

Evaluation of the Frequency of Asthma Attack and Disease Severity in Children in the COVID-19 Pandemic

COVID-19 Pandemisinde Çocuklarda Astım Atağı Sıklığı ve Hastalık Şiddetinin Değerlendirilmesi

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ABSTRACT

Objective: As with any lower respiratory tract infection, it is thought that coronavirus disease 2019 (COVID-19) infection may trigger asthma attacks, and the infection may be more severe in patients with asthma. The objective of this study was to establish the incidence of COVID-19 in children with asthma and to assess the disease severity in this patient group.

Material and Methods: We retrospectively analyzed patients who were admitted to the pediatric emergency clinic at our hospital between March and December 2020 with asthma attacks. The patients underwent a real-time polymerase chain reaction (RT-PCR) test to diagnose COVID-19.

Results: The study involved 155 patients, with 85 (54.8%) being male and the median age (IQR) was 122.0 (66.0-163.0) months. The most common symptoms presented by these patients were cough (70.3%), fever (39.4%), and dyspnea (29.7%). Within the patients who required hospitalisation, 18 (81.8%) were diagnosed with moderate attack and 4 (18.2%) with severe attack ($p < 0.001$). Of the patients who were hospitalised, 10 (45.5%) were partially controlled and 8 (36.4%) were uncontrolled with respect to their medical condition ($p < 0.001$). In the study, COVID-19 was detected in 22 (14.2%) out of 155 patients. According to the diagnosis of COVID-19, there was no difference in the severity of attacks or the requirement for ward hospitalization ($p = 0.633$, $p = 0.288$, respectively).



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Conclusion: COVID-19 infection does not increase the severity of asthma attacks or the need for hospitalization in children. This information is particularly important in the context of pediatric emergency care for asthma patients during the COVID-19 pandemic.

Key Words: Asthma, COVID-19, Pediatric emergency

ÖZ

Amaç: Her türlü alt solunum yolu enfeksiyonunda olduğu gibi, koronavirus hastalığı 2019 (COVID-19) enfeksiyonunun da, astım ataklarını tetiklenebileceği ve astımı olan hastalarda enfeksiyonun daha ağır geçebileceği düşünülmektedir. Bu çalışmada COVID-19 hastalığının astımlı çocuklardaki sıklığının saptanması ve bu hastalardaki hastalık şiddetinin belirlenmesi amaçlanmıştır.

Gereç ve Yöntemler: Hastanemiz çocuk acil kliniğine Mart- Aralık 2020 tarihleri arasında astım atağı ile başvurmuş ve COVID-19 tanısı için gerçek zamanlı polimeraz zincir reaksiyonu (RT-PCR) testi bakılmış hastalar geriye dönük olarak incelendi.

Bulgular: Çalışmaya alınan 155 hastanın 85'i (%54.8) erkek cinsiyette ve ortalama yaş (IQR), 122.0 (66.0- 163.0)'dı. En sık başvuru şikayetlerinin öksürük (%70.3), ateş (%39.4) ve nefes darlığı (%29.7) olduğu belirlendi. Hastaneye yatışı yapılan hastaların 18'i (%81.8) orta atak, 4'ü (%18.2) ağır atak olarak değerlendirildi ($p < 0.001$). Yatış yapılan hastaların 10'u (% 45.5) kısmi kontrollü, 8'i (%36.4) kontrolsüzdü ($p < 0.001$). Çalışmaya alınan 155 hastanın 22'sinde (%14.2) COVID-19 saptandı. Hastaların COVID-19 tanısına göre atak şiddetinde ve servis yatış ihtiyacında farklılık saptanmadı (sırasıyla $p=0.633$, $p=0.288$).

Sonuç: COVID-19 enfeksiyonunun çocuklarda astım atak şiddetini ve hastaneye yatış ihtiyacını arttırmadığı saptanmıştır. COVID-19 pandemisi sırasında astım hastaları için çocuk acil servis değerlendirmesinde bu durum önemlidir.

Anahtar Sözcükler: Astım, COVID-19, Çocuk acil

INTRODUCTION

Asthma is a prevalent chronic inflammatory lung illness of childhood that features airway obstruction and hypersensitivity responses. Its development is influenced by hereditary and environmental factors. In the United States of America (USA), asthma diagnosis follows over 6 million children, accounting for an 8.4% prevalence, and more than 700.000 children attend the emergency unit every year for asthma-related problems (1,2). Approximately 2%–5% of hospitalizations are attributed to asthma (1).

Asthma is characterized by recurrent episodes of wheezing, coughing, shortness of breath, and chest pain. Patients' complaints usually occur with triggering factors such as cigar smoke, air pollution, cold air, exercise, and infection. This worsening of the disease state is called asthma attacks (3). Because there is impairment in the production of antiviral IFNs (IFN- α /b/l) in airway epithelial cells and leukocytes in asthma patients, viruses with weak virulence, such as rhinovirus and respiratory syncytial virus, which are generally upper respiratory tract infection agents in healthy individuals, cause attacks in asthma patients (4).

COVID-19 is an infection caused by the coronavirus identified as SARS-CoV-2, which causes severe acute respiratory syndrome (4,5). Since the declaration of COVID-19 as a global pandemic in March 2020, it continues to affect both adults and children worldwide. Chronic diseases can increase the risk of severe COVID-19 infection. However, data on whether childhood asthma poses a risk for COVID-19 is not clear, however it is thought that asthma patients with impaired antiviral responses may be at high risk for COVID-19 morbidity and mortality. In this study, we aimed to evaluate SARS-CoV-2 positivity and its effect on attack severity in children admitted to the pediatric

emergency department because of an acute asthma attack during the pandemic period.

MATERIALS and METHODS

This study was conducted retrospectively between March 31 and December 31, 2020, in the pediatric emergency department of Ankara City Hospital, Children's Hospital. Cases who presented to the emergency department with asthma attack and who had COVID-19 real-time reverse transcriptase-polymerase chain reaction (RT-PCR) were included in the study.

On 23 March 2020, the World Health Organization published a guideline recommending the use of RT-PCR test in the detection of cases infected with COVID-19 (5). In a short time after SARS-CoV-2 transmission, viral RNA is detected in the upper respiratory tract by RT-PCR method and viral load is high in upper respiratory tract samples within the first week after the onset of symptoms (6). Swab samples taken from the nasopharyngeal and then oropharyngeal regions of patients who came to the emergency department with asthma attacks were placed in transport medium, labelled, request forms and clinical information of the patient were filled and sent to the laboratory by following the cold chain rules and the samples were studied by a special method called RT-PCR free of charge. In the study, only PCR results for COVID-19 were analysed, it is not known whether patients were tested for respiratory viral screening.

Chest radiographs of the patients were taken anteroposteriorly (AP); radiographs with atelectasis and/or hyperinflation, peribronchial thickening and consolidation were interpreted as abnormal (7).

The severity of asthma attacks and asthma control status of the patients were determined according to the Global Initiative for

Asthma (GINA) guideline (3). In the GINA guideline, for asthma control evaluation, the patient was questioned whether the patient had asthma symptoms for more than a few minutes, more than once a week, activity limitation due to asthma, the need for reliever medication more than once a week, and night cough/waking due to asthma in the last 4 weeks. It was considered well-controlled if the patient did not have these symptoms, partially controlled if 1-2 of these symptoms were present, and uncontrolled if 3-4 of these symptoms were present. In the early stages of the COVID-19 pandemic, especially in children with underlying diseases, the isolation of patients with COVID-19 was higher than normal because we did not know how the course would follow in patients with underlying diseases.

Permission was obtained from Ankara City Hospital Clinical Research Ethics Committee (meeting date: 14.10.2020, decision no: E1/1183/2020) for the study.

Statistical Analysis

IBM SPSS Statistics 22.0 (SPSS Inc., Chicago, IL, USA) program was used for statistical evaluation. Frequency distributions were evaluated as numbers and percentages, continuous variables (measurements) were evaluated as median (IQR). The Kolmogorov-Smirnov test was used to determine whether the data were normally distributed. In statistical evaluation, T-test was used for data showing normal distribution and Mann-Whitney U test was used for data not showing normal distribution in the comparison of paired groups. Categorical variables were compared using Chi-square test. The level of significance set was $p < 0.050$.

RESULTS

During the study period, the number of admissions to the pediatric emergency department was 55.664 and 6070 (10.9%) of the patients were hospitalized and followed up. In this period, the number of patients admitted to the emergency department with asthma attack was 155 (3%) and the hospitalization rate was 23.9%. The number of children diagnosed with COVID-19 in our hospital was 7214. 22 (0.3%) of these patients presented to the emergency department with asthma attacks and non of them has underlying diseases except asthma.

Of the 155 patients included in the study, 85 (54.8%) were male. The median age (IQR) was 122.0 (66.0- 163.0) months and 71 (45.8%) of the patients were younger than 120 months. The most common presenting complaints were cough (70.3%), fever (39.4%) and dyspnoea (29.7%). The most common findings on physical examination were rhonchus (41.3%) and rales (9.0%). 125 (80.6%) had mild, 26 (16.8%) moderate and 4 (2.6%) severe attacks. Thirty-seven (23.9%) of the patients were hospitalized and followed up; 15 (40.5%) of these patients were discharged from the emergency department (median (IQR)

Table I: Demographical and clinical characteristics of patients

	n (%)
Age (mo)*	122.0 (66.0- 163.0)
Sex	
Male	85 (54.8)
Female	70 (45.2)
Type of admission to the hospital	
EMS	6 (3.9)
With their own means	149 (96.1)
Time of Emergency department (ED)	
8:00 AM to 4:00 PM	68 (43.9)
4:01PM to 11:59 PM	68 (43.9)
12 midnight to 07:59 AM	19 (12.3)
Complaints	
Cough	109 (70.3)
Fever	61 (39.4)
Dyspnea	46 (29.7)
Nasal discharge	25 (16.1)
Sorethroat	22 (14.2)
Vomiting	16 (10.3)
Diarrhea	12 (7.7)
Headache	11 (7.1)
Wheezing	9 (5.8)
Chest pain	5 (3.2)
Abdominal pain	6 (3.9)
Rash	1 (0.6)
Other	27 (17.4)
Complaint period (hour)*	2 (1-4)
Physical examination findings	
Rhonchus	64 (41.3)
Ral	14 (9.0)
Wheeze	4 (2.6)
Tachypnea	4 (2.6)
Asthma attack severity	
Mild	125 (80.6)
Moderate	26 (16.8)
Severe	4 (2.6)
Hospitalization Rates	
Discharged	118 (76.1)
Hospitalization	37 (23.9)
Emergency Department	37 (100.0)
Pediatric ward	22 (59.5)
Pediatric intensive care unit	2 (5.4)

*median (IQR)

emergency department observation time, 3 (2.0- 5.0) hours) and 22 (59.5%) were hospitalized in the pediatric ward (Table I).

The distribution of patients according to months was analyzed. The highest rate of presentation with asthma attacks was found in October (20.0%), September (18.1%) and April (16.1%). The rate of COVID-19 positivity in patients presenting with asthma attacks was higher in September (33.3%) and October (27.3%) (Figure 1).

There was no difference between patients with and without COVID-19 infection in terms of lymphocyte count, D-dimer, AST, ALT, BUN, and creatinine values ($p = 0.435$, $p = 0.422$, 0.938, 0.550, 0.517, 0.126, respectively). Among patients who

Table II: Laboratory results of the patients

	Total (Mean±SD)	Positive RT-PCR (n=22)	Negative RT-PCR (n=133)	p
WBC (x10 ⁹ /L)	9.3±4.0	7.8±4.5	9.5±3.9	0.172
Hemoglobin at presentation (gr/dL)	14.7±1.2	13.8±1.0	14.8±12.9	0.767
Platelets (x10 ⁹ /L)	315.2±86.2	282.2±643.5	321.2±886.6	0.122
ANC x10 ⁹ /L	5.4±3.3	4.3±2.8	5.5±3.3	0.206
ALC x10 ⁹ /L	9.2±1.7	2.2±2.9	2.7±1.5	0.435
Percentage of eosinophils (mm ³ /L)	0.7±1.3	0.7±1.6	0.7±1.2	0.944
ALT (U/L)	25.8±36.0	20.5±18.2	26.6±38.6	0.550
AST (U/L)	26.9±14.2	26.6±12.6	26.9±14.6	0.938
BUN (mg/dL)	24.2±6.2	25.3±6.6	23.9±6.1	0.517
Creatinine (mg/dL)	0.5±0.2	0.6±0.1	0.5±0.1	0.126
CRP (mg/dL)	18.7±48.2	3.6±3.3	21.6±52.1	0.006*
PT	12.2±0.8	12.2±0.5	12.2±0.9	0.914
aPTT (sec)	25.9±3.8	26.5±2.9	25.7±4.1	0.569
INR	1.0±0.08	1.0±0.06	1.0±0.09	0.504
D-dimer	0.8±1.9	1.5±3.8	0.6±0.6	0.422

RT-PCR: Real-Time Reverse Transcriptase-Polymerase Chain Reaction, **WBC:** white blood cell, **ANC:** Absolute Neutrophil Count, **ALC:** Absolute Lymphocyte Count, **ALT:** Alanine aminotransferase, **AST:** aspartat aminotransferase, **BUN:** blood urea nitrogen, **CRP:** C-reactive protein, **PT:** Prothrombin time, **aPTT:** Partial thromboplastin time, **INR:** International Normalized Ratio

Table III: Asthma conditions and hospitalization characteristics.

	Hospitalized patients n (%)	Patients not hospitalized n (%)	p
Asthma attack severity*			< 0.001
Mild	9 (24.3)	116 (98.3)	
Moderate	24 (64.9)	2 (1.7)	
Severe	4 (10.8)	0 (0.0)	
Asthma symptom control*			0.002
Well controlled	13 (35.2)	79 (67.0)	
Partly controlled	12 (32.4)	24 (20.3)	
Uncontrolled	12 (32.4)	15 (12.7)	

*column percentage is given

presented to the emergency department with asthma attack, C-reactive protein value was found to be significantly higher in those without COVID-19 infection (p= 0.006) (Table II).

The relationship between asthma control status and hospitalization was evaluated. Of the 37 patients hospitalised, 24 (64.9%) were classified as moderate attack and 4 (10.8%) as severe attack (p< 0.001); 12 (32.4%) of the hospitalized patients were partially controlled and 12 (32.4%) were uncontrolled (p= 0.02) (Table III).

COVID-19 was detected in 22 (14.2%) of 155 patients included in the study, 19 (86.4%) of these patients were evaluated as mild, 3 (13.4%) as moderate attacks, and 3 (16.6%) of the patients were hospitalized in the ward. There was no difference in the severity of attacks and the need for ward hospitalisation according to the COVID-19 diagnosis (p=0.633, p=0.288, respectively) (Table IV). It was determined that the asthma

control status of 3 patients who were hospitalized in the ward was partially controlled.

When the imaging modalities performed in patients with and without COVID-19 were evaluated, no difference was found in terms of abnormal X-ray and CT examination (p= 0.630, p=0.243, respectively) (Table IV).

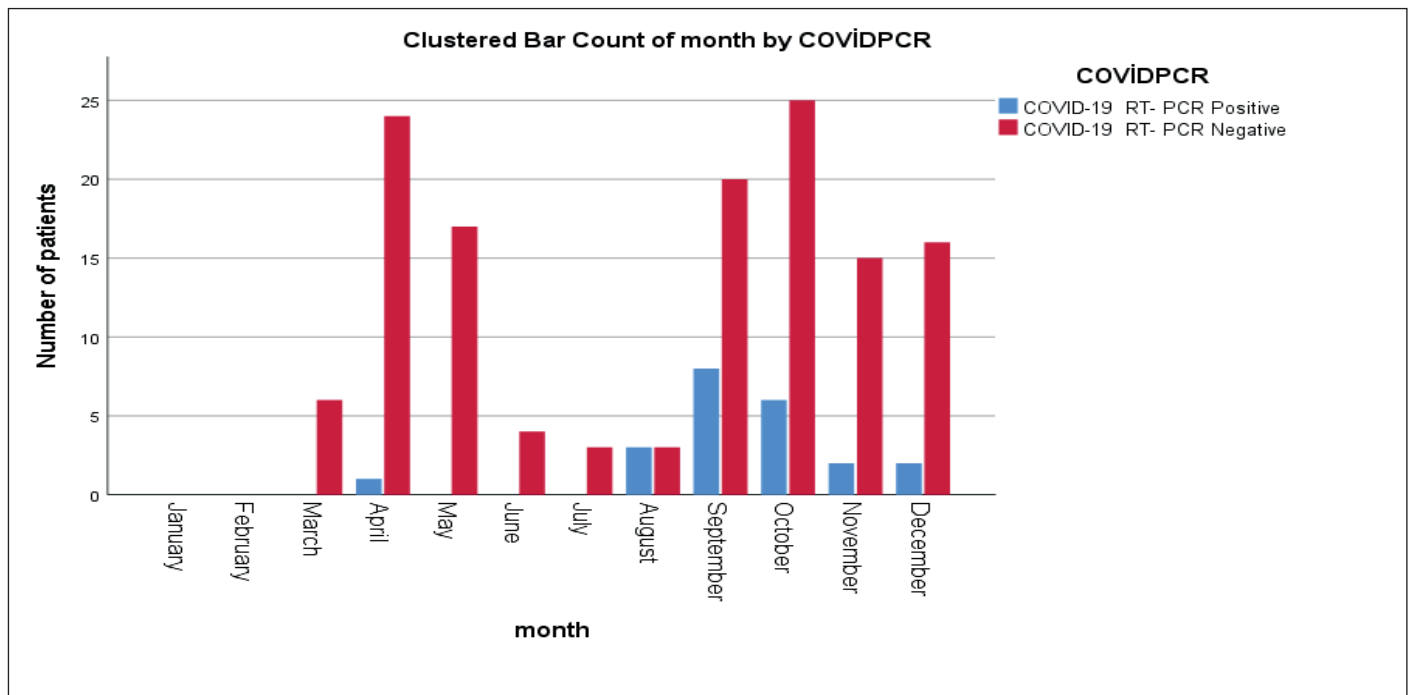
Chest radiographs were performed in 131 (84.5%) patients, and 62 (47.3%) patients had abnormal radiographs. Computed tomography (CT) of the lung was performed in only 5 (3.2%) patients (Table IV).

RT-PCR was positive in only 1 of the patients who underwent chest CT; a 9.5-year-old patient was found to have lobar consolidation on chest radiography and ground-glass opacity in the lower lobe of the right lung on CT examination. This patient was considered to have an intermediate attack and was hospitalized in the ward for 4 days.

Table IV: Clinical Features and Characteristics of Patients Based on Real-Time RT-PCR Results

	Total n (%)	COVID-19 Real-Time RT-PCR Positive n (%)	COVID-19 Real-Time RT-PCR Negative n (%)	p
Asthma attack severity [*]				0.633
Mild	125(80.6)	19 (86.4)	106 (79.7)	
Moderate	26 (16.8)	3 (13.6)	23 (17.3)	
Severe	4 (2.6)	0 (0.0)	4 (3.0)	
Hospitalisation [*]				0.288
Yes	37 (23.9)	3 (13.6)	34 (25.6)	
No	118 (76.1)	19 (86.4)	99 (74.4)	
Chest x-ray				0.630
Normal	69 (52.7)	9 (47.4)	60 (53.6)	
Abnormal	62 (47.3)	10 (52.6)	52 (46.4)	
Chest computed tomography				0.243
Normal	0 (0.0)	0	0	
Abnormal	5 (100.0)	1 (20.0)	4 (80.0)	

* column percentage is given

**Figure 1:** Patient distribution by months

DISCUSSION

Acute asthma attacks are the most important factor determining morbidity/mortality in asthma, which is the most common chronic disease of childhood, and viral infections play a role in most of the attacks. In this study, the rate of patients presenting to the emergency department with asthma attacks was 3% and the hospitalization rate was 23.9%. Of the 155 patients included in the study, COVID-19 was detected in 22 (14.2%), 19 (86.4%) of these patients were evaluated as mild, 3 (13.4%) as moderate attacks, and 3 (16.6%) of the patients were hospitalized in the service. There was no difference in the severity of asthma attacks and the need for ward hospitalization in patients infected with COVID-19.

Asthma attack is a common cause of admission to the pediatric emergency department. Studies have reported that the number of asthma attack admissions was lower than that in the pre-pandemic period (8-10). Similar to previous studies, we found an increase of 13 in emergency department admissions with asthma attacks in the post-pandemic period. The decrease in the hospital admissions with asthma attacks during the pandemic period may be due to quarantine measures for the transmission of respiratory viruses such as rhinovirus and RSV, decreased pollution in the atmosphere, and decreased exposure to outdoor allergens. The use of asthma medication under parental control may also increase medication compliance (10).

Studies have reported that the prevalence of asthma in children and adults diagnosed with COVID-19 was 0-14% and 0.3%-17.9%, respectively (11-13). In two studies conducted in our

country (14,15), the rate of chronic lung disease as a comorbid disease was 0.9% and 1.8% in children with COVID-19 infection, respectively. In our study, similar to these results, we found that the rate of presentation to the emergency department with asthma attack in children diagnosed with COVID-19 was 0.3%.

In the study by Wang L et al. (16), it was reported that especially male gender was a risk factor for hospitalization in adult patients with asthma who had COVID-19 infection. Swann et al. (17) reported that 53.5% of 1612 children with COVID-19 were male and 60.3% were younger than 10 years. Metbulut et al. (11) reported that the mean age of children with COVID-19 enf diagnosed with asthma was 10.5 years and 53.7% were male. Although male gender is not reported as a risk factor for the disease in children, we determined that 53.7% of the cases were male and the median age was 122 months.

COVID-19 symptoms are similar to asthma attack symptoms (2). Jin et al. (18) reported that the most common complaints were fever, cough, chest pain, shortness of breath, and chest pain in both groups in their study in which they evaluated adult patients with (21) and without (100) a diagnosis of asthma with COVID-19. Lu X et al. (19) reported that cough (48.5%) and fever (41.5%) were the most common symptoms in their study in which they evaluated 171 cases with COVID-19 between the ages of 1 day and 15 years. Metbulut et al. (11) reported that 54 (0.87%) of 6.205 children with COVID-19 were diagnosed with asthma; cough, shortness of breath complaints, and hospitalization rate were found to be higher in the asthma group. In our study, we found that cough, fever, and dyspnea were the most common presenting complaints in patients presenting to the emergency department with asthma attack.

Different studies have been conducted on which laboratory parameters should be used to evaluate disease severity in patients with COVID-19. In the study by Jin et al.(18) evaluating adult patients with and without a diagnosis of asthma with COVID-19, leukocytosis was found in the asthma group; no difference was found between the groups in PT, PTT, AST, ALT, urea, and hs-CRP (high sensitivity CRP) values.

Some studies have reported that leukocytosis and increased CRP levels are observed in COVID-19 infection (20, 21). In our study, we found no difference between patients with and without COVID-19 infection in terms of lymphocyte count, D-dimer, AST, ALT, BUN, creatinine, and C-reactive protein values. C-reactive protein level was significantly higher in patients without COVID-19 infection. It can be said that laboratory data vary according to different hospitals and patient groups and have no diagnostic value.

It has not been proven that asthma in children poses a risk of severe COVID-19 (1). Studies have reported that asthma is not a risk factor for morbidity/mortality in pediatric COVID-19 cases (22, 23). In our study, we found no difference in terms of attack severity and the need for ward hospitalization in asthma attack

patients with COVID-19. According to these findings, asthma is thought not to affect the course of COVID-19 in children.

Studies have reported that lung radiograph findings were mostly normal in pediatric patients with COVID-19 (24- 27). Consistent with the literature, no difference was found in terms of abnormal chest radiograph examination in our patients with and without COVID-19 ($p= 0.630$).

There are different data regarding thoracic CT in COVID-19 cases in children. Ma et al. (26) reported that 85% of pediatric patients had abnormal thorax CT findings. In some studies, it was reported that thorax CT examination was normal in asymptomatic and mild clinical stage COVID-19 cases (25, 27). Das et al. (28) reported that although thorax CT can detect specific radiological findings as well as early lung abnormalities, such as ground-glass opacity, it is an appropriate imaging method to evaluate COVID-19-related complications only in symptomatic pediatric patients with COVID-19 pneumonia whose clinic worsens despite treatment. In our study, there was no difference in CT examination between our patients with and without COVID-19 ($p=0.243$). Because we did not have any patients with a severe clinical condition, the number of patients who underwent CT imaging of the thorax was very low; therefore, there may not have been a difference.

The main limitation of this study is that it is retrospective and single-centre. Since it was retrospective, diagnosis codes and medical records were found to be incomplete and some asthma attack patients could not be included in the study.

In conclusion, the most important factor determining morbidity/mortality in asthma is acute asthma attacks, and viral infections play a role in most of these attacks. It was observed that there was no difference in the severity of asthma attacks and the need for ward hospitalization in COVID-19 infection, and it is thought that asthma is not a risk factor for morbidity/mortality in COVID-19 cases.

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