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Original Article

# Impact of COVID-19 on Pediatric Asthma: Practice Adjustments and Disease Burden

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***What is already known about this topic?*** Coronavirus disease 2019 has a mild disease course in children and adolescents. Chronic respiratory conditions, including asthma, have been suggested as risk factors; however, asthma in children is highly variable in both triggers and severity.

***What does this article add to our knowledge?*** During the pandemic, pediatric asthma services limited consultations and established virtual clinics. However, respondents perceived their patients' asthma control to be retained or even improved, while treatment adherence was considered increased. Children with asthma were not disproportionately affected by coronavirus disease 2019.

***How does this study impact current management guidelines?*** Trigger avoidance and treatment adherence can rapidly improve asthma control in children, even under lockdown pressure. Children/adolescents with asthma do not appear to need additional prophylactic measures from coronavirus disease 2019 when asthma is well-treated.

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*Abbreviations used*
*COVID-19- coronavirus disease 2019*
*IQR- interquartile range*
*SARS-CoV-2- severe acute respiratory syndrome coronavirus 2*

**BACKGROUND: It is unclear whether asthma may affect susceptibility or severity of coronavirus disease 2019 (COVID-19) in children and how pediatric asthma services worldwide have responded to the pandemic.**

**OBJECTIVE: To describe the impact of the COVID-19 pandemic on pediatric asthma services and on disease burden in their patients.**

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**METHODS: An online survey was sent to members of the Pediatric Asthma in Real Life think tank and the World Allergy Organization Pediatric Asthma Committee. It included questions on service provision, disease burden, and the clinical course of confirmed cases of COVID-19 infection among children with asthma.**

**RESULTS: Ninety-one respondents, caring for an estimated population of more than 133,000 children with asthma, completed the survey. COVID-19 significantly impacted pediatric asthma services: 39% ceased physical appointments, 47% stopped accepting new patients, and 75% limited patients' visits. Consultations were almost halved to a median of 20 (interquartile range, 10-25) patients per week. Virtual clinics and helplines were launched in most centers. Better than expected disease control was reported in 20% (10%-40%) of patients, whereas control was negatively affected in only 10% (7.5%-12.5%). Adherence also appeared to increase. Only 15 confirmed cases of COVID-19 were reported among the population; the estimated incidence is not apparently different from the reports of general pediatric cohorts.**

**CONCLUSIONS: Children with asthma do not appear to be disproportionately affected by COVID-19. Outcomes may even have improved, possibly through increased adherence and/or reduced exposures. Clinical services have rapidly responded to the pandemic by limiting and replacing physical appointments with virtual encounters.**  **(J Allergy Clin Immunol Pract 2020;8:2592-9)**

***Key words:*** *Asthma; Children; Virus; Adherence; COVID-19; SARS-CoV2; Control*

## INTRODUCTION

The ongoing coronavirus disease 2019 (COVID-19) pandemic, induced by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is driving an unprecedented international research and clinical mobilization, to understand and contain the disease.[1] COVID-19 has less direct impact on children and adolescents than on adults, although all ages are affected.[2] In children, as in adults, preexisting chronic conditions appear to increase the risk for severe or fatal disease.[3,4] Despite initial clinical reports that did not identify asthma to be overrepresented among patients with COVID-19,[5] it has been suggested that asthma, particularly when uncontrolled, may be included among the underlying conditions imposing a risk for severe COVID-19.[3] Further evaluation is urgently required, because children with wheezing illness/asthma constitute a significant proportion throughout the pediatric age span and asthma is the most frequent chronic condition managed by pediatricians.[6,7]

To rationalize management and instruct the public health care system, it is crucial to understand whether asthma, allergy, or their treatments add risk, protect, or have no discernible effects on the health of children with asthma.[8,9]

Symptoms of COVID-19 in children usually include dry cough and often fever. In contrast with infected adults, most infected children appear to have a milder clinical course.[10] Dyspnea may be present; however, wheeze has not been reported as part of the clinical presentation.[2,11,12] There is currently no published information about the clinical course or other characteristics of COVID-2019 in children with asthma. In parallel, the COVID-19 pandemic introduced a need to change clinical practice, including minimizing face-to-face contact and limiting the use of aerosolising procedures.[13] A need for guidelines in the context has been expressed[14]; however, this is challenged by the lack of evidence.

In this context, pediatric asthma services around the world are being reorganized to face the new, uncertain, reality. Pediatric Asthma in Real Life, a think tank initiated by the Respiratory Effectiveness Group, comprising pediatric asthma experts from all around the world, aims to develop recommendations that will improve patient care.[15] To identify and share best practices, and in collaboration with the World Allergy Organization Pediatric Asthma Committee, we assessed the impact of COVID-2019 on pediatric asthma services and their patients through a survey addressed to large pediatric asthma clinics worldwide.

## METHODS

An online questionnaire was constructed with input from the Pediatric Asthma in Real Life steering group. It included questions about the operation of pediatric asthma clinics during the COVID-19 pandemic, changes in the methods used to communicate with and assess patients, estimates of overall disease activity and patient attitudes, as well as known cases of COVID-19 infection, within the respondents' pediatric asthma cohorts. The survey questionnaire can be found in Table E1 in this article's Online Repository at www.jaci-inpractice.org. Sixty-two members of the participating groups, actively involved in the assessment and management of children with asthma, as assessed by a previous survey,[15] and representing clinical services in different health care systems, were invited to complete the survey on April 9, 2020. The recipients were allowed to further forward the survey to additional clinical practices in their country. Because of the extraordinary circumstances and urgency, the allowed response time was 10 days; no reminders were sent.

Responses are presented descriptively, as proportions or median (interquartile range [IQR]) for numeric variables. We report pertinent differences in the responses across different responder groups:

A. Participants from countries with different COVID burden: (1) less than 10 deaths per million population (limited burden), (2) between 10 and 100 deaths per million population (intermediate burden), and (3) more than 100 deaths per million population (high burden), as of April 19, 2020, the last day of the survey.
B. Participants from different continents. Adequate responses were collected from the Americas, Asia, and Europe, which allowed meaningful comparisons.
C. Participants from countries with different economies. Countries with high versus low and middle income, according to the World Bank classification.
D. Participants from different practice settings, namely, primary care/private clinics, secondary care, and tertiary/university hospitals.

We used Fisher exact test for comparing dichotomous data, given the relatively limited number of participants in each group. Kruskal-Wallis test was used for comparing continuous data, assuming a non-normal distribution. Between-group differences were formally tested only for findings around asthma control and treatment adherence, to avoid multiple comparisons and the risk of type 1 and/or type 2 statistical error. In an exploratory analysis, we extrapolated the

estimates of respondents about asthma control, treatment changes, and treatment adherence in their actual case numbers during the preceding month and we present the risk ratios of patients with favorable versus unfavorable outcomes. Given the limitations of this analysis, we chose to use the 99% CIs.

Although completion of questions was optional, each question was answered by more than 75% of the eligible participants for that question. Missing responses data were disregarded when evaluating the findings.

## RESULTS

### Survey responses and patient population represented

All invited responded to the survey; response from additional centers, invited by the participants, led to an overall response rate of 146% over the original invitations. Ninety-one experts, each representing a different clinical practice from different care settings, economies, and countries, including the whole spectrum of COVID-19 disease burden, completed the survey. Respondents were from 27 countries and 5 continents (Africa, Asia, Americas, Europe, and Oceania), consulting a median of 20 (IQR, 10-25) children with asthma per week, corresponding to 89,804 annual visits in the 61 centers reporting this question, or an estimated 133,969 visits in the complete cohort. Characteristics of the respondent's practices are summarized in Tables I and II and in Tables E2 to E4 in this article's Online Repository at www.jaci-inpractice.org.

### Effect of the COVID-19 pandemic on pediatric asthma practices worldwide

Over the recent time period, pediatric asthma clinics across the world have markedly changed their practice because of the COVID-19 pandemic (Table I). Almost half the participants (47%) reported that their clinics did not accept/receive new patients during the epidemic, with responders from Asia being a notable exception, as 78% received new patients. Among the participating practices, 39% have ceased physical appointments; this proportion exceeded 60% in the more heavily burdened countries. Among centers that continued to run physically, 75% reported a decrease in the number of evaluated cases during the pandemic period. During the month preceding the completion of the survey, participants reviewed a median of 35 cases (IQR, 20-60), approximately half their normal rate, in parallel to the escalating measures to avoid patient contact.

In pediatric asthma clinics that continued accepting physical appointments, several practice changes were implemented to minimize these encounters. Further to the reduction of evaluated cases, most (62%) clinics limited the frequency of planned monitoring encounters, with 28% reviewing only children with severe asthma, while 8% accepted only patients receiving biologics. Access to asthma medications was an issue in 30% of the participating centers, predominantly in Asia (44%).

Importantly, more than 90% of participating centers have launched virtual online or telephone consultations to substitute or complement clinical visits, while 73% have used a helpline to address the needs of their patients. About half the participants considered virtual visits a suboptimal clinical encounter, viable only in the short-term. Nevertheless, a considerable proportion (42%) found them acceptable, or, occasionally, as good as face-to-face visits. Several tools were used by all respondents to facilitate better distal monitoring of asthma control. Validated tools for evaluating asthma control, such as the Asthma Control Test or the Asthma Control Questionnaire, were used by 72% of the participants. Peak expiratory flow readings (31%) or portable spirometer readings (8.5%) were less often used, while treatment adherence was formally monitored in 42% of practices. Symptom recording apps or telemedicine platforms were used in 27% of centers.

There were some between-group differences in monitoring. First, validated asthma control questionnaires were less favored in private/primary care practices (33%), compared with proportions exceeding 80% in secondary, tertiary, and university hospitals. On the contrary, 67% of the private practices opted for telemedicine platforms, in contrast to only 28% of the clinics in secondary care and 13% of the university/tertiary care hospitals. Peak expiratory flow rate was more often used in less affluent countries (42% in low-/middle- vs 27% in high-income countries), while portable spirometers were solely available in high-income countries. Treatment adherence was more extensively evaluated in Asia (78%), than in Europe (44%), or in the Americas (16%).

### Pediatric asthma burden during the COVID-19 pandemic

Evaluation on pediatric asthma burden during the pandemic was queried as proportions improving, remaining stable, or worsening within each individual clinic, for a number of clinically relevant aspects (Table II). Within each practice, a median of 70% (IQR, 60%-80%) of evaluated patients were well controlled, 20% (IQR, 10%-30%) partially controlled, and 10% (IQR, 0%-10%) uncontrolled. In subjectively evaluating their patients' asthma control status, participants considered that while in 85% (IQR, 70%-100%) of cases this was in line with their previous symptom trajectories (as expected), in 20% (IQR, 10%-40%) this exceeded their expectations, while control had deteriorated in only 10% (IQR, 7.5%-12.5%). The risk ratio of the children with better than expected versus worse than expected asthma control was 2.69 (99% CI, 2.17-3.34), while all subgroup analyses yielded consistent findings. Apart from the prespecified subgroup analyses (by the countries' COVID-19 burden, countries' economy, continent, and clinical setting), we evaluated separately centers using or not using a validated questionnaire for evaluating asthma control and centers formally evaluating treatment adherence or not. In line with this impression of the clinical status, no treatment changes were required for 80% of patients (IQR, 60%-90%), while a similar proportion of patients (~10%) required treatment escalation or deescalation. Treatment adherence was estimated to be unchanged in 80% (IQR, 60%-100%) of patients, whereas it improved in 20% (IQR, 10%-40%) of children with asthma, especially in the Americas (IQR, 20%-63%). Reduced adherence was reported in only up to 10% of patients (IQR, 0%-10%). Increased treatment adherence was consistently observed both in the overall study population (relative risk, 1.97; 99% CI, 1.66-2.33) and in all the subgroup analyses.

Countries that were less severely hit by the COVID-19 epidemic reported a higher proportion of well-controlled patients. However, there were no between-group differences in the expected symptom trajectories.

**TABLE I.** Effects of the COVID-19 pandemic on pediatric asthma practices

| Pediatric asthma clinics metrics | Overall cohort | COVID-19 burden (deaths/million) | | | Clinical setting | | |
|---|---|---|---|---|---|---|---|
| | | <10 | 10-100 | >100 | Primary | Secondary | Tertiary/university |
| No. of participants in each category, N | 91 | 31 | 15 | 26 | 15 | 11 | 47 |
| Measures to limit physical contact | | | | | | | |
| Did not receive/accept new cases during pandemic | 33/70 (47) | 13/25 (52) | 6/15 (40) | 13/25 (52) | 5/15 (33) | 7/11 (64) | 20/40 (50) |
| Ceased physical appointments | 35/91 (39) | 11/31 (35) | 4/15 (27) | 16/26 (62) | 8/15 (53) | 3/11 (27) | 21/47 (45) |
| Reduced no. of cases* | 39/52 (75) | 15/20 (75) | 9/11 (82) | 8/10 (80) | 6/7 (86) | 5/8 (63) | 21/26 (81) |
| Reduced planned monitoring visits* | 32/52 (62) | 12/20 (60) | 8/11 (73) | 5/10 (50) | 6/7 (86) | 5/8 (63) | 14/26 (54) |
| Only monitoring patients receiving biologics | 6/71 (9) | 1/25 (4) | 0/15 (0) | 3/25 (12) | 1/15 (7) | 0/11 (0) | 4/40 (10) |
| Only monitoring children with severe asthma | 20/71 (28) | 4/25 (16) | 7/15 (47) | 8/25 (32) | 2/15 (13) | 2/11 (18) | 15/40 (38) |
| Nonphysical services launched to address health needs | | | | | | | |
| Launched virtual online or telephone consultations | 79/87 (91) | 25/31 (81) | 15/15 (100) | 25/26 (96) | 15/15 (100) | 11/11 (100) | 40/47 (85) |
| Launched helpline for children with asthma | 57/78 (73) | 23/31 (74) | 10/15 (67) | 19/26 (73) | 11/15 (73) | 9/11 (82) | 33/47 (70) |
| Shared any advisory material | 45/78 (58) | 22/31 (71) | 6/15 (40) | 13/26 (50) | 11/15 (73) | 8/11 (73) | 23/47 (49) |
| Shared advisory material via email | 24/78 (31) | 8/31 (26) | 4/15 (27) | 11/26 (42) | 5/15 (33) | 4/11 (33) | 14/47 (30) |
| Shared advisory material via social media | 18/78 (23) | 12/31 (39) | 2/15 (13) | 1/26 (4) | 4/15 (27) | 6/11 (55) | 5/47 (11) |
| Shared advisory material through Web site | 14/78 (18) | 7/31 (23) | 1/15 (7) | 3/26 (12) | 3/15 (20) | 2/11 (19) | 7/47 (15) |
| Tools for evaluating asthma control | | | | | | | |
| Using at least 1 tool for evaluating asthma control | 71/71 (100) | 25/25 (100) | 15/15 (100) | 25/25 (100) | 15/15 (100) | 11/11 (100) | 40/40 (100) |
| A validated questionnaire, such as ACT or ACQ | 51/71 (72) | 16/25 (64) | 11/15 (73) | 20/25 (80) | 5/15 (33) | 9/11 (82) | 33/40 (83) |
| A standardized questionnaire | 19/71 (27) | 4/25 (16) | 5/15 (33) | 9/25 (36) | 1/15 (7) | 1/11 (9) | 16/40 (40) |
| Peak flow meter reading | 22/71 (31) | 10/25 (40) | 6/15 (40) | 4/25 (16) | 5/15 (33) | 4/11 (36) | 11/40 (28) |
| Portable spirometer reading | 6/71 (9) | 0/25 (0) | 3/15 (20) | 1/25 (4) | 0/15 (0) | 0/11 (0) | 4/40 (10) |
| Diary cards | 5/71 (7) | 2/25 (8) | 2/15 (13) | 0/25 (0) | 0/15 (0) | 0/11 (0) | 4/40 (10) |
| Symptom-recording applications or telemedicine platforms | 19/71 (27) | 10/25 (40) | 4/15 (27) | 3/25 (12) | 10/15 (67) | 3/11 (28) | 5/40 (13) |
| Adherence evaluation | 30/71 (42) | 9/25 (36) | 7/15 (47) | 10/25 (40) | 5/15 (33) | 4/11 (36) | 17/40 (43) |
| Acceptability of virtual clinics | | | | | | | |
| As good as face-to-face clinics | 3/71 (4) | 1/25 (4) | 1/15 (7) | 0/25 (0) | 2/15 (13) | 0/11 (0) | 1/40 (3) |
| Somehow compromised, but still acceptable | 27/71 (38) | 8/25 (32) | 6/15 (40) | 11/25 (44) | 4/15 (27) | 3/11 (28) | 18/40 (45) |
| Only viable for a short period of time | 34/71 (48) | 12/25 (48) | 7/15 (47) | 12/25 (48) | 7/15 (47) | 5/11 (46) | 19/40 (48) |
| Unsatisfactory, low-quality medical advice | 3/71 (4) | 2/25 (8) | 1/15 (7) | 0/25 (0) | 1/15 (7) | 1/11 (9) | 1/40 (3) |

*ACQ*, Asthma Control Questionnaire; *ACT*, Asthma Control Test.
Values are n (%).
*Among those with physical appointments.

**TABLE II.** Pediatric asthma burden during the COVID-19 pandemic

| | | COVID-19 burden (deaths/million) | | | | Clinical setting | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Pediatric asthma burden** | **Overall cohort** | **<10** | **10-100** | **>100** | ***P*** | **Primary** | **Secondary** | **Tertiary** | ***P*** |
| No. of participants contributing data, N | 61 | 22 | 10 | 23 | | 13 | 9 | 34 | |
| Asthma control: What percentage of your pediatric asthma patients are currently | | | | | | | | | |
| Well controlled | 70 (60-80) | 80 (70-90) | 70 (60-85) | 60 (50-80) | <.01 | 80 (80-90) | 70 (65-80) | 70 (60-80) | |
| Partially controlled | 20 (10-30) | 20 (10-20) | 20 (15-30) | 20 (20-30) | | 20 (10-20) | 20 (20-35) | 20 (10-30) | |
| Uncontrolled | 10 (0-10) | 10 (0-10) | 10 (0-10) | 10 (10-20) | | 0 (0-10) | 10 (10-15) | 10 (10-13) | |
| Asthma control: How does the current control of your patients compare with your expectations for these patients? | | | | | | | | | |
| Better than expected | 20 (10-40) | 30 (10-50) | 20 (10-25) | 20 (10-40) | | 35 (20-43) | 25 (10-48) | 20 (10-30) | |
| As expected | 85 (70-100) | 90 (65-100) | 80 (70-95) | 80 (70-100) | | 90 (65-100) | 90 (75-100) | 80 (70-100) | |
| Worse than expected | 10 (8-13) | 10 (0-10) | 10 (10-10) | 10 (10-20) | | 0 (0-8) | 10 (3-18) | 10 (10-20) | .03 |
| Risk ratio of better vs worse asthma control, RR (99% CI) | 2.69 (2.17-3.34) | 5.19 (3.06-8.81) | 2.90 (1.89-4.47) | 1.99 (1.50-2.64) | | 12.67 (5.29-30.32) | 4.00 (1.30-12.33) | 2.07 (1.65-2.61) | |
| What proportion of your patients required a change in their asthma treatments? | | | | | | | | | |
| Treatment escalation | 10 (10-30) | 10 (10-30) | 10 (10-20) | 20 (10-25) | | 10 (10-30) | 15 (10-30) | 10 (10-30) | |
| Unchanged treatment | 80 (60-90) | 80 (60-90) | 80 (80-85) | 80 (60-90) | | 90 (70-90) | 80 (65-90) | 80 (60-90) | |
| Treatment de-escalation | 10 (0-20) | 10 (0-20) | 10 (0-10) | 10 (0-20) | | 10 (0-10) | 10 (5-15) | 10 (0-20) | |
| Risk ratio escalation vs deescalation, RR (99% CI) | 1.41 (1.21-1.65) | 1.78 (1.27-2.50) | 5.21 (3.15-8.60) | 0.95 (0.79-1.16) | | 2.22 (1.52-3.25) | 2.42 (1.05-5.55) | 1.24 (1.04-1.47) | |
| Have you observed changes in the adherence to controller medications? | | | | | | | | | |
| Increased adherence | 20 (10-43) | 20 (10-30) | 25 (13-38) | 30 (10-50) | | 30 (20-45) | 10 (8-15) | 20 (10-50) | |
| Unchanged adherence | 80 (60-100) | 90 (70-100) | 80 (60-100) | 70 (53-100) | | 70 (65-95) | 100 (95-100) | 80 (50-100) | .03 |
| Reduced adherence | 10 (0-10) | 10 (0-10) | 10 (5-10) | 10 (0-30) | | 10 (3-10) | 0 (0-3%) | 0 (0-18%) | |
| Risk ratio of increased vs reduced adherence, RR (99% CI) | 1.97 (1.66-2.33) | 3.00 (2.01-4.47) | 3.79 (2.41-5.98) | 1.43 (1.16-1.77) | | 3.11 (2.08-4.64) | 6.00 (0.38-94.23) | 1.73 (1.43-2.09) | |
| Limited availability/access to asthma medications, n (%) | 21/69 (30) | 8/25 (32) | 2/15 (33) | 9/25 (36) | | 6/15 (40) | 3/11 (28) | 12/42 (29) | |

Values are median (IQR) unless otherwise indicated.

### COVID-19 among children with asthma within the participating centers

Suspected cases of COVID-19 in children with asthma were reported in only 13 of 91 participating centers (14%). There were 100 such cases (a median of 3 suspected cases in each of these centers; IQR, 2-10). Of these, only 15 (15%) were confirmed, 10 in 1 center in Italy, 2 in Portugal, and the remaining in 2 French centers. The most frequent presenting symptoms of the confirmed cases included nasal discharge or blockage and cough, whereas breathlessness, fever, and wheeze were less often reported (see details in Table E5 in this article's Online Repository at www.jaci-inpractice.org). Half the reported cases also experienced nonrespiratory symptoms, such as myalgia and fatigue. Eleven of these children (73%) experienced a mild clinical syndrome, 3 (20%) a moderate illness, and only 1 case (6.7%) required hospitalization. None required an admission to the intensive care unit or ventilation, and all made a complete recovery.

## DISCUSSION

There is no doubt that pediatric asthma clinics are among health care services significantly affected by the COVID-19 pandemic. The number of new patients evaluated is restricted, while there is also a reduction in the frequency and/or the total number of patients monitored. In addition, use of several diagnostic modalities, including lung function testing, fractional exhaled nitric oxide, or methacholine tests, is limited, along with therapeutic interventions, such as nebulized treatments.[16] However, many services have actively responded to these challenges, most often by "virtual" clinics or other telehealth appliances, which flourished in all medical specialties during the COVID-19 epidemic.[17] Clinicians consider such clinics suboptimal, nonetheless adequate for the, hopefully, short time period under lockdown. Standard tools such as the Asthma Control Test or the Asthma Control Questionnaire were used, whereas objective measures, such as spirometry or peak expiratory flow rate, were less often feasible. The observed approaches are consistent with recent ad-hoc recommendations.[18]

Despite the above challenges, there was no apparent deterioration in asthma in the large majority of patients. In fact, based on the perceptions of the participants, improvement exceeded expectations in 20% of subjects. This was accompanied, and possibly partially mediated, by increased adherence to treatment plans—normally a major challenge in pediatric asthma management. Contrasting and very often unproven information has been circulated through the media in regard to maintenance medications and management. Among others, inhaled and/or systemic corticosteroids have been of particular interest, as both a potential COVID-19 treatment and as an increased susceptibility factor.[19] Our findings suggest that parents of children with asthma monitored in specialist clinics have responded to messages on the need for treatment continuation, rather than unfounded fears about potentially detrimental effects of inhaled steroids. Furthermore, social distancing, sheltering at home, and reduced school days may reduce exposure to the main triggers of acute asthma events, most notably rhinovirus infections, outdoor allergens, physical exercise, and air pollution,[20,21] contributing to sustained, or even improved, outcomes during this period. Nevertheless, a small proportion of children (~10%) have deteriorated; confinement in children sensitized to indoor allergens and/or psychological factors may have contributed to this.

Despite the differences between countries regarding COVID-19 infection and policies, the number of pediatric patients with asthma with suspected and, even more, confirmed COVID-19 was small, coming mostly from 1 tertiary center in Italy. It is noteworthy that even in these cases, the clinical course was benign, and wheezing, the hallmark of asthma, was observed in only 40%, while the simultaneous presence of other viruses was not assessed.

Our data cannot provide a concrete estimate of the clinically relevant COVID-19 incidence among children with asthma. However, taking into account (1) the reported COVID-19 incidence in the more severely affected countries (the United States, Spain, Italy, France, and the United Kingdom; 2.2-4.8 cases per thousand population[22]) and (2) data suggesting that COVID-19, severe enough to lead to seeking medical advice and thus diagnosed, is about 12.8 times less frequent in children than in adults,[3] 17 to 38 such cases per 100,000 of a nonselected pediatric population can be assumed. This is consistent with recent data on the burden of COVID-19 in children in China, South Korea, and the United States, where it is uniformly very low.[3,23,24] In our survey, the estimated population of pediatric patients with asthma represented within these countries was 20,000 to 40,000; that is, the expected range of potential patients with COVID-19 would be 3 to 15, suggesting that COVID-19 is not associated with severe asthma exacerbations.

It is possible that SARS-CoV-2 does not induce bronchial hyperreactivity and asthma-like pathophysiology; nevertheless, this does not exclude the possibility of children with asthma, particularly uncontrolled asthma, developing more severe COVID-19, as we have previously reported for influenza.[25] Furthermore, the impact of atopy on SARS-CoV-2 susceptibility needs to be further evaluated, in light of recent findings suggesting that allergic sensitization and allergen exposure may reduce the SARS-CoV-2 receptor, angiotensin-converting enzyme 2.[26] However, only 1 case requiring hospitalization was identified through this survey, drawing information from a large number of children with asthma, including a large proportion with severe asthma, given the large proportion of respondents from tertiary centers. Further evaluation of children with asthma, poor symptom control, and high severity in regard to the individual response to SARS-CoV-2 will be needed to draw a firm conclusion.

There are several limitations to this survey. Most importantly, the clinical data that are described are not based on direct evaluation of patients, but on the subjective evaluation of the respondents and therefore, there is a risk of recall bias. In addition, respondents might have been unaware of some of the acute presentations of their patients to alternative clinical sites. However, clinicians are well aware of this issue that is not specific to the COVID-19 era. There is a chance that changes in clinical practice due to COVID-19 may have led more patients to seek medical advice from alternative sources; however, all participating centers offered either physical or virtual appointments or helplines for patients with acute symptoms.

In parallel, children with asthma tend to have less controlled disease at the time of the initial referral to the expert clinic. Therefore, the significant decrease in new referrals may partially account for the respondents' perception that asthma control has improved during the pandemic. However, clinicians were

specifically asked to compare their perceptions about disease control among patients during monitoring visits, during versus before the epidemic. As a result of these limitations, all findings described about the clinical burden of COVID-19 on children with asthma should be considered exploratory and further studies directly evaluating the clinical course of children with asthma are needed.

Moreover, responders are clinicians with high expertise and interest in the domain; therefore, they may not be representative of all pediatric asthma services. Nevertheless, our findings of limited COVID-19 burden within the included cohorts that are potentially selective for children with more severe or uncontrolled asthma, including patients treated with biologics, further supports our conclusions. Moreover, expertise and increased interest, as confirmed by the rapid response of the totality of invited, may also be considered a strong point. Input came from a wide geographical spread; unfortunately, Africa and Oceania were minimally represented. Similarly, the responses do not include many low-income countries, in which health services, underlying susceptibility to illness, and disease impact may be different.

## CONCLUSIONS

Children with asthma do not appear to be disproportionately affected by COVID-19; relevant high-end services have rapidly responded, medication adherence has not been negatively affected, and outcomes are promising. Ongoing epidemiological studies, including one initiated by this group, will be able to quantify any added and long-term risk of COVID-19 on children with asthma.

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## ONLINE REPOSITORY

**TABLE E1.** Survey questions and response options

| |
|---|
| Q1. Does your Pediatric Asthma clinic continue to run physically? |
| Yes |
| No |
| Q2. Has the number of evaluated cases changed in the last month? |
| Increased |
| Stable |
| Decreased |
| Q3. Has the planned monitoring frequency of patients changed? |
| No |
| More frequently |
| Less frequently |
| Currently unstable/unknown |
| Q4. Do you offer a virtual (online or telephone) clinic/consultation? |
| Yes |
| No |
| Q5. In the last few weeks, has the number of evaluated cases |
| Increased? |
| Remain stable? |
| Decreased? |
| Q6. Approximately how many patients do you see per week (number)? |
| Number: _____ |
| Q7. Has the type/severity/priority of patients changed? |
| No |
| Yes—more severe |
| Yes—patients receiving biologicals only |
| Yes—other priority please specify |
| Q8. Which of the following methods do you use to monitor your patients? |
| A standardized questionnaire |
| An asthma control test (ACT, ACQ, other) |
| Peak flow meter reading |
| Portable spirometer reading |
| Adherence evaluation |
| Diary cards |
| Symptom-recording app/telemedicine platform |
| Other (please specify) |
| Q9. What has been your experience with your virtual clinic so far? |
| As good as the face-to-face clinic |
| Somehow compromised but still okay |
| Only viable for a short period of time |
| Unsatisfactory—low-quality medical service |
| Other (please specify): _____ |
| Q10. Do you offer a helpline for your pediatric asthma patients? |
| Yes |
| No |
| Q11. If you do not offer physical or virtual clinic, please describe expectations/plans around pediatric asthma patients in the near future. |
| Free text: _____ |
| Q12. Do you actively send advice to your asthma patients? |
| No |
| By email |
| Through social media |
| Through website |
| Q13. In the last few weeks have you received any new patients? |
| No |
| Yes—a few |
| Yes—several |
| Q14. If yes, how many new patients do you receive every week, during the COVID-19 pandemic? |
| Number: _____ |
| Q15. In your asthma clinic, do you have any patients receiving biologicals? |
| Yes |
| No |
| Q16. If yes, how many? |
| Number: _____ |
| Q17. Do they continue their regular dosage? |
| Yes |
| No—stopped |
| No—reduced frequency |
| Q18. Has any of your pediatric asthma patients had confirmed COVID? |
| No |
| Yes |
| Q19. If yes, approximately how many? |
| Number: _____ |
| Q20. Their symptoms at presentation included: |
| Runny/blocked nose. Percentage: _____ |
| Cough. Percentage: _____ |
| Wheeze. Percentage: _____ |
| Shortness of breath. Percentage: _____ |
| Fever. Percentage: _____ |
| Nonrespiratory symptoms/other. Percentage: _____ |
| Q21. Their clinical course in regard to their asthma has been: |
| Mild. Percentage: _____ |
| Moderate (treated at home). Percentage: _____ |
| Severe exacerbation (emergency visit or hospital admission). Percentage: _____ |
| Required ICU admission or intubation. Percentage: _____ |
| Death. Percentage: _____ |
| Q22. Has any of your pediatric asthma patients had suspected, but not confirmed COVID? |
| No |
| Yes |
| Q23. If yes, approximately how many? |
| Number: _____ |
| Q24. Their symptoms at presentation included: |
| Runny/blocked nose. Percentage: _____ |
| Cough. Percentage: _____ |
| Wheeze. Percentage: _____ |
| Shortness of breath. Percentage: _____ |
| Fever. Percentage: _____ |
| Nonrespiratory symptoms/other. Percentage: _____ |
| Q25. Their clinical course in regard to their asthma has been: |
| Mild. Percentage: _____ |
| Moderate (treated at home). Percentage: _____ |

**TABLE E1.** *(Continued)*

| |
|---|
| Severe exacerbation (emergency visit or hospital admission). Percentage: _____ |
| Required ICU admission or intubation. Percentage: _____ |
| Death. Percentage: _____ |
| Q26. In the last month, approximately how many patients have you monitored (either physically or virtually)? |
| Number: _____ |
| Q27. From the patients you have monitored, what is the proportion with |
| Well-controlled asthma. Percentage: _____ |
| Partially controlled asthma. Percentage: _____ |
| Uncontrolled asthma. Percentage: _____ |
| Q28. How does this compare with your expectations for the same patients? |
| As expected. Percentage: _____ |
| Better that expected. Percentage: _____ |
| Worse than expected. Percentage: _____ |
| Q29. What was the proportion of patients with regard to treatment changes? |
| Increased treatment. Percentage: _____ |
| Continued treatment. Percentage: _____ |
| Decreased treatment. Percentage: _____ |
| Q30. Is availability or access to medication an issue? |
| Yes |
| No |
| Q31. Have you observed changes in adherence to controller medications? |
| No changes in adherence. Percentage: _____ |
| Increased adherence. Percentage: _____ |
| Reduced adherence. Percentage: _____ |
| Any comment on adherence changes? _____ |
| Q32. Number of your patients (approximately) who have suffered an exacerbation during the last month and treated at outpatients (independent of COVID)? |
| Number: _____ |
| Q33. Number of your patients (approximately) who have suffered an exacerbation during the last month and were hospitalized (independent of COVID)? |
| Number: _____ |
| Q34. In which country do you practice? |
| Q35. In what setting do you practice? |
| Tertiary/university hospital |
| Secondary hospital |
| Primary care |
| Community center |
| Q36. Your email (optional) |
| Q37. Your name (optional) |

*ACQ*, Asthma Control Questionnaire; *ACT*, Asthma Control Test; *ICU*, intensive care unit.

**TABLE E2.** Respondents by country of practice

| Continent<br>Country | N |
|---|---|
| Europe | 39 |
| Czech Republic | 1 |
| Finland | 4 |
| France | 11 |
| Germany | 2 |
| Greece | 1 |
| Italy | 2 |
| Lithuania | 1 |
| Poland | 7 |
| Portugal | 1 |
| Romania | 1 |
| Spain | 2 |
| Sweden | 1 |
| United Kingdom | 5 |
| Asia | 9 |
| China | 2 |
| India | 2 |
| Pakistan | 1 |
| Russian Federation | 2 |
| Singapore | 1 |
| Turkey | 1 |
| Americas | 22 |
| Argentina | 1 |
| Brazil | 1 |
| Canada | 2 |
| Chile | 1 |
| Mexico | 12 |
| United States | 5 |
| Africa, Oceania | 2 |
| Egypt | 1 |
| Australia | 1 |
| Undeclared | 19 |

**TABLE E3.** Respondent distribution by domain

| Domains | Participants |
|---|---|
| Setting | Tertiary/university hospital (47)<br>Secondary care (11)<br>Primary care, private practice (15)<br>Not declared (18) |
| COVID burden | <10 deaths per million population (31)<br>10-100 deaths per million population (15)<br>>100 deaths per million population (26)<br>Not declared (19) |
| Country income (World Bank) | High income (49)<br>Upper middle income (19)<br>Low middle income (4)<br>Not declared (19) |

**TABLE E4.** Pediatric patients with asthma reviewed by the participating centers, in the past and during the COVID-19 pandemic

| | | COVID-19 burden (deaths/million) | | | Clinical setting | | |
|---|---|---|---|---|---|---|---|
| **Patients reviewed** | **Overall cohort** | **<10** | **10-100** | **>100** | **Primary** | **Secondary** | **Tertiary** |
| No. of consultations per respondent per week, median (IQR) | 20 (10-25) | 12.5 (5-20) | 18 (14-28) | 20 (10-25) | 20 (10-25) | 5 (5-10) | 20 (11-24) |
| No. of participants contributing data, N | 61 | 22 | 10 | 23 | 13 | 9 | 34 |
| Total no. of patients evaluated weekly by respondents, N | 1,727 | 326 | 301 | 785 | 292 | 69 | 1081 |
| Annualized estimate of patients evaluated, N | 89,804 | 16,952 | 15,652 | 40,820 | 15,184 | 3,588 | 56,212 |
| No. of patients evaluated per respondent during the preceding month, median (IQR) | 35 (20-60) | 25 (10-40) | 38 (21-60) | 48 (20-68) | 50 (10-100) | 25 (10-30) | 40 (20-60) |
| No. of participants contributing data, N | 59 | 22 | 14 | 22 | 13 | 9 | 37 |
| Total no. of patients evaluated during the preceding month by participants, N | 3,593 | 820 | 728 | 1,925 | 870 | 214 | 2,509 |
| Annualized estimate of patients evaluated, N | 43,116 | 9,840 | 8,736 | 23,100 | 10,440 | 2,568 | 30,108 |
| No. of new patients per respondent per week, during COVID-19, median (IQR) | 5 (3-9) | 3.5 (2-5) | 4 (3-6) | 5 (3-10) | 5 (2-8) | 4 (4-5) | 5 (3-10) |
| No. of participants contributing data, N | 27 | 10 | 4 | 9 | 8 | 2 | 14 |
| Total no., N | 194 | 63 | 20 | 74 | 62 | 8 | 97 |
| No. of patients receiving biologics in the clinic, median (IQR) | 11 (5-20) | 5 (3-10) | 9 (5-15) | 20 (10-30) | 10 (5-17) | 3 (3-3) | 11 (6-20) |
| No. of participants contributing data, N | 38 | 8 | 9 | 20 | 4 | 1 | 32 |

**TABLE E5.** Clinical presentation of children with asthma and confirmed COVID-19

| **Symptoms** | **No. (proportion)** |
|---|---|
| Nasal discharge or blockage | 9 of 15 (60%) |
| Cough | 11 of 15 (73%) |
| Wheeze | 6 of 15 (40%) |
| Breathlessness | 6 of 15 (40%) |
| Fever | 6 of 15 (40%) |
| Nonrespiratory symptoms | 9 of 15 (60%) |