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Original Article

COVID-19 in a group of children with asthma: presentation, severity, and outcome

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Abstract: Background: There are insufficient data concerning COVID-19 severity among asthmatic children. Aim: to evaluate the impact of asthma on COVID-19 severity and outcome. Patients and methods: We carried out an observational study that comprised 2 matched groups of children with confirmed/probable COVID-19: 30 with and 32 without asthma aged 6-18 years, who were enrolled consecutively from Children's Hospital, Ain Shams University, Egypt. COVID-19 clinical presentations, laboratory and radiological abnormalities, severity and outcome were compared between the 2 groups. Asthma severity and control were assessed based on GINA 2020. Results: The asthmatic COVID-19 children were 9 boys and 21 girls, with median age 9 years, IQR: 8-12 years. The non-asthmatic COVID-19 group included 18 males and 14 females with median age 9.5 years, IQR: 7-12.5 years. Clinical manifestations of COVID-19 were comparable among the 2 groups, except for wheezes which were more frequently encountered as a COVID-19 manifestation among the asthmatics (p=0.001). Multisystem inflammatory syndrome (MIS-c) was diagnosed in one asthmatic and 3 non-asthmatic patients. The asthmatic group had higher frequency of serum ferritin, LDH and D-dimer elevations compared to the non-asthmatic peers (*p* values 0.014, 0.001, and 0.015 respectively). Based on CO-RAD classification, 70% of the asthmatic patients had CO-RAD score of 5 versus 6.3 % among the non-asthmatic group with significant differences between the 2 groups in their CO-RAD scores (P=0.002). COVID-19 severity was comparable among the studied groups (P=0.775), as well as COVID-19 outcome and duration of hospital stay (*p* values 0.999, and 0.655, respectively). Conclusion: From our limited sample sized study, childhood asthma did not pose a significant impact on COVID-19 severity and outcome. Further longitudinal studies are warranted to validate our conclusion and investigate the relation of COVID-19 severity and outcome to allergen immunotherapy and the use of biologicals for asthma treatment.

Keywords: Bronchial asthma, COVID-19, CO-RAD, children

Introduction

COVID-19 is a respiratory disease caused by the SARS-CoV-2 virus which is a highly transmissible virus that emerged in December 2019. It was declared as a pandemic by the World Health Organization (WHO) on March 11, 2020. COVID-19 infection in children has a less severe course if compared to adults [1]. On June 17th, 2022, the number of reported confirmed cases was around 536 million cases worldwide. In the United States, the period from February 2020 to September 2021, COVID-19 was reported among 25.8 million children and adolescents [2].

Asthma was not proved as a significant risk factor for complicated COVID-19 [3]. Children with respiratory allergic diseases like asthma and allergic rhinitis did not suffer from a higher incidence, severer forms or worse prognosis of COVID-19 compared to non-allergic children [4]. However, data concerning the situation of COVID-19 severity and outcome among asthmatic children in Egypt is lacking. We aimed to study the differences in presentation, severity and outcome of COVID-19 infection between asthmatic and non-asthmatic children, to determine the impact of asthma on COVID-19 severity and outcome and if they need further precautions.

Patients and methods

Study settings

This cross-sectional study was conducted in the Pediatric Allergy, Immunology and Rhe-

umatology Unit, emergency room (ER), isolation ward and Pediatric Intensive Care Unit (PICU) of Children's hospital, Ain Shams University in the period from May 2020 to April 2021. The study protocol gained approval of the Research Ethics Committee of the Department of Pediatrics, Ain Shams University, with approval number FWA 000017858.

Study population

Two groups of COVID-19 patients were enrolled: a group of 30 children (aged 6-18 years) with physician diagnosed asthma for at least 6 months before enrollment in the study, based on the Global Initiative of Asthma (GINA) guidelines for asthma diagnosis [5], and a group of 32 children without asthma after exclusion of patients with chronic respiratory disorders such as chronic interstitial lung disease, cystic fibrosis and bronchiectasis, and those with chronic illnesses such as diabetes mellitus, chronic cardiac, renal or liver disorders, patients on immunosuppressive or chemotherapy for treatment for immunological or malignant disorders or on radiotherapy and patients with evidence of primary of secondary immunodeficiency.

Definition of probable and confirmed COVID-19 matched the criteria of definition of the Center for Disease Control (CDC) [6]. Classification of COVID-19 severity into asymptomatic/mild, moderate, severe and critical illness was according to the World Allergy Organization (WHO) criteria, 2020 [7].

Study tools: all enrolled patients were subjected to the following

1) Detailed clinical history taking including, demographic data, and history of recent contact with a COVID-19 positive patient. Parents were asked about the initial symptoms including fever, respiratory symptoms (cough, dyspnea, cyanosis, chest pain), gastrointestinal symptoms (abdominal pain, vomiting, diarrhea), anosmia, ageusia, skin rash, conjunctivitis, mucositis, symptoms of organ dysfunction for instance, symptoms of pulmonary venous congestion and/or low cardiac output, symptoms of renal impairment, and neurological affection (agitation, convulsions, impaired consciousness, etc.).

2) Clinical examination was performed for detection of signs of respiratory distress and asthma exacerbation (if any) and evaluation for different systems' affection.

3) Severity of COVID-19 illness was assessed based on manifestations, need of oxygen supplementation, and the need for PICU admission [7]. Patients were classified into: i- *Asymptomatic* with positive PCR, ii- *Mild:* fever and/or fatigue and/or upper airways symptoms without radiological evidence of pneumonia, iii- *Moderate:* fever and/or fatigue and/or upper airways symptoms and/or radiological evidences of pneumonia, iv- *Severe:* fever and cough, in addition to at least one of the followings: low oxygen saturation <92%, severe respiratory distress, tachypnea, toxemia; and v- *Critical:* patients with respiratory failure, acute respiratory distress syndrome (ARDS), cardiac, renal or neurological affection.

4) Asthmatic patients were additionally asked about asthma duration, frequency of symptoms and treatments given. Severity and control of asthma over the 4 weeks prior to the COVID-19 infection were assessed according to GINA, 2020 [5]. Mild asthma was defined when the patient's symptoms were controlled on low-intensity inhaled corticosteroids (ICS). Moderate disease was defined when the patient is controlled on ICS, leukotriene receptor antagonists (LTRA) and/or long-acting B2 agonist (LABA), whereas severe illness was considered in patients who needed high doses of ICS-LABA or even systemic steroids.

5) Laboratory and imaging data were recorded. Laboratory data included: polymerase chain reaction (PCR) for COVID-19 (VIASURE Real Time PCR detection kits), complete blood counts (CBC) using (XT-1800i Automated Hematology Analyzer by Symex) machine, C-Reactive protein, erythrocyte sedimentation rate (ESR), serum ferritin, lactate dehydrogenase (LDH), D-dimer, serum amylase, serum creatinine, alanine transaminase (ALT) using (Dia Sys Response 920) machine. Imaging studies included chest X-ray (using GE DX300 X-Ray machine) and computed tomography (CT) (using GE Optima CT 660 64-128 slice machine). Chest CT scan findings were classified according to COVID-19 Reporting and Data System (CO-RADS) classification [8].

6) Length of hospital stay, treatment modalities and outcome of the patients on discharge from the hospital, whether it was complete cure, cure with residual illness, or death were all recorded from the hospital records.

Statistical analysis

Data were collected, revised, coded and entered to the statistical package for Social Science (IBM SPSS) version 26. The numerical variables were presented as median and interquartile range, and intergroup differences were compared with the Mann-Whitney test. Categorical variables were presented as number and percentage. The comparison between groups was done by using the Pearson chi-squared test or Fisher exact test. Ordinal data including CO-RAD scoring and COVID-19 severity were compared with the chi-squared test for trend. *P*-value was considered significant when less than 0.05.

Results

Description of studied population

We recruited 62 children infected with COVID-19. The asthmatic children were 30, including 9 males (30%) and 21 females (70%) with median age of 9 years (IQR: 8-12 years). Non-asthmatic children were 32 patients, including 18 (56%) males and 14 (44%) females, and their median age was 9.5 years (IQR: 7-12.5 years). Both groups were comparable with respect to age with a *p* value 0.876. Confirmed COVID-19 infection was detected in 25 out of the 30 (83.3%) asthmatic patients and 26 out of the 32 (81.3%) non-asthmatic patients, while the rest were probable cases of COVID-19.

Description of COVID-19 presentations

Clinical manifestations of COVID-19 and different systems affection were comparable among the studied groups (**Table 1**). However, wheeze as a presentation of COVID-19 was more frequently encountered among asthmatics versus the non-asthmatic cases (P=0.001). Multisystem inflammatory syndrome related to COVID-19 (MIS-c) was diagnosed in one asthmatic and 3 non-asthmatic patients. Distribution of patients according to the severity of COVID-19 illness is shown in **Table 2** with comparable severity among the asthmatic and the non-asthmatic cases (P=0.775).

Concerning laboratory investigations, data showed lower median hemoglobin concentration and higher median platelet count among asthmatic versus the non-asthmatic COVID-19 cases (**Table 3**). D dimer, ferritin and LDH levels, were more frequently elevated among the non-asthmatic group (**Table 4**).

Radiological and laboratory findings

Chest x-ray was done in all patients while CT scan of the chest was performed in 10 asthmatic and 16 non asthmatic patients. Data analysis showed abnormal x-ray findings in 36.7% of the asthmatic children and 37.5% of the non-asthmatics. Among the studied 62 COVID-19 patients, X-ray findings included focal opacities (11.3%), heterogenous patches (9.7%), pneumonia and interstitial infiltrations (14.5%), and pleural effusion (1.6%), with comparable findings between the asthmatic and non-asthmatic patients. CO-RAD classification varied significantly between the studied groups as shown in **Table 5**. The need of oxygen therapy, parenteral corticosteroids, intravenous immunoglobulins (IVIG), anti- interleukin 6 (IL-6) or anticoagulant therapy was comparable between the studied asthmatic and non-asthmatic children (**Table 6**).

COVID-19 severity and outcome

PICU admission was needed in 2 non-asthmatic patients who had MIS-C diagnosis. Both patients suffered from hypotension, pericarditis, decreased O_2 saturation, elevated levels of LDH, ferritin, and D-dimer. None of them required mechanical ventilation. According to the hospital policy, the duration of hospital stay was related not only to the clinical condition, but also to obtaining a negative swab result. Median duration of hospital admission among the asthmatic patients was 10 days (IQR: 8-13.8), and was 11 days (IQR: 8-13) among the non-asthmatic group, not necessarily a reflection of the illness duration. The outcome of COVID-19 among enrolled patients in both asthmatic and non-asthmatic groups was complete resolution, except for one non-asthmatic patient who had MIS-C and continued with residual cardiac affection (mild pericardial effusion).

Neither asthma control, severity nor asthma-controller therapy represented a significant risk

Table 1. Clinical presentations of COVID-19 in asthmatic and non-asthmatic patients

Clinical Presentation	Asthmatic (n=30)		Non-Asthmatic (n=32)		χ^2	*P*-value
	N	%	N	%		
General (constitutional)						
Fever	22	73.3%	24	75.0%	0.022	0.881†
Maculopapular skin rash	0	0.0%	4	12.5%	-	0.114‡
Discolored/Painful extremities	1	3.3%	3	9.4%	-	0.613‡
Oral ulcers	1	3.3%	2	6.3%	-	>0.999‡
Non-purulent conjunctivitis	1	3.3%	2	6.3%	-	>0.999‡
ENT						
Anosmia	13	43.3%	9	28.1%	1.564	0.211†
Ageusia	13	43.3%	9	28.1%	1.564	0.211†
Sore throat	11	36.7%	15	46.9%	0.663	0.416†
GIT						
Diarrhea	6	20.0%	5	15.6%	0.203	0.652†
Vomiting	6	20.0%	5	15.6%	0.203	0.652†
Anorexia	10	33.3%	9	28.1%	0.198	0.657†
Abdominal pain	7	23.3%	8	25.0%	0.023	0.878†
Circulatory						
Hypotension	2	6.7%	2	6.3%	-	>0.999‡
Tachycardia	5	16.7%	8	25.0%	0.649	0.421†
Respiratory						
Cough	21	70.0%	15	46.9%	3.401	0.065†
Expectoration	11	36.7%	7	21.9%	1.644	0.200†
Chest pain	4	13.3%	5	15.6%	-	>0.999‡
Dyspnea	0	0.0%	5	15.6%	-	0.053‡
Tachypnea	5	16.7%	7	21.9%	0.269	0.604†
Generalized wheezes	12	40.0%	2	6.3%	10.089	0.001†
Rales	0	0.0%	1	3.1%	-	>0.999‡
Decreased air entry	0	0.0%	1	3.1%	-	>0.999‡
Pneumonia	2	6.7%	2	6.3%	-	>0.999‡
Decreased O_2 saturation below 92%	0	0.0%	2	6.3%	-	0.492‡

N=number, χ^2=chi-squared test. †. Pearson Chi-squared test. ‡. Fisher's exact test.

Table 2. Severity of COVID-19 infection in asthmatic and non-asthmatic children

Variable		Asthmatic (n=30)		Non-Asthmatic (n=32)		χ^2	*P*-value
		N	%	N	%		
COVID-19 severity	Asymptomatic	2	6.7%	7	21.9%	0.08	0.775†
	Mild	20	66.7%	10	31.3%		
	Moderate/Severe	8	26.7%	15	46.9%		

N=number, χ^2=chi-squared statistic. †. Pearson Chi-squared test.

factor for COVID-19 severe disease in our studied patients as shown in **Table 7**.

Discussion

As respiratory tract viral infections are thought to be associated with a more severe course and worse prognosis in asthmatic children [9], we were stimulated to investigate the presentation, severity and outcome of COVID-19 infection in asthmatic children compared to non-asthmatic COVID-19 patients.

We observed that the clinical manifestations of COVID-19 were similar in both asthmatic and non-asthmatic groups, including constitutional,

Table 3. Laboratory investigations among asthmatic and non-asthmatic children with COVID-19

Variable	Asthmatic (N=3)			Non-Asthmatic (N=3)			Z	*P*-value
	Min-Max	Median	IQR	Min-Max	Median	IQR		
TLC (count/mm^3)	3600-22000	7,000	5,000 to 13,000	2700-19000	7,275	5,200 to 9,275	-0.049	0.961
ANC (count/mm^3)	1400-16300	4,200	3,000 to 7,000	1400-16200	4,450	3,839 to 6,450	-0.296	0.767
ALC (count/mm^3)	550-6500	2,000	900.0 to 3,000.0	200-6600	1,945	1,025.0 to 2,625.0	-0.120	0.905
NLR	0.7-11.7	2.20	1.30 to 4.90	0.8-32	2.50	1.70 to 3.85	-0.162	0.871
Monocytes (count/mm^3)	100-2500	325.0	230.0 to 700.0	116-1000	437.5	285.0 to 625.0	-1.312	0.190
Hemoglobin (g/dl)	8-13	11.0	9.0 to 12.0	9-15	11.6	10.8 to 12.5	-1.998	0.046
MCV (fl)	68-90	77.5	71.0 to 83.0	68-90	80.0	77.0 to 85.5	-1.094	0.274
Platelets (count/mm^3)	152000-935000	323,000	272,000 to 400,000	142000-714000	287,500	204,000 to 335,500	-2.015	0.044
ESR (mm/h)	7-110	25.0	15.0 to 35.0	10-110	25.0	15.0 to 52.5	-0.917	0.359

ALC: absolute lymphocyte count, ANC: absolute neutrophil count, ESR: erythrocytes sedimentation rate, IQR: interquartile range, Max: maximum, MCV: mean corpuscular volume, Min: minimum, N: number, NLR: neutrophil/lymphocyte ratio, TLC: total leukocytes count.

Table 4. Frequency of laboratory abnormalities among asthmatic and non-asthmatic groups with COVID-19

Test	Asthmatic Total tests n=27		Non-Asthmatic Total tests n=19		χ^2	*P*-value
	N	%	N	%		
High D-Dimer	3	11.1%	9	47.4%	-	0.015§
High ferritin	6	22.2%	11	57.9%	6.091	0.014‡
High LDH	7	25.9%	15	78.9%	12.564	<0.001‡

LDH: lactate dehydrogenase, N: number. χ^2=chi-squared test, ‡. Pearson chi-squared test, §. Fisher's exact test.

Table 5. Radiological findings among asthmatic and non-asthmatic children with COVID-19

Variable		Asthmatic (n=30)		Non-Asthmatic (n=32)		χ^2	*P*-value
		N	%	N	%		
Chest X ray (CXR)	Abnormal CXR	11	36.7%	12	37.5%	0.005	0.946†
	Focal opacities	4	13.3%	3	9.4%	-	0.703‡
	Patchy opacities	2	6.7%	4	12.5%	-	0.672‡
	Bronchopneumonia/ Interstitial infiltration	5	16.7%	4	12.5%	-	0.728‡
	Effusion	0	0.0%	1	3.1%	-	>0.999‡
COVID-19 reporting and data system (CO-RAD) classification		Total tests (n=10)		Total tests (n=16)			
	CO-RADS 1	0	0.0%	4	25.0%	9.344	0.002§
	CO-RADS 2	1	10.0%	5	31.3%		
	CO-RADS 3	0	0.0%	1	6.3%		
	CO-RADS 4	2	20.0%	5	31.3%		
	CO-RADS 5	7	70.0%	1	6.3%		
Echocardiography		Total tests (n=8)		Total tests (n=3)			
	Pericardial effusion	1	12.5%	2	66.7%	-	0.152‡

χ^2=chi-squared test, †. Pearson chi-squared test, ‡. Fisher's exact test, §. Chi-squared test for trend.

Table 6. Management received for COVID-19 infection in asthmatic and non-asthmatic children

Variable		Asthmatic (n=30)		Non-Asthmatic (n=32)		χ^2	*P*-value
		N	%	N	%		
Management	Hospital admission	19	63.3%	28	87.5%	4.931	0.026†
	Oxygen therapy	1	3.3%	3	9.4%	-	0.613‡
	PICU admission	0	0.0%	2	6.3%	-	0.492‡
	Mechanical ventilation	0	0.0%	0	0.0%		-
Medications for COVID-19	Paracetamol/Ibuprofen	21	70.0%	20	62.5%	0.389	0.533†
	Antibiotics	23	76.7%	30	93.8%	-	0.077‡
	HCQ	2	6.7%	1	3.1%	-	0.607‡
	Antivirals	4	13.3%	1	3.1%	-	0.189‡
	IVIG	1	3.3%	2	6.3%	-	>0.999‡
	Systemic corticosteroids	7	23.3%	12	37.5%	1.462	0.227†
	Tocilizumab	0	0.0%	3	9.4%	-	0.238‡
	Prophylactic anticoagulants	4	13.3%	9	28.1%	2.044	0.153†

HCQ: Hydroxychloroquine, IVIG: Intra-venous immunoglobulin, N: number, χ^2=chi-squared test, †. Pearson chi-squared test, ‡. Fisher's exact test.

respiratory, gastrointestinal, cardio-vascular, and dermatological manifestations save the wheeze which was more frequently encountered in asthmatics 12/30 (40%) compared to the non-asthmatics 2/32 (6.3%). Although rare, COVID-19 infection in children may trigger viral

Table 7. Regression analysis for predictors of COVID-19 severity in asthmatic children

Predictor	Odds ratio	95% CI		*P*-value
		Lower bound	Upper bound	
Male sex	1.60	0.29	8.86	0.590
Age (yr)	1.16	0.88	1.53	0.298
Duration of asthma (yr)	1.24	0.87	1.76	0.227
Daily low dose ICS or daily low dose ICS-formetrol	2.00	0.35	11.44	0.436
Daily medium dose ICS	2.00	0.13	30.16	0.617
Intake of LTRA	2.41	0.46	12.72	0.301
Oral bronchodilators	1.75	0.34	8.98	0.503
Oral corticosteroids	0.49	0.05	4.94	0.542
Moderate asthma	0.25	0.03	2.18	0.210
Severe asthma	4.50	0.25	80.57	0.307
Moderate/Severe asthma	0.47	0.06	3.54	0.466
Uncontrolled/Partly controlled asthma	4.33	0.71	26.53	0.113

LTRA: leukotriene receptor antagonists, ICS: inhaled corticosteroid.

induced wheezes [10]. The same observation was reported by Ruano and colleagues [11].

GIT manifestations were the presenting symptoms in 23% of asthmatics and 25% of non-asthmatic children infected with COVID-19 in our series. The most prominent symptom was anorexia followed by abdominal pain, then vomiting and diarrhea. Generally, GIT manifestations of COVID-19 were more linked to pediatric infection rather than adults [12]. One of the major metanalysis studies referred to GIT symptoms as the leading presentation in up to 22.8% of children infected with COVID-19, with diarrhea being the most common presentation, followed by vomiting and abdominal pain [13].

In our study, loss of taste and smell was observed in asthmatic children (43.3% each) in higher, albeit insignificant rates than their non-asthmatic peers (28.1%). Lower rates were reported by a study conducted on Spanish children wherein anosmia was found in 7% and dysgeusia in 3% of their cohort [11]. The associated allergic rhinitis and chronic rhinosinusitis may have some impact on smell and taste sensation [14, 15]. Furthermore, it is difficult for children to distinguish between anosmia and ageusia [16]. Although widely described with COVID-19, anosmia has been also reported in association with other viruses affecting the upper respiratory tract [17, 18].

COVID-19 was asymptomatic in 9 patients, mild in 30, and moderate to severe in 23 including 4 MIS-C patients. Only 2 patients (3%) needed ICU admission. Thus, more than half of the enrolled children had asymptomatic/mild COVID-19, reflecting the generally milder nature of the disease in children. These mild COVID-19 patients were more of the asthmatic than of the non-asthmatic group with the former group having a lower frequency-although non-significant- of moderate-to-severe COVID-19 infection. Previous reports suggested a protective role of asthma and asthma treatment against severity and invasion of COVID-19. Milder courses of COVID-19 infection in childhood asthma were explained by the lower expression of ACE2 receptors in nasal and bronchial epithelia of allergic children [19]. Furthermore, eosinophils seem to play a role in attenuating the COVID-19 burden in asthmatic children [20, 21]. Another possible explanation is the use of corticosteroids in controlling asthma, wherein steroid therapy was found to be associated with lower cell expression of ACE2 [22] and had a suppressor effect on IL6 and IL8 production [23]. Conclusions about the possible positive impact of asthma on the prognosis of COVID-19 infections were raised by other studies as well [11, 20, 24, 25].

Abnormal high levels of ferritin, LDH and D-dimer, which have been described as markers of COVID-19 severity, were more frequently encountered in non-asthmatic patient, as finding which goes hand in hand with the more severe course of COVID-19 and the higher number of MIS-C patients in the non-asthmatic group. Other laboratory data in our study, including CBC, ESR, electrolytes, kidney and

liver function tests were comparable in asthmatic and non-asthmatic patients. These findings matched other reports addressing the laboratory differences during COVID-19 infection between asthmatic and non-asthmatic children [26-28].

The finding in the present study of normal chest-x ray in 2/3 of both the asthmatic and the non-asthmatic COVID-19 patients, confirms the previous observation by other investigators that normal radiology does not exclude COVID-19 diagnosis [29]. The high frequency of normal chest X ray among our cases would not be attributed to the inclusion of non-confirmed COVID-19 cases in our study since they constituted only 10/62 (16%) of the whole sample. Furthermore, over 60% of the confirmed cases had normal chest-x ray. Chest-x ray is not as sensitive as the CT scan in detection of the radiological abnormalities in COVID-19 and a negative result does not exclude lung affection [29]. Patients with abnormal chest x-ray and those with respiratory manifestations despite their clear x ray, were subjected to CT scan. Asthmatic patients with abnormal radiological findings were mainly in CO-RAD 5 category (7/10, 70%). Non-asthmatic children showed radiological changes matching CO-RAD 2 and 4 in 10/16 (32.6%) of patients. In a systematic review that included imaging for 3670 children with laboratory-confirmed COVID-19, 44% had abnormalities on chest radiograph or CT scan of the chest [30]. In a separate meta-analysis of 1026 children with laboratory-confirmed COVID-19, 28% had abnormal radiological lesions, mainly ground glass opacities (37%) and consolidation or pneumonic infiltrates (22%) [31]. The higher frequency of CO-RAD 5 among asthmatic patients might denote a more severe COVID-19 illness. Worth to note that the chest CT scan was done in only 10/30 asthmatic and 16/32 non-asthmatics, and despite the significant difference between the 2 groups in their CORAD score, yet the findings are limited by the small number of patients who performed the CT, and thus the results should be interpreted with caution especially that they were not reflected on the clinical COVID-19 severity. CO-RAD score was reported to be useful in detecting COVID-19 disease, even if RT-PCR testing is negative [32]. In addition to its good performance in predicting moderate to severe disease [33]. However, wider studies are needed to investigate the relation between COVID-19 severity and asthma.

Duration of hospital stay of admitted patients ranged between 8 and 14 days (median 10 days). Negative PCR testing was a prerequisite for discharging admitted patients. Hence, this might have resulted in a more than needed hospital stay as a kind of isolation rather than the need for hospital medical care. This was obvious when compared to the shorter duration of hospital admissions mentioned by other authors. In Chao and colleagues' study, the median length of hospital stay in the hospitalized group was 3 days [24]. Another study has mentioned a median length of hospital stay of 5.5 days for infected asthmatic children [20].

MIS-C was diagnosed in one asthmatic and 3 non-asthmatic patients. Three patients had cured completely, and one non-asthmatic patient had suffered from residual mild pericardial effusion. In a study conducted on 49 COVID-19 infected children, MIS-C was diagnosed in 18/49 (9%) of patients, two out of the 18 were asthmatic (11%), presenting mild MIS-C though [16]. Complete resolution was the outcome for all patients in both groups except for the patient with MIS-C in the non-asthmatic group who had residual mild pericardial effusion. COVID-19 infection outcome was generally good in asthmatic children, according to literature, leaving no residuals [11, 25, 27, 34].

Asthmatic patients were maintained on their asthma controllers such as inhaled steroids, antileukotrienes, and oral steroids on some occasions. None of them needed to increase the doses of the long-term controller therapies. This finding was in contrast to a Spanish study in which 14% of their studied asthmatic patients had to increase the doses of the long-term asthma controller medications [11]. Several authors, however, reported that benign courses of treatment were the general rule for COVID-19 infected asthmatic children [27, 34, 35].

Finally, neither asthma severity nor control represented a risk factor for COVID-19 severity in our study. Lack of negative impact of asthma on COVID-19 severity and outcome was reported in a study conducted on asthmatic adults [36]. A possible protective effect of asthma, in

general, and atopy, in particular, against severe COVID-19 infection in children was suggested by many authors [21, 22, 27, 28].

In conclusion, in children, asthma severity and control did not have a significant negative impact on COVID-19 course severity or outcome in our study. However, the small sample size in our study constituted a limitation. More research onto the impact of the atopic nature of asthma and the effect of other asthma therapies such as biologics on the course and outcome of COVID-19 in asthmatic children is recommended.

Disclosure of conflict of interest

None.

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