COVID-19 and having a positive PCR test for SARS-CoV-2; and (3) patients hospitalized for COVID-19 and having a negative PCR test for SARS-CoV-2 but having a chest computed tomography (CT) scan compatible with COVID-19 (ie, bilateral distribution of ground-glass opacities with or without consolidation in posterior and peripheral lungs; multifocal, patchy, or segmental consolidation distributed in subpleural areas or along with bronchovascular bundles; and reticular pattern with interlobular septal thickening, crazy paving pattern, and air bronchogram)[10] and direct contact with people with SARS-CoV-2 confirmed by PCR testing.

Patients were evaluated in the pediatric emergency department or the pediatric COVID-19 outpatient clinic by a pediatric infectious disease specialist during their first admission, and hospitalization was determined according to the hospitalization criteria of the American Academy of Pediatrics as follows: (1) hypoxemia (peripheral capillary oxygen saturation of <92%); (2) infants less than 3 to 6 months of age; (3) tachypnea; (4) respiratory distress; (5) signs of dehydration or reduced oral intake; (6) capillary refill of more than 2 seconds; (7) toxic appearance; (8) underlying comorbidities; (9) complications; and (10) failure of outpatient therapy.[11]

Study Protocol

The patients were evaluated in the pediatric allergy immunology and pediatric pulmonology departments 1 to 4 months after discharge or having a negative PCR test for SARS-CoV-2. The patients' demographic data, symptoms, physical examination findings, laboratory, and imaging studies at the time of the COVID-19 infection, hospitalization status, medications, and duration of hospitalization were obtained from hospital records.

The patients were grouped as hospitalized (Group 1) and nonhospitalized (Group 2), and further statistical analyses were conducted among these 2 groups.

Evaluation of Allergic Diseases

Allergic symptoms were evaluated by the International Study of Asthma and Allergies in Childhood (ISAAC) Phase 3 questionnaire.[12] The questionnaire was translated into Turkish, and the questions were asked directly by the physicians in the clinical setting. Allergic work-up was carried out using skin prick testing (SPT) for the following: (1) aeroallergens (*Dermatophagoides farinea*, *D pteronyssinus*, *Alternaria alternata*, *Aspergillus fumigatus*, *Cladosporiun herberatum*); (2) grass mix (*Dactylis*, *Festuca*, *Lolium Phleum*, *Poa*); (3) weed mix (*Artemisia*, *Chenopodia*, *Parietarie*, *Plantago*); (4) tree mix (*Alnus*, *Betula*, *Corylus*); (5) cat epithelia, dog epithelia, cockroach (Alk Abello, Madrid, Spain); and (6) food allergens (cow's milk, egg yolk, egg white, peanut, hazelnut, walnut, almond, wheat flour) (Alk Abello, Madrid, Spain). Specific immunoglobulin E (IgE) levels (*D farinea*, *D pteronyssinus*, cow's milk, egg white, and fX5-food mix) (Immulite 2000, Siemens Medical Solutions Diagnostics, Tarrytown, New York) and spirometry were also performed. Written informed consent was taken from the patients and their parents before the tests.

Spirometry (Quark pulmonary function test [PFT], Cosmed, Rome, Italy) was performed following the American Thoracic Society and European Respiratory Society guidelines at a minimum of 2 months after complete recovery or having a negative PCR test for SARS-CoV-2.[13] Personal protective equipment, including an N95 or FFP2 face mask, goggles, face shield, gloves, and gown, were used by the technician. The tests were performed in a well-ventilated room with only 1 patient in the room at a time, and all the surfaces and the turbine of the device were disinfected after each patient.[14] Recorded pre- and postbronchodilator spirometry parameters included forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), FEV1/FVC ratio, forced expiratory flow at 25% to 75% of the vital capacity (FEF25–75), and peak expiratory flow (PEF).

The asthma diagnosis was based on respiratory symptoms typical of asthma plus documentation of variable airflow limitation by pulmonary function tests (PFTs) (FEV1 <80%, FEV1/FVC <80%, and >12% reversibility of FEV1) for children older than 5 years[15] and based on the modified asthma predictive index for children 5 years old and younger.[16] A diagnosis of allergic rhinitis (AR) was made with 2 or more nasal symptoms (ie, congestion, rhinorrhea, sneezing, and itching) persisting for at least 1 hour a day for more than 2 weeks plus aeroallergen sensitization noted on SPT or allergen-specific IgE.[17] A diagnosis of atopic dermatitis (AD) was made on the basis of Hanifin-Rajka criteria.[18]

Statistical Analysis

The Kolmogorov-Smirnov test and histogram were used to test the normality of the distribution of the data. Continuous variables were expressed as median (25 percentile–75 percentile) and categorical variables were expressed as numbers (percent). The categorical variables were compared using a χ^2 test, and the numerical variables were compared using a Mann-Whitney *U* test. Correlations between continuous variables were made using Spearman's correlation analysis. For multivariate analysis, the possible factors identified by univariate analysis were further entered into the logistic regression model to determine the predictors of hospitalization because of COVID-19. A *P* value of <.05 was considered statistically significant. The International Business Machines

Corporation Statistical Package for the Social Sciences software package, version 25 (SPSS Inc, Chicago, Illinois) for Windows was used for all the statistical analyses.

Results

Patient Characteristics

A total of 107 patients aged 1 month to 18 years of age (median, 102 months; interquartile range [IQR], 35-180 months) were included in the study, of which 49 (45.9%) were women and 58 (54.2%) were men. The median time for the allergic and immunologic evaluation was 79 days (IQR, 68-92 days) after a COVID-19 diagnosis. Of note, 61 (57%) patients were hospitalized for a median of 8 days (IQR, 6-10 days), and 46 (43%) patients were followed closely in the outpatient clinic. In addition, 21 (19.6%) of the hospitalized patients were given oxygen support but none of them needed noninvasive or invasive mechanical ventilation. SARS-CoV-2 PCR results were positive for all nonhospitalized patients and 75.4% for hospitalized patients. The hospitalized and nonhospitalized patient characteristics during COVID-19 are detailed in Table 1.

Thorax CT findings compatible with COVID-19 were present in 37 of 50 (74%) of hospitalized patients and 2 of 16 (12.5%) of nonhospitalized patients ($P < .001$), respiratory acidosis was detected in 19 of 52 (36.5%) of hospitalized patients and 2 of 23 (8.7%) of nonhospitalized patients ($P = .01$), and the median C-reactive protein level was 2.65 g/dL (IQR, 0.93-19.4 g/dL) for hospitalized patients and 0.58 g/dL (IQR, 0.31-4.8 g/dL) for nonhospitalized patients ($P < .001$).

Inquiry of Allergic Symptoms on the Basis of the ISAAC Questionnaire

The ISAAC Phase 3 questionnaire, including 8 questions for asthma, 7 questions for AR, and 6 questions for AD, was filled out by the parents of all 107 patients.

Of note, 15 (14%) patients indicated ever having asthma, 8 (7.5%) patients ever having hay fever, and 6 (5.6%) patients ever having eczema. There was no difference in terms of allergic symptoms on the basis of the ISAAC questionnaire results between the hospitalized and nonhospitalized patients (Table 2).

Evaluation of Allergic Diseases

The number of patients diagnosed with AR, asthma, AD, and episodic wheezing after allergy evaluation (allergic symptoms, SPT, allergen specific IgE, and spirometry) was 11 (10.3%), 7 (6.5%), 5 (4.7%), and 4 (3.7%), respectively. Aeroallergen sensitization was found in 22 (22.2%) patients, with the most common sensitized allergen being *Dermatophagoides* sp. (n = 12) followed by grass mix (n = 8), weed mix (n = 3), trees mix (n = 3), dog (n = 2), cat (n = 1), and *Alternaria alternata* (n = 1). Food allergen sensitization was found in 2 (1.9%) patients without any symptoms related to food allergy. The distribution of allergic diseases between hospitalized and nonhospitalized patients is given in Table 3.

Spirometry Results

A total of 70 (64.4 %) patients were older than 6 years of age and 37 patients (34.6 %) were 6 years old and below. The number of patients with valid spirometry was 44 (41.1 %). Spirometry could not be performed on 63 patients because of their lack of cooperation (37 patients ≤6 years old and 26 patients >6 years old). In addition, 2 (4.5%) patients had a restrictive spirometry pattern (FVC <80% and FEV1/FVC >0.7) and 4 (9%) patients had an FEV1 and FEV1/FVC ratio less than 80% of predicted values without bronchodilator reversibility. All patients diagnosed as having asthma had symptoms related to asthma plus FEV1 reversibility greater than or equal to 12% but a normal FEV1 and FEV1/FVC ratio. We found higher FEV1/FVC ratios and PEF reversibility in hospitalized patients than in nonhospitalized ones ($P = .02$ and $P = .003$, respectively). A comparison of the spirometry results of

Table 1
Patient Characteristics Related to COVID-19

Clinical manifestations of SARS-CoV-2	Group 1 (Hospitalized patients) (n = 61)	Group 2 (Nonhospitalized patients) (n = 46)	*P* value
Asymptomatic, n (%)	6 (9.8)	7 (15.2)	.40
Fever, n (%)	36 (59)	24 (52.2)	.48
Respiratory symptoms			
Cough, n (%)	33 (54.1)	15 (32.6)	.03
Respiratory distress, n (%)	9 (14.8)	3 (6.5)	.18
Gastrointestinal symptoms			
Abdominal pain, n (%)	6 (9.8)	12 (26.1)	.03
Diarrhea, n (%)	14 (23)	12 (26.1)	.71
Nausea or vomiting, n (%)	13 (21.3)	9 (19.6)	.83
Influenza-like symptoms			
Myalgias, n (%)	0	2 (4.3)	.18[a]
Headache, n (%)	2 (3.3)	7 (15.2)	.04[a]
Sore throat, n (%)	3 (5)	0	.26[a]
Other			
Arthralgias, n (%)	1 (1.6)	1 (2.2)	>.99[a]
Rash, n (%)	1 (1.6)	2 (4.3)	.58[a]
Malaise, n (%)	7 (11.5)	4 (8.7)	.75[a]
Loss of smell or taste, n (%)	1 (1.6)	3 (6.5)	.31[a]
Laboratory evaluation			
Hemoglobin (g/dL), median, (IQR)	12.6 (11.6-14.3)	12.7 (11.8-14.0)	.94
Leucocyte count (cells/mm^3), median, (IQR)	6820 (5100-9695)	6755 (5125-9485)	.61
Platelet count (cells/mm^3), median (IQR)	244.000 (208.000-309.000)	273.000 (186.000-353.000)	.55
Neutrophil count (cells/mm^3), median (IQR)	3160 (1870-5405)	3505 (2000-4807)	.83
Lymphocyte count (cells/mm^3), median (IQR)	2100 (1600-4050)	2550 (1725-3350)	.75
CRP (g/dL), median (IQR)	2.65 (0.93-19.4)	0.58 (0.31-4.8)	<.001
Positive thorax CT finding compatible with COVID-19, n (%)	36 (59)	2 (4.3)	<.001

Abbreviations: COVID-19, coronavirus disease 2019; CRP, C-reactive protein; CT, computed tomography; IQR, interquartile range; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
[a]Fisher's exact test.

Table 2
Comparison of Allergic Symptoms Between Hospitalized and Nonhospitalized Patients On the basis of ISAAC Questionnaire[a]

Allergic symptoms	Group 1 (Hospitalized patients), n (%)	Group 2 (Nonhospitalized patients), n (%)	*P* value
Asthma			
Wheezing ever	21 (34.4)	16 (34.8)	.97
Wheezing in the past y	8 (13.1)	7 (15.2)	.76
Number of wheezing episodes in the past year			
1-3	8 (13.1)	4 (8.7)	N/A
4-12	0	2 (4.3)	
>12	0	1 (2.2)	
Sleep disturbance owing to wheezing in the past y			
None	57 (93.4)	40 (87)	.25
<1/wk	4 (6.6)	6 (13)	
>1/wk	0	0	
Wheezing limiting speech in the past y	0	2 (4.3)	.43[b]
Ever had asthma	9 (14.8)	6 (13)	.80
Wheezing after exercise in the past y	3 (4.9)	4 (8.7)	.43
Night waking because of cough in the past y	3 (4.9)	4 (8.7)	.46[b]
Allergic rhinitis			
Ever had a problem with sneezing, or a runny, or blocked nose while not having a cold or the flu	9 (14.8)	11 (23.9)	.23
Problem with sneezing, or a runny, or blocked nose while not having a cold or the flu in the past 12 mo	8 (13.1)	12 (26.2)	.09
Accompanying itchy-watery eyes in the past 12 mo	4 (6.6)	6 (13)	.25
Rhinitis symptoms			
Seasonal	4 (6.6)	5 (10.8)	.71
Perennial	4 (6.6)	7 (15.2)	
Rhinitis symptoms interfering with daily activities in the past 12 mo	6 (9.8)	11 (23.9)	.54[b]
Ever had hay fever	4 (6.6)	4 (8.7)	.68
Eczema			
Ever had an itchy rash coming and going for at least 6 mo	6 (9.8)	3 (6.5)	.54
Having this itchy rash at any time in the past 12 mo	3 (4.9)	2 (4.3)	>.99[b]
Itchy rash at any time affecting any of the places specific to AD	1 (1.6)	3 (6.5)	.31[b]
Rash starting at <2 y of age	1 (1.6)	3 (6.5)	.05[b]
He rash cleared completely at any time in the past 12 mo	5 (8.2)	2 (4.3)	>.99[b]
Night waking owing to cough in the past 12 mo	1 (1.6)	2 (4.3)	.58[b]
Ever had eczema	3 (4.9)	3 (6.5)	>.99[b]

Abbreviations: AD, atopic dermatitis; ISAAC, International Study of Asthma, and Allergies in Childhood; N/A, not applicable.
[a]Represents the parent-reported allergic symptoms.
[b]Fisher's exact test.

the hospitalized and nonhospitalized patients is detailed in Table 3.

A total of 14 (13.1%) patients described pulmonary symptoms, such as ongoing cough, shortness of breath, chest pain, and exercise dyspnea after SARS-CoV-2 infection, with 9 of these patients having pulmonary function tests. None of these patients had a diagnosis of asthma, but 3 of them had AR. Pulmonary function tests were also not different for patients with post–COVID-19 pulmonary symptoms and symptom-free patients, including PEF reversibility (median, −11% [IQR: −21.5% to 28.5%] PEF reversibility for the former and −1.5% [IQR, −10.2% to 11.8%] for the latter) and FEV1/FVC ratio (median, 91.5 % [IQR: 58.5%-108.8%] for the former and 98 % [IQR, 91.8%-106 %] for the latter) (P = .47 and P = .26, respectively).

Factors Associated With Hospitalization Because of COVID-19 Severity

We found no differences in terms of age, sex, prematurity, passive tobacco exposure, having asthma, AR, AD, aeroallergen sensitization, or food allergen sensitization among hospitalized and nonhospitalized patients (P = .84, P = .45, P = > .99, P = .27, P = .46, P = .14, p=0.09, P = 0.39, and P = > .99, respectively). There was no difference in the IgE levels and eosinophil counts either (P = .99 and P = .93, respectively) (Table 3). A total of 12 patients had pets at home—with 10 of them having birds and 2 of them having cats—and the number of patients having a pet was significantly higher in nonhospitalized patients compared with the hospitalized ones (P = .02).

A logistic regression model was conducted according to factors that might interfere with hospitalization. Although having asthma with or without AR, AD, and passive tobacco exposure were not found to be related to severe COVID-19, having a pet at home was found to decrease the risk for severe disease (odds ratio, 0.191; 95% confidence interval, 0.047-0.779; P = .02) (Table 4).

Having asthma with or without AR was also not found to be associated with prolonged hospitalization (median, 8 days [IQR, 5.5–9 days] for patients with asthma with or without AR vs median, 8 days [IQR, 6-10 days] for patients not having asthma with or without AR) (P = .88).

Table 3
Clinical and Laboratory Characteristics and Pulmonary Function Tests of Hospitalized and Nonhospitalized Patients with COVID-19

Characteristic	Group 1 (Hospitalized patients)	Group 2 (Nonhospitalized patients)	*P* value
Clinical characteristics	n = 61	n = 46	
Age (mo), median (IQR)	102 (26.5-190)	103.5 (39.8-170.3)	.84
Sex			
Female	26 (42.6)	23 (50)	.45
Male	35 (57.4)	23 (50)	
BMI, median (IQR)	21.6 (18-28)	20.9 (18.7-23.4)	.35
Asthma[a]	3 (4.9)	4 (8.7)	.46[b]
AR[a]	4 (6.6)	7 (15.2)	.14
Asthma ± AR[a]	5 (8.2)	9 (20)	.08
AD[a]	1 (1.6)	4 (8.7)	.09[b]
Episodic wheezing	2 (3.3)	2 (4.3)	>.99[b]
Aeroallergen sensitization	10 (16.4)	12 (26.1)	.39
Food allergen sensitization	1 (1.6)	1 (2.2)	>.99[b]
IgE (kU/L), median (IQR)	36.9 (13.7- 84.7)	30.7 (19.5-72)	.99
Eosinophil (cells/μL), median (IQR)	140 (80-275)	150 (75-245)	.93
Parental allergy	10 (16.4)	3 (6.5)	.12
Prematurity	4 (6.6)	3 (6.5)	>.99[b]
Passive tobacco exposure	22 (36.1)	12 (26.1)	.27
Pet at home	3 (4.9)	9 (19.6)	.02
Pulmonary function tests (% of predicted), median (IQR)	n = 26	n = 18	
FVC—pre	105 (94-112)	105 (99-116)	.48
FEV1—pre	100 (91-109)	99 (94-109)	.88
FEV1/FVC—pre	99 (92-107)	94 (83-98)	.06
FEF 25-75—pre	94 (79-124)	87 (75-94)	.21
PEF—pre	80 (66-91)	88 (77-93)	.59
FVC—post	107 (99-118)	106 (98-117)	.95
FEV1—post	106 (96-114)	101 (76-113)	.38
FEV1/FVC—post	101 (94-109)	94 (83-99)	.02
FEF 25-75—post	104 (83-145)	85 (59-105)	.05
PEF—post	87.5 (47-120)	73 (36-145)	.08
FEV1—rev	5 (0-8)	0.5 (−7 to 7)	.13
FEF 25-75—rev	7 (−5 to 22)	6.5 (−25 to 22)	.62
PEF—rev	6.5 (−9 to 23)	−8 (−20 to 0)	.003

Abbreviations: AD, atopic dermatitis; AR, allergic rhinitis; BMI, body mass index; COVID-19, coronavirus disease 2019; FEF 25-75, forced expiratory flow at 25% to 75% of the vital capacity; FEV1, forced expiratory volume in the first second; FVC, forced vital capacity; IQR, interquartile range; IgE, immunoglobulin E; PEF, peak expiratory flow; post, postbronchodilator; pre, prebronchodilator; rev, reversibility. NOTE: The categorical variables were compared with the χ^2 test, whereas the numerical variables were compared with the Mann-Whitney *U* test.
[a]Physician-diagnosed.
[b]Fischer's exact test.

Discussion

It is now well established that age, history of smoking, and certain comorbidities including hypertension, diabetes, obesity, and coronary artery disease pose a higher risk for severe COVID-19,[19-21] but the context of asthma is controversial. There is scarcely any data on whether childhood asthma constitutes a risk factor for SARS-CoV-2 infection or hospitalization because of COVID-19. In our study population, although the ISAAC questionnaire–based asthma prevalence was 14%, the physician-diagnosed asthma prevalence was 6.5%, which is lower than the general prevalence of asthma in Turkish children (6.9% in 2003[22] and 17.8% in 2006).[23] It was a limitation for us not having spirometry before the SARS-COV-2 infection, but it seems impossible to design such a study because of the impossibility of predicting who will get COVID-19. There is also a possibility of a post–COVID-19 bronchial reactivity, however, we made the asthma diagnosis not just with spirometry but also with asthma-related symptoms before they got COVID-19 and allergic evaluation.

The prevalence of asthma among adult patients with COVID-19 illustrates marked regional differences, with an incidence lower than the general population in People's Republic of China (0.9%),[24] Italy (1.96% and 1.92%),[25] Sweden (1.8% and 2.6%),[26] Russia (1.8%),[27] and Brazil (1.5%),[28] but a higher incidence in Spain (5.2%),[29] Ireland (8.8%),[30] the United Kingdom (17.9%),[31] and the United States (7.4% and 14%).[32,33] Prevalence data on asthma among pediatric patients with COVID-19 are quite scarce. Ibrahim et al[34] retrospectively evaluated 433 pediatric patients admitted to an Australian children's hospital over a 30-day period and reported a 25% asthma prevalence for COVID-19, but there were only 4 patients who were SARS-CoV-2–positive and 1 patient with asthma. Du et al[35] recently published the data of 182 pediatric patients hospitalized because of COVID-19; 43 (22.8%) patients were reported as having an allergic disease, most typically AR, according to electronic medical records, but they did not find any difference between patients with allergy and those without in terms of clinical and immunologic findings and disease severity.[35] Because all the previously published epidemiologic studies have been conducted retrospectively and the asthma diagnosis was mostly on the basis of patient declaration, we conclude that the actual prevalence of asthma might be lower. The proposed hypotheses for a relatively decreased COVID-19 prevalence in patients with asthma are self-protection awareness, regular intake of asthma medication during the pandemic, markedly reduced levels of angiotensin-converting enzyme 2 (ACE2) expression in atopic individuals, and inhaled corticosteroid treatment.[36]

In our study, AR was detected in 10.3% of our patients and was not found to be related to the hospitalization in patients with COVID-19. Similarly, Chibba et al[33] found an 11.6% prevalence of AR among patients with COVID-19 and a trend toward lower hospitalization in AR. Recently, several studies found that interleukin-13–down-regulated ACE-2 expression not only in bronchial epithelial cells but also in nasal epithelial cells.[37] Considering the studies done so far, AR does not seem to be a risk factor for COVID-19 either.

We investigated factors affecting hospitalization in patients with COVID-19; none of the allergic conditions were found to be a risk factor for hospitalization. Similar to our finding, a previous epidemiologic study of 1526 patients from the United States reported that 14% of patients with COVID-19 had asthma, but the presence of asthma and the use of inhaled or systemic corticosteroids were not found to be risk factors for hospitalization.[6] Rosenthal et al[38] retrospectively evaluated 727 patients with COVID-19 (median age: 49 years), and asthma was not found to be associated with hospitalization, intensive care unit (ICU) admission, or death. However, intubation was found to be 2-fold higher among people with asthma compared with those without asthma, without a difference in duration of intubation or hospitalization.[38]

It has been recently reported that patients with COVID-19 pneumonia have residual abnormalities, most typically ground-glass opacity in chest CT scans during discharge, which may affect pulmonary functions.[39] However, few studies have performed PFTs for patients with COVID-19. To the best of our knowledge, our study is the first to perform spirometry on COVID-19 survivors in the pediatric age group. We found higher FEV1/FVC ratios and PEF reversibility in hospitalized patients. Similar to our finding, Fumagalli et al[40] found lower FVC and higher FEV1/FVC ratios in 13 adult patients with COVID-19 than the upper limit of normality, with an improvement in FEV1/FVC after 6 weeks, but not for FVC. Recently, Mo et al[41] performed spirometry and diffusing capacity for carbon monoxide (DLCO), for 110 adult patients with COVID-19 during discharge. They found an impairment in diffusion capacity and

Table 4
Multivariate Logistic Regression Model for Factors Affecting Hospitalization Because of COVID-19

Risk factor	Regression coefficient	SE	Wald χ^2 value	*P* value	OR	95% CI for OR	
						Lower	Upper
Asthma ± AR	−0.899	0.718	1.566	.21	0.407	0.100	1.664
AD	−0.741	1.340	0.306	.58	0.477	0.034	6.586
Pet at home	−1.653	0.716	5.331	.02	0.191	0.047	0.779
Passive tobacco exposure	0.467	0.455	1.055	.30	1.596	0.654	3.892

Abbreviations: AD, atopic dermatitis; AR, allergic rhinitis; CI, confidence interval; COVID-19, coronavirus disease 2019; OR, odds ratio.

restrictive ventilatory defects, both associated with disease severity. Liu et al[42] investigated the effect of 6 weeks of pulmonary rehabilitation on pulmonary functions in patients with COVID-19; they found a significant improvement in FEV1, FVC, FEV1/FVC, DLCO, and 6-minute walk tests in the intervention group compared with the control group. There is a relatively old but well-designed study by Trigg et al[43] that reported a reduction in FEV1 and an increase in bronchial responsiveness during viral respiratory tract infections, including coronaviruses, accompanying bronchial eosinophilic inflammation irrespective of atopy. During the H1N1 influenza pandemic in 2009, Zarogoulidis et al[44] performed spirometry on patients (aged 14-65 years) at 3-month intervals after the resolution of H1N1 influenza pneumonia and found an improvement in FEV1, FVC, and DLCO over time. Interpreting the data in the literature and our findings together, it might be speculated that the impairment in respiratory functions after COVID-19 is not only restrictive.

An interesting finding of our study was the inverse relationship between pet ownership and hospitalization because of COVID-19. To the best of our knowledge, our study is the first to evaluate this topic. At this time, there is no evidence that domestic pets can transmit new coronaviruses to humans.[45] The CDC has pointed out a variety of health benefits from having a pet, including decreased blood pressure, lowered cholesterol levels, increased opportunities for exercise and outdoor activities, and reduced feelings of loneliness.[46] Pet ownership may affect reduced COVID-19 severity because of these factors.

There are some limitations to our study. First, we did not have any patients treated in an ICU; we, thus, do not have data for intubation risk or duration. Further multicenter studies are needed to investigate the relationship between asthma and ICU outcomes in pediatric patients. Other limitations were the number of patients having spirometry in our study group, the simple spirometric approach we used, and having no spirometry before COVID-19. However, we did not find any difference in PFTs between patients with and without post–COVID-19 pulmonary symptoms; we can comment though that COVID-19 may cause a change in pulmonary functions even if patients were asymptomatic.

The strength of our study is that the diagnosis of allergic disorders did not rely on patient declarations or medical records, rather on clinical and laboratory evaluation. Moreover, our study is the first pediatric study performing spirometry in patients with COVID-19. Further studies with a larger number of children are needed to understand whether there is long-term lung damage because of COVID-19. Pulmonary function monitoring after COVID-19 recovery also seems important even in asymptomatic children.

In conclusion, our study adds to the growing COVID-19 literature that asthma and allergic diseases are not risk factors for hospitalization in children with COVID-19; in fact, having a pet at home may be a protective effect. COVID-19 pneumonia may result in impaired lung function that needs to be further evaluated in pediatric follow-up studies, including detailed PFTs such as DLCO and lung capacity.

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