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CASE SERIES

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Pre and post-COVID 19 infection pulmonary functions in children with chronic respiratory disease: A case series

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Abstract

As functional respiratory impairment following COVID-19 infection (COVID-19) is increasingly reported in adult, data regarding children especially with pre-existing chronic respiratory disease (PCRD) remain scarce. We retrospectively assessed clinical presentation, duration of symptoms related to COVID-19 from paediatric patients with PCRD and compared their pre/post COVID-19-I spirometry values. Data from 12 patients were analysed. Timing between COVID-19 diagnosis and subsequent functional evaluation ranged from 26 to 209 days (mean 77). The PCRD in these patients included asthma, cystic fibrosis, bronchiolitis obliterans and bronchomalacia. During COVID-19, all clinical presentations were mild. One patient displayed persistent post-COVID-19 symptoms for 8 weeks after infection. Two patients presented significant deterioration of post-COVID-19 spirometric values with a return to pre-COVID-19 values in subsequent measures. We concluded that children with PCRD are not at increased risk for severe COVID disease and that most of them have no or only transient pulmonary functional impairment 1 to 7 months after COVID-19.

KEYWORDS
COVID-19 associated symptoms, COVID-19 infection in children, pre-existing chronic respiratory disease, pulmonary functional test

INTRODUCTION

Coronavirus-19 disease (COVID-19) is a primarily respiratory viral infection caused by a novel coronavirus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease displays highly heterogenous patterns of presentation and evolution, ranging from asymptomatic infection to severe acute respiratory with multiorgan failure. Multiple studies have shown that children are less frequently and less severely affected than adults.[1–3] Studies in adults have shown that pre-existing chronic respiratory diseases (PCRD) such as asthma and chronic obstructive lung disease do not confer an increased risk of infection but a possible increased risk of progression to a severe disease.[4] Medium-term functional impairment is also increasingly reported in adult patients following COVID-19.[5] However, paediatric data remain scarce regarding the short- and medium-term impact of COVID-19 in children with PCRD. In this case series, we report the changes in lung function and symptomatology after COVID-19 of 12 children with PCRD.

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Methods

We included patients aged ≥6 years who were followed for a PCRD at the respiratory clinic of the Sainte-Justine University Hospital Center in Montreal, Canada, a tertiary paediatric care center. Pulmonologists identified their patients who had documented COVID-19 by polymerase chain reaction (PCR) tests from March 2020 to April 2021, covering the first 2 waves and the beginning of the third wave of the

TABLE 1 Patients' characteristics and COVID-related symptoms

Patients	Sexe (F/M)	Pre-existing respiratory condition(s)	Comorbidities	Age at COVID (years)	Associated COVID symptoms	Symptoms duration (days)	Post-COVID symptoms
1	F	Asthma	DMA	16.6	Muscular stiffness Odynophagia	10 7	Fatigue × 8 weeks
2	M	Asthma	CID	12.4	Odynophagia, mild cough Fatigue	10 14	Nil
3	F	Asthma	N/A	10.6	Nil	N/A	Nil
4	F	OB	AML	12.4	Mild fever	3	Nil
5	M	Asthma	ALL	10.6	Mild dry cough, headache Mild fever	4 1	Nil
6	F	Asthma, CF	N/A	7.5	Nil	N/A	Nil
7	F	Asthma, CF	N/A	7.2	Mild dry cough	4	Nil
8	M	CF	N/A	9.7	Rhinorrhea	3	Nil
9	M	Asthma, bronchomalacia	N/A	9.9	Mild dry cough	4	Nil
10	M	Asthma	N/A	14.7	Rhinorrhea, mild dyspnea Mild fever, headache Ageusia, anosmia	9 3 15	Mild effort dyspnea × 2 weeks
11	M	Asthma	N/A	9.0	Mild dry cough	7	Nil
12	F	OB	N/A	15.9	Nil	N/A	Nil

Abbreviations: ALL, acute lymphoblastic leukaemia; AML, acute myeloid leukaemia; CF, cystic fibrosis; CID, congenital immunodeficiency; DMA, dust mites allergy; F, female; M, male; N/a, not applicable; OB, obliterative bronchiolitis.

pandemic in Quebec. Children who were unable to perform spirometry were excluded. After obtaining consent, we collected patient- or parent-reported COVID-associated symptoms (nature and duration). We retrospectively collected clinical information from the patient's medical chart, including the last spirometry values pre-COVID and the first spirometry post-COVID. These include forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC), and forced expiratory flow between 25% and 75% of FVC curve (FEF_{25-75}). Spirometry was performed according to the American Thoracic Society (ATS) and European Respiratory Society (ERS) technical standards.[6] Global lung initiative (GLI) references were used.[7] Obstructive ventilatory defect (OVD) was defined according to the ATS/ERS definition.[8]

Results

We identified 12 children meeting study criteria. The mean (SD) age at COVID diagnosis was 11.3 years (range 7.2–16.6 years) and 6 patients (50%) were female (Table 1). Pre-existing lung disease included asthma ($n = 9$, 75%), bronchiolitis obliterans ($n = 2$, 16.7%), cystic fibrosis ($n = 3$, 25%), and bronchomalacia ($n = 1$, 8.3%). All patients showed relatively mild symptoms at the time of diagnosis and none required hospitalization. Symptoms were mainly of upper airways origin with mild dry cough being the most common ($n = 5$, 41.7%). Mild dyspnea was a complaint in only 1 (8.3%) patient. Systemic symptoms were also infrequent with mild fever and headache in 3 (25%) and 2 (16.7%) patients respectively. Only one patient (8.3%), Patient 1, presented persistent symptoms following COVID infection with general fatigue for 8 weeks.

Timing between COVID diagnosis and subsequent spirometry ranged from 26 to 137 days (mean 77 days). At the post-COVID evaluation, only 1 patient (patient 10, male, 14.6 years at COVID diagnosis) presented a new and persistent symptom since his COVID diagnosis, consisting of mild exertional dyspnea.

Patient 1 ($n = 1$, 8.3%) had normal spirometry pre-COVID but presented a mild OVD at 1 month post-COVID with a FEV_1/FVC Z-score of −1.92 (decrease of 0.31 compared to pre-COVID) and FVC and FEV_1 values within normal rage (Table 2). *Z*-score value for FEF_{25-75} in this patient also showed a decrease of 0.40, reaching −1.94 in post-COVID-19. This patient was followed for asthma and had sub-optimal adherence to prescribed treatments. Given that these results were suggestive of increased obstructive disease, asthma treatment was optimized and both functional and clinical control were documented at the subsequent follow-up appointment at 4.6 months post-COVID. While a short-term and transient deterioration in lung function cannot be ruled out, other factors could have contributed to this observation such as poor adherence to baseline therapy.

Patient 4 and 12 ($n = 2$, 16.7%) had post-infectious bronchiolitis obliterans and already presented severe OVD pre-COVID. At approximately 2 months post-COVID,

TABLE 2 Pre and post-COVID spirometry values in the 12 reported cases

	FVC *Z*-score		FEV_1 *Z*-score		FEV_1/FVC *Z*-score		FEF_{25-75} *Z*-score		Time after COVID (days)
	Pre-COVID	Post-COVID	Pre-COVID	Post-COVID	Pre-COVID	Post-COVID	Pre-COVID	Post-COVID	
1	0.82	0.67	−0.22	−0.63	−1.61	−1.92	−1.54	−1.94	26
2	−1.44	−1.35	−0.68	−0.81	1.59	0.98	−0.20	0.34	44
3	0.95	0.59	1.57	1.08	0.97	0.8	1.37	0.68	105
4	−1.25	−2.68	−3.24	−4.24	−3.00	−3.09	−4.25	−4.51	66
5	0.78	0.16	1.322	0.68	0.763	0.85	1.18	1.12	137
6	0.29	0.14	−0.29	−0.01	−1.12	−0.39	−1.7	−0.2	46
7	0.15	0.13	−0.16	−0.46	−0.66	−1.12	−0.77	−1.13	75
8	−0.13	0.69	0.18	1.14	0.45	0.6	0.18	0.38	126
9	1.05	0.67	0.77	0.15	−0.50	−0.83	−1.51	−0.74	102
10	−0.86	−0.64	−0.94	−0.72	−0.26	−0.23	−0.41	−0.38	39
11	−0.34	−0.63	0.20	0.20	0.93	1.61	1.43	1.57	98
12	−2.57	−2.34	−4.02	−4.24	−2.92	−3.29	−4.26	−4.63	209

Note: *Z*-scores are calculated using the global lung initiative references. Time after COVID is the time between COVID-19 diagnosis and post-COVID spirometry, expressed in days.

Patient 4 displayed a notable worsening in in both FVC (−1.43 in *Z*-score) and FEV_1 (−1.00 in *Z*-score). FEV_1/FVC (−0.09 in *Z*-score) and FEF_{25-75} (−0.26 in *Z*-score) showed a relative stability post-COVID. A subsequent control of lung function at 10 months post-COVID showed a return to baseline values. A review of the patient's previous spirometries revealed similar variations in lung function following viral upper respiratory tract infections despite a stable clinical state, thus a transient deterioration in lung function secondary to COVID could not be ruled out.

In Patient 12, the post-COVID spirometry acquired at approximatively 7 months from diagnosis showed no major variations compared with pre-COVID values. *Z*-score values for FEV_1, FEV_1/FVC, and FEF_{25-75} decreased by −0.22, −0.37, and −0.37, respectively, while FVC Z-score values increased by +0.23.

For all remaining patients, pre- and post-COVID spirometric values were within normal limits, with the mean change between pre- and post-COVID Z-score values for FVC, FEV_1, and FEV_1/FVC being 0.15, −0.08, and 0.01, respectively.

DISCUSSION

In this case series of 12 children with PCRD, we found that these children were only mildly symptomatic from COVID-19 and that the majority did not show deterioration of their lung function or aggravation of respiratory symptoms after the infection. For the two patients with a deterioration in lung function, the impact was transient and a full recovery was subsequently observed. Despite being a tertiary care referral center for respiratory disease that actively follows over 1400 children in general pulmonology and cystic fibrosis clinics, we only identified 12 patients meeting inclusion criteria. While this suggests that underlying lung disease may not be a risk factor for COVID-19 in children, it may also reflect the heightened awareness of the families of children with lung disease, which may lead to increased adoption of sanitary and protective measures.

While we now have a better understanding of COVID-19 in children in general, we know little about the impact of COVID-19 on children with pre-existing lung disease and its short- to medium-term consequences on lung function and symptomatology. As respiratory involvement remains the main feature in COVID-19, association between respiratory chronic conditions and the risks of infection and severe disease is of particular concern. Asthma, the most common paediatric chronic respiratory disease, does not seem to be a risk factor for COVID-19 infection for children nor adults.[9–11] A recent review on comorbidities associated with severe COVID-19 disease in children showed a prevalence of 10% of asthma in these patients which is similar to the prevalence in the general paediatric population.[12] In a systematic review by Castro-Rodriguez et al, only two studies specifically examined asthma as a possible risk factor for COVID-19 infection in children and both did not show an association with mortality nor severity.[13] The association between asthma and severe COVID-19 in adults also remains a subject of controversy with multiple studies advocating for[14,15] or against[16–19] asthma as a risk factor. Conversely, chronic obstructive pulmonary disease in adults seem to confer an increased risk of severe COVID-19.[4]

Data on the impact of COVID-19 on lung function is scarce. Amat et al reported 46 cases of COVID-19 in children with asthma attending an outpatient paediatric respiratory rehabilitation center in France. Half of the patients were asymptomatic during the infection. FEV_1 at 1 month post-COVID showed no significant change from baseline values, which corroborates with our findings.[20]

We could not find similar studies for children with other underlying pulmonary conditions such as cystic fibrosis or bronchiolitis obliterans. In adults studies not restricting to patients with underlying lung disease, concerns were raised for persistent functional impairment after moderate-to-severe COVID-19 with decreased DLCO at hospital discharge and at 6 months follow-up.[5,21] Similarly, studies on previous coronavirus epidemics have shown that a significant proportion of adults with severe acute respiratory syndrome (SARS) and middle-east respiratory syndrome (MERS) developed pulmonary complications such as lung fibrosis and functional impairment, including decreased DLCO.[22]

Our study presents several limitations. First, by focusing on children who could perform spirometry in a paediatric tertiary care health center, the number of cases included remains small. Furthermore, none of our cases developed severe COVID-19. This may limit the generalizability of the observed results to other populations or those presenting with severe COVID-19. Conversely, the relatively small number of cases identified in our large tertiary care pulmonary clinic could reflect the greater adoption of sanitary measures by our patient population overall. Second, all the presented cases were infected before the emergence of the Omicron SARS-CoV-2 variant, which appeared durably in Quebec around the end of November 2021. Thus, our findings might not be applicable to the population infected by this newer or future variants. Finally, we only report spirometric data. More detailed pulmonary functional testing, such as diffusion capacity or cardiopulmonary exercise testing, could highlight other functional impairments, especially during effort. Nonetheless, such anomaly would probably represent sub-clinical or mild as the majority of our patients were asymptomatic 8 weeks after the infection.

Our observations suggest that children with a variety of underlying chronic pulmonary conditions are not at increased risk for severe COVID-19 disease and most have no or transient pulmonary functional impairment 1–7 months after the infection. While larger studies are needed to validate our findings, these represent reassuring observations for patients, parents, and clinicians on the favourable clinical and functional evolution of these children in the face of COVID-19.

AUTHOR CONTRIBUTIONS

Salim Ramadan: Obtained oral and written consent, collected the data from the subjects' medical charts, analysed and interpreted the collected data, and wrote the manuscript. **The Thanh Diem Nguyen**: Obtained oral consent and corrected the article's draft. **Sophie Laberge**: Obtained oral consent and corrected the article's draft. **Jacques-Edouard Marcotte**: Obtained oral consent and corrected the article's draft. **Zofia Zisman-Colman**: Obtained oral consent and corrected the article's draft. **Sze Man Tse**: Obtained oral consent, interpreted the data, participated in the writing of the manuscript, and corrected the article's draft. All authors read and approved the final manuscript.

CONFLICT OF INTEREST

None declared.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

ETHICS STATEMENT

After consultation of our local ethics committee, as this case series is a retrospective analysis of data that were already collected for usual follow-up with no specific intervention, no ethics approval was necessary. However, for all of the subjects, written consent to participate was obtained from parents and/or children aged 14 years old or more. After an "in person" or telephone conversation with parents and/or children aged 14 years old, a form with detailed information about the study was given or sent by e-mail to the parents and/or child. After written signature/e-signature and validation of consent to participate, that form was integrated to the child's computerized file.

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