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COVID-19 in Children and the Dynamics of Infection in Families

Klara M. Posfay-Barbe, MD¹, Noemie Wagner, MD¹, Magali Gauthey, MD², Dehlia Moussaoui, MD³, Natasha Loevy, MD⁴, Alessandro Diana, MD^{5,6}, Arnaud G. L'Huillier, MD^{1,7}

¹Pediatric Infectious Diseases Unit, Department of Woman, Child and Adolescent Medicine, Geneva University Hospitals and Faculty of Medicine, University of Geneva, Geneva, Switzerland

²Pediatric Department, Hôpital de La Tour, Geneva, Switzerland

³Division of General Pediatrics, Department of Woman, Child and Adolescent Medicine, Geneva University Hospitals and Faculty of Medicine, University of Geneva, Geneva, Switzerland

⁴Pediatric Platform for Clinical Research, Department of Woman, Child and Adolescent Medicine, Geneva University Hospitals and Faculty of Medicine, University of Geneva, Geneva, Switzerland

⁵Lecturer, Primary Care Unit, University of Geneva, Geneva, Switzerland

⁶Clinique des Grangettes, Geneva, Switzerland

⁷Division of Infectious Diseases and Laboratory of Virology, Division of Laboratory Medicine, Geneva University Hospitals and Medical School, Geneva, Switzerland

Corresponding author:

Arnaud G. L'Huillier, MD

Department of Woman, Child and Adolescent Medicine, Geneva University Hospitals and Medical School, Geneva, Switzerland Pediatric Infectious Diseases Unit

6 rue Willy-Donze, 1211 Geneva 14, Switzerland

+41 79 55 31 385; arnaud.lhuillier@hcuge.ch

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Abbreviations:

COVID-19: coronavirus disease; HHC: household contact; IQR: interquartile range; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

Contributors' Statement: Klara Posfay-Barbe, Noemie Wagner and Arnaud G. L'Huillier conceived and designed the study, designed the data collection instruments, coordinated and supervised data collection, carried out the initial analyses, drafted the initial manuscript, and reviewed and revised the manuscript. Magali Gauthey, Dehlia Moussaoui, Natasha Loevy and Alessandro Diana coordinated and supervised data collection, critically reviewed the manuscript for important intellectual content, and reviewed and revised the manuscript. All the authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Introduction

Since the onset of coronavirus disease (COVID-19) pandemic, children have been less affected than adults in terms of severity¹⁻³ and frequency, accounting for <2% of the cases²⁻⁵. Unlike with other viral respiratory infections, children do not seem to be a major vector of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission, with most pediatric cases described inside familial clusters⁶ and no documentation of child-to-child or child-to-adult transmission^{7,8}. The aim of this work was to describe the clinical presentation of the first 40 pediatric cases of COVID-19 in our city and the dynamics of their familial clusters.

Methods

From March 10th to April 10th 2020, all patients <16 years old with SARS-CoV-2 infection were identified by means of the Geneva University Hospital's surveillance network (Switzerland). The network notifies the institution's pediatric infectious diseases specialists about results of nasopharyngeal specimens tested for SARS-CoV-2 by reverse-transcription polymerase-chain-reaction. This study was approved by the Regional Ethics Committee. After informed oral parental consent and its documentation in the medical charts, chart reviews were used to retrieve clinical data and parents were called for patients and household contacts (HHC) follow-up. HHC were considered suspect if they had fever or acute respiratory symptoms, as per the Swiss Federal Office for Public Health's case definition⁹ (Supplementary Methods).

Categorical data were compared using the chi-squared test, with p-values <0.05 considered significant. Statistics were performed using SPSS version 23.0.

Results

Among a total of 4310 SARS-CoV-2 cases, 40 were <16 years old (0.9%). One patient for which telephone follow-up was not possible was excluded because of the inability to evaluate clinical evolution and household contact (HHC) symptoms. The median follow-up of the households was 18 days (interquartile range [IQR] 14-28).

Clinical presentation, diagnosis and management. Demographics, clinical presentation and diagnosis of the study children are detailed in Table 1. Of note, 29 (74%) patients were previously healthy; the most frequently reported comorbidities were asthma (10%), diabetes (8%), obesity (5%), premature birth (5%) and hypertension (3%). Seven patients (18%) were hospitalized to the ward, for a median duration of 3 days (IQR 2-4); reasons for admission were surveillance for non-hypoxemic viral pneumonia (n=2), fever without source (n=2), apparent life-threatening event (n=1), sepsis-like event (n=1) and one paucisymptomatic child admitted because both parents had severe COVID-19 (n=1). No patient required intensive care unit admission or SARS-CoV-2 specific therapies. The others 32 patients were managed as outpatients. All patients had a complete resolution of symptoms by day seven after diagnosis.

Familial clusters. Familial cluster evaluation revealed a t number of four household members per family (IQR 3-4). Among the 111 HHC of study children, mothers predominated (n=39), followed by fathers (n=32), pediatric siblings (n=23), adult siblings (n=8) and grand-parents (n=7) (Figure 1). Adult HHC were suspected or confirmed with COVID-19 prior to the study child in 79% (31/39) of cases. In only 8% (3/39) of households did the study child develop symptoms prior to any other HHC (Figure 1). Interestingly, 85% (75/88) of adult HHC developed symptoms at some point, compared to 43% (10/23) of pediatric HHC (p<0.001). Also, 92% (36/39) of mothers developed symptoms, compared to 75% (24/32) of fathers (p=0.04).

Discussion

Most children in our study had mild or atypical presentations: headache and nasal discharge were described in more than half of cases, and anosmia and abdominal symptoms in more than 20%, which is more frequent than previously described². Some of these symptoms might be underreported because younger children may not be able to describe them.

In 79% of households, at least one adult family member was suspected or confirmed for COVID-19 prior to symptom onset in the study child, confirming that children are infected mainly inside familial clusters⁶. Surprisingly, in 33% of households, symptomatic HHC tested negative despite belonging to a familial cluster with confirmed SARS-CoV-2 cases, suggesting an underreporting of cases. In only 8% of households did a child develop symptoms prior to any other HHC, which is in line with previous data showing that children are index cases in less than 10% of SARS-CoV-2 familial clusters¹⁰; however, our study design cannot confirm that child-to-adult transmission occurred.

This study has some limitations. The study sample likely doesn't represent the total number of pediatric SARS-CoV-2 cases during this time period. Indeed, patients with milder or atypical presentation might not have sought medical attention. Moreover, the recall of symptom onset among HHC might be inaccurate, even though this seems for once less likely due to the confinement measures and anxiety in the community.

The results of this study are important because of the extensive household contact tracing and the almost absence of loss to follow-up. Extended diagnostic screening of suspected cases and thorough contact tracing are needed to better understand the dynamics of transmission within households.

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Table 1. Demographics and clinical presentation of study patients

| | n=39 |
|--|-----------------|
| <u>Demographics</u> | |
| Median age, years (IQR) | 11.1 (5.7-14.5) |
| Female gender, No. (%) | 22 (56) |
| <u>Clinical presentation</u> | |
| <u>Median time between symptom onset and diagnosis, days (IQR)</u> | 2 (1-3) |
| <u>Reported symptoms, No. (%)</u> | |
| Cough | 32 (82) |
| Fever | 26 (67) |
| Nasal discharge | 25 (64) |
| Headache | 22 (56) |
| Sore throat | 14 (36) |
| Shortness of breath | 13 (33) |
| Myalgia | 13 (33) |
| Abdominal pain | 11 (28) |
| Anosmia | 8 (21) |
| Arthralgia | 7 (18) |
| Diarrhea | 7 (18) |
| Fatigue | 5 (13) |
| Rash | 5 (13) |
| Dysgeusia | 4 (10) |
| Nausea | 4 (10) |
| Vomiting | 3 (8) |
| Thoracic pain | 2(5) |
| Conjunctivitis | 1 (3) |
| <u>Diagnosis, No. (%)</u> | |
| Upper respiratory tract infection | 27 (69) |
| Influenza-like illness | 2(5) |
| Fever without source | 2(5) |

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| Pneumonia | 2(5) |
| Obstructive bronchitis | 2(5) |
| Sepsis-like event | 1 (3) |
| Croup | 1 (3) |
| ALTE | 1 (3) |
| Asymptomatic | 1 (3) |

IQR: interquartile range; ALTE: Apparent life-threatening events

Figure 1. Description of individual household clusters with asymptomatic, suspected and confirmed SARS-CoV-2 cases

| Patient → | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 | Total | Symptomatic | | | | |
|---------------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|-------|-------------|---------|---|---------|---------|
| RT-PCR CT value | 16 | 22 | 21 | 22 | 30 | 34 | 34 | 19 | 32 | 33 | 26 | 31 | 16 | 16 | 14 | 17 | 24 | 33 | 16 | 19 | 13 | 28 | 20 | 23 | 24 | 38 | 24 | 32 | 34 | 37 | 34 | 28 | 35 | 32 | 31 | 35 | 36 | 32 | 36 | n | n (%) | | | | |
| Mother | + | | | + | + | - | | | | + | - | | | | | - | + | + | + | + | + | + | + | + | | + | | | - | + | + | | - | + | + | + | - | - | | 39 | 36 (92) | | | | |
| Father | - | | | + | | + | | + | | | + | | | | | + | | | + | + | + | + | + | + | + | | | | | | | | | | | | | + | + | | 32 | 24 (75) | | | |
| Adult Sibling 1 | | | | | | | | | | | | | | | | | + | | | | | | + | + | | | | | | | | | | | | | | | | | | | | | |
| Adult Sibling 2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | 8 | 8 (100) | |
| Grand-Parent 1 | | | | | | | + | | | | | | | | | + | | | | | | | | | | | | | | | | | | | | | | | + | + | | | | | |
| Grand-Parent 2 | | | | | | | | | | | | | | | | + | | | | | | | | | | | | | | | | | | | | | | | | | | | 7 | 5 (71) | |
| Other Adult | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | 2 | 2 (100) | |
| Pediatric Sibling 1 | | | | | - | | | | | - | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Pediatric Sibling 2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Pediatric Sibling 3 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Pediatric Sibling 4 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | 23 | 10 (43) |

Green, yellow and red squares correspond to symptomatic household contacts who developed symptoms respectively, before, simultaneously and after study patients. White squares correspond to asymptomatic household contacts. The “+” and “-” signs correspond to the results of SARS-CoV-2 nasopharyngeal RT-PCR; patients without testing have an empty square. The absence of a family member inside a given household cluster is shown in grey.

The study patient was the first to develop symptoms in clusters #2, #3 and #13 only.

CT values correspond to the number of PCR cycles required to amplify the virus; hence the CT value is inversely proportional to the viral load.

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; RT-PCR: reverse-transcription polymerase chain reaction; CT: cycle threshold.

Supplementary Methods

Study setting. The study was performed while schools, daycares, restaurants, bars and shops were closed. Citizens were allowed to circulate outside their housing in groups of five or less while respecting social distance measures.

RT-PCR testing criteria. For epidemiological purposes and to maximize contact tracing, every patient with respiratory symptoms or fever who came to the hospital was tested for SARS-CoV-2 by RT-PCR, independently of epidemiological links. There was no significant shortage of testing capacity in our institution during this time period. The data and results of household contacts (HHC) RT-PCR testing was available to the study team through the hospital's surveillance network.

Definitions. HHCs were defined as persons living in the same housing as the SARS-CoV-2 RT-PCR positive study patient. HHC were asked whether they developed symptoms before, after or at the same time as the study patient; no minimal threshold was used for this definition.

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