Original Article

Isolated rhinorrhea in the presentation of SARS-CoV-2 infection among preschool- versus school-aged children

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ABSTRACT

Objectives: Rapid identification and isolation of SARS-CoV-2 cases are priorities in school and child care settings to prevent further outbreaks. The objective of this study was to compare the clinical presentation of SARS-CoV-2 infections among preschool (<5 years) versus school-aged (\geq 5 years) children diagnosed with SARS-CoV-2 infection, and, specifically, the probability of presenting with an isolated symptom, such rhinorrhea or sore throat.

Methods: Retrospective study of children (\leq 18 years of age) diagnosed with SARS-CoV-2 in the outpatient COVID-19 clinic or the Emergency Department at the Centre Hospitalier Universitaire Sainte-Justine (Montreal, Quebec, Canada) February through May 2020.

Results: Of 3,789 children tested, 105 (3%) were positive for SARS-CoV-2, and 104 included in the analysis (n=49 age <5 years and n=55 age \geq 5 years). While fever was the most common presenting symptom across both age groups, in the absence of fever, the presence of a combination of two or more symptoms identified the majority (92%) of cases. Isolated single symptom presentations were uncommon (<5% of cases). Most importantly, not a single child in either age group presented with isolated rhinorrhea or sore throat.

Conclusions: While there are differences in the clinical manifestations of COVID-19 in preschool- versus school-aged children, in both age groups, isolated rhinorrhea was not a manifestation of SARS-CoV-2 infection. These results could help further guide testing criteria and exclusion criteria in child care and school settings.

Keywords: Clinical manifestations; Paediatric; SARS-CoV-2; Rhinorrhea; Testing criteria.

As Canada grapples with its fourth wave of the SARS-CoV-2 pandemic, paediatric patients (0 to 19 years old) represent a significantly higher proportion of cases across the country (1). Although children have a lower risk of infection than do adults and seem to be infrequently the index case, there is evidence that they can contribute to household and community transmission (2-4). Rapid identification and isolation of cases are therefore priorities in school and child care settings to prevent further outbreaks (5).

While it is now widely acknowledged that symptomatic children most frequently present with fever and cough, generally experience a milder disease course, and have a drastically lower mortality risk than do adults (6–10), there remains little data on age-specific characteristics of mild infection and the predictive value of isolated, mild, common paediatric symptoms such as rhinorrhea (6,11,12). As a result, local guidelines differ regarding paediatric testing and isolation criteria (13–15), with frequent school and child care exclusions for nonspecific

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With the rise of other viral respiratory pathogens known to cause rhinorrhea (18), understanding specific symptoms of SARS-CoV-2 may help provide greater evidence for testing and exclusion criteria. The objectives of this study were to compare the clinical presentation of SARS-CoV-2 infections among preschool- (<5 years) versus school-aged (\geq 5 years) children and, specifically, to determine the probability of presenting with an isolated symptom, such as rhinorrhea.

METHODS

This was a retrospective cohort study of all children of less than 18 years of age diagnosed with SARS-CoV-2 infection at the Centre Hospitalier Universitaire Sainte-Justine (CHU-SJ) March 8, 2020 through May 31, 2020. The study was approved by the CHU-SJ research ethics board. Children were tested using SARS-CoV-2 RNA real-time reverse transcriptase–polymerase chain reaction on nasophayngeal swabs; diagnostic testing indications followed Quebec public health guidelines. From March 8 to March 20, 2020, only children with symptoms of fever and cough returning from travel outside of Canada were tested. From March 21 onwards, any child with fever, or with a known COVID-19 exposure, or requiring hospitalization, elective surgery, or any aerosol generating procedure, was also tested. The study was conducted before the local emergence of variants of concern.

Baseline demographics, epidemiological risk factors, presenting symptoms, and clinical outcomes were extracted manually from the electronic chart. Data for preschool- (age <5 years) and school-aged (age \geq 5 years) children were compared via the Wilcoxon rank sum or Fisher exact test where appropriate, using a two-sided α level, with a P value<0.05 considered statistically significant. Symptoms were grouped by system, and specific individual symptoms within the upper respiratory and gastrointestinal symptom groups compared as the primary outcomes of interest. Statistical analysis was performed using Stata v.12.1 (StataCorp LLC).

RESULTS

A total of 3,789 children were tested for SARS-CoV-2 at CHU-SJ during the study period, of whom 105 (3%) were positive. One case was excluded for missing data. Epidemiological and clinical characteristics of the 104 children included in the analysis are shown in Table 1.

Cases were equally distributed between both age groups (47% versus 53% in <5 versus \geq 5 years of age) and sex categories (51% versus 55% female in <5 versus \geq 5 years of age). Twothirds (66%) of children were diagnosed through the ED, and one-third (34%) through the outpatient COVID-19 clinic. Indications for testing included a known contact (49%), symptomatic patients with a travel history outside of Canada (7%) or symptoms only (39%), with only 4% diagnosed in the absence of symptoms through pre-procedure screening. The majority of children (63%) had a known contact, and this proportion was significantly higher in school-aged versus preschool-aged children (76% versus 43%, P<0.01).

Clinical signs and symptoms

The most common presenting symptom was fever (70%), followed by systemic symptoms (54%), gastrointestinal symptoms (48%), lower respiratory tract symptoms (45%), and upper respiratory tract symptoms (37%) (Table 1). Overall, 92% of children had either fever, or in the absence of fever, a combination of two or more individual symptoms (including two symptoms from the same system category, i.e., vomiting and diarrhea). Among the eight (8%) children who were afebrile and with less than two symptoms, five (6%) were asymptomatic, one (1%) had isolated vomiting, one (1%) isolated cough, and one (1%) isolated neurological symptoms (vertigo and ataxia). None presented with isolated rhinorrhea or sore throat.

Overall, younger children were more likely to have fever at presentation than older children (84% versus 58%, P=0.02), while older children were more likely to present with systemic symptoms (64% versus 48%, P=0.03), upper respiratory tract symptoms (49% versus 22%, P=0.008), and abdominal pain (20% versus 6%, P=0.006). Nonrespiratory bacterial co-infections were common (13% of all cases) and more frequent in younger children (22% versus 4%, P=0.006). These co-infections included urinary tract infection (n=8), otitis media (n=2), cervical adenitis (n=1), Group A streptococcus pharyngitis (n=1), and a branchial cleft cyst infection (n=1). Finally, there was a higher proportion of mild disease (no hospitalization or return/follow-up visit) among older children versus younger children (65% versus 39%, P<0.001), with a higher proportion of the younger children being scheduled for a follow-up in the outpatient clinic within a month of diagnosis (12% versus 5%, P=0.01).

DISCUSSION

In this study, we describe the clinical manifestations of SARS-CoV-2 infection in preschool- versus school-aged children with the aim of better understanding when to suspect SARS-CoV-2 in these different age groups. Overall, single symptom presentations of SARS-CoV-2 infection were rare (<5% of all cases), and no child presented with isolated rhinorrhea or sore throat. Perhaps most importantly, fever or a combination of two or more individual symptoms (other than fever) identified the majority (92%) of cases. These results suggest that in the absence of fever, isolated symptoms, notably rhinorrhea, were not a primary manifestation of SARS-CoV-2 infection in children. These findings mirror adult data showing that isolated rhinorrhea and sore throat are rarely associated with a positive SARS-CoV-2 nasopharyngeal swab (19,20).

These findings are consistent with previous studies reporting that children mainly present with fever and mild disease (6–10). Fever was the most common symptom across both age groups, followed by systemic symptoms, gastrointestinal manifestations, lower respiratory tract, and upper respiratory tract symptoms. The incidence of gastrointestinal symptoms was higher than in two paediatric meta-analysis (18% (21) and 23% [22]). Moreover, there were notable age-specific differences in clinical presentation. Fever stood out as the primary manifestation of SARS-CoV-2 infection in younger children, whereas older children presented with a wider constellation of symptoms, including both upper and lower respiratory tract symptoms and systemic manifestations. Of note, the only symptom

Table 1. Epidemiological and clinical characteristics of SARS-CoV-2 infection in children <5 versus ≥5 years of age

	n=104*	Age <5 years n=49 [*]	$\frac{\text{Age} \ge 5 \text{ years}}{n=55^{*}}$	P value [†]
 Demographics				
Age (median, range)	6 years (6 days–18 years)	1 (6 days-5 years)	13 (5–18 years)	NA
Female	55 (53%)	25 (51%)	30 (55%)	0.72
Indications for testing (n=103)				
Travel and symptoms	7 (7%)	1 (2%)	6 (11%)	< 0.001
Symptoms and known contact [§]	51 (50%)	19 (39%)	33 (60%)	
Symptoms only	41 (40%)	29 (59%)	12 (22%)	
Pre-procedure screening	4 (4%)	0	4 (7%)	
Symptoms				
Fever	73 (70%)	41 (84%)	32 (58%)	0.02
Fever or ≥2 symptoms (excluding fever)	96 (92%)	47 (96%)	49 (89%)	0.17
Fever alone	8 (8%)	7 (14%)	1 (2%)	0.02
Systemic (headache, myalgia, or decreased oral intake)	56 (54%)	21 (48%)	35 (64%)	0.03
Systemic alone	0	0	0	NA
Lower respiratory (cough, shortness of breath, wheeze)	47 (45%)	18 (37%)	29 (53%)	0.05
Lower respiratory alone	1 (1%)	0	1 (2%)	1.0
Upper respiratory	38 (37%)	11 (22%)	27 (49%)	0.008
Sore throat	14 (14%)	4 (8%)	10 (18%)	0.38
Rhinorrhea	24 (23%)	7 (14%)	17 (31%)	0.03
Sore throat alone	0	0	0	NA
Rhinorrhea alone	0	0	0	NA
Gastrointestinal	50 (48%)	23 (47%)	27 (49%)	0.83
Abdominal pain	14 (14%)	3 (6%)	11 (20%)	0.006
Vomiting	22 (21%)	12 (25%)	10 (18%)	0.43
Diarrhea	14 (14%)	8 (16%)	6 (11%)	0.44
Gastrointestinal alone	1 (1%)	0	1 (1%)	1.0
Other symptoms				
Ocular	4 (4%)	0	4 (7%)	0.05
Dermatological ⁹	6 (6%)	5 (10%)	1 (2%)	0.22
Anosmia	5 (5%)	0	5 (9%)	0.03
Asymptomatic	5 (5%)	1 (2%)	4 (7%)	0.37
Co-infection [#]	13 (13%)	11 (22%)	2 (4%)	0.006
Outcomes				
Death	0	0	0	NA
Intensive care unit	2 (2%)	1 (2%)	1 (2%)	1.0
Hospitalization ward	16 (15%)	10 (20%)	6 (11%)	0.07
Duration of hospitalization: Median [range] (days)	3 [2-6]	3 [1-4]	7 [3–9]	0.006
Emergency department return visit	16 (15%)	7 (14%)	9 (16%)	0.80
Outpatient clinic follow-up	15 (14%)	12 (24%)	3 (5%)	0.01
No return visit	55 (53%)	19 (39%)	36 (65%)	< 0.001

^{*}Unless specified otherwise in the row header, results in the columns below are presented as 'n (%)';

⁺P<0.05 was considered statistically significant;

*NA, nonapplicable;

[§]A contact was defined as a symptomatic individual or laboratory-confirmed SARS-CoV-2 infection;

Included ocular pain and conjunctivitis;

[¶]Included urticaria, macules, pustules, and petechiae;

*Co-infection diagnosed clinically (otitis media, cervical adenitis, branchial cleft cyst infection) or by a positive bacterial culture (urinary tract infection, pharyngitis);

"No return visit to the emergency department or follow-up at the outpatient clinic after screening positive in the COVID-19 clinic or the emergency department.

category that equally affected both younger and older children was gastrointestinal manifestations, potentially due to SARS-CoV-2 tropism for ACE-2 receptors lining the epithelium of the gastrointestinal tract in children (23). Ocular, dermatological, and neurological symptoms were not common features of infection in this cohort, and only one patient reported neurological symptoms (vertigo) in isolation. Finally, nonrespiratory bacterial co-infections were frequently reported (13% of cases), and may have been the primary cause of symptoms. While a few studies have evaluated the presence of viral co-infections in children, there are little reported data on concurrent urinary tract infections, especially among younger children (24).

Our study is limited by the fact that the study occurred before the emergence of SARS-CoV-2 variants of concern (25), and may therefore not reflect the clinical presentation of these new variants. Moreover, due to its small sample size and its retrospective nature relying on self-reported symptoms, we may have underestimated the prevalence of some symptoms (i.e., anosmia), not recognized early on as manifestations of COVID-19. Finally, given that the indications for testing followed evolving public health guidelines, most of the children included in this cohort were symptomatic from their infection such that we have likely underestimated asymptomatic infections. Based on seroprevalence data obtained following the study period, an estimated 3.3% of Montreal's 850,000 children acquired SARS-CoV-2 infection during the first wave, suggesting that there were many unrecognized infections (26). Nonetheless, whereas the majority of previous studies focused on symptoms among hospitalized patients (27) or report population-level epidemiological data (28,29), one of the main strengths of this study is the detailed information on clinical manifestations and outcomes captured for mildly symptomatic children in Canada.

In summary, our findings suggest that while there are differences in the clinical manifestations of SARS-CoV-2 infection in preschool- versus school-aged children, the majority (92%) of children across both age groups presented with a fever, or a combination of two or more symptoms other than fever. As such, an isolated symptom in the absence of fever is not likely to be a manifestation of SARS-CoV-2 in children. Most importantly, isolated rhinorrhea was not a manifestation of SARS-CoV-2 infection in this cohort. These results could help further guide testing criteria and infection control measures in child care and school settings, though further study among larger paediatric cohorts with the new variants of concern are needed.

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POTENTIAL CONFLICTS OF INTEREST

All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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