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### Contributor's Statement:

Dr. Rabia Agha conceptualized and designed the study, collected and analyzed the data, drafted the initial manuscript and reviewed and revised the manuscript.

Dr. Tsoline Kojaoghlanian conceptualized and designed the study, collected and analyzed the data, reviewed and revised the manuscript.

Dr. Jeffrey R. Avner critically reviewed the manuscript, assisted in data analysis and revised the manuscript.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

## Abstract

COVID-19 has affected children differently than adults worldwide. Data on the clinical presentation of the infection in children is limited. We present a detailed account of pediatric inpatients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus at our institution during widespread local transmission, aiming to understand disease presentation and outcomes. A retrospective chart review was performed of children, ages 0-18 years, with a positive PCR test for SARS-CoV-2 on nasopharyngeal specimens admitted to our hospital over a four weeks period. We present clinical data from 22 patients and highlight the variability of the presentation. In our study, most children presented without respiratory illness or symptoms suggestive of COVID-19; many were identified only because of universal testing. Since children may have variable signs and symptoms of COVID-19 infection, targeted testing may miss some cases.

## Introduction

Children account for < 5% of the cases of SARS-CoV-2 infections in the United States to date (1,2). While some general epidemiologic data of Coronavirus Disease 2019 (COVID-19) in children has been published (3-6), there is limited reporting of the actual clinical presentation. We present a detailed account of pediatric patients who presented to our institution during the early stages of the COVID-19 pandemic to provide a better understanding of the disease presentation and outcomes in children.

## Methods

A retrospective review was performed of patients, ages 0-18 years old, admitted to our inpatient pediatric service at a children's hospital in Brooklyn, New York from March 18<sup>th</sup> to April 15<sup>th</sup>, 2020 who tested positive by PCR (polymerase chain reaction) for SARS-CoV-2 virus on a nasopharyngeal specimen. Patients were identified using the hospital's daily log that listed all institutional testing results for SARS-CoV-2. Our initial testing strategy was in accordance with CDC guidelines, recommending testing if there were symptoms of fever, cough and shortness of breath, travel to high risk countries or close contact with a confirmed case. As the incidence of infection increased, in the latter half of our study, from March 27<sup>th</sup> onwards, we implemented PCR testing for all admitted patients irrespective of symptomatology. This study was approved by the institutional internal review board (IRB) for expedited review.

## Results

Of the 22 patients who tested positive, 55% were male (Table). Children ranged in age from 11 days to 18 years. Infants under one year of age made up 45% of hospitalizations. No patient had a travel history and 6/22 (27%) had confirmed SARS-CoV-2 exposure. Six patients had underlying co-morbidities (3 with malignancy, 2 with chronic lung disease and one with cardiac disease). The majority of patients 18/22 (82%) were admitted to the hospital within 3 days of symptom onset. No patient died during the study period.

The most common clinical presentation was fever without a source in otherwise healthy infants 5/22 (23%), age range 11-35 days. All 5 patients had a sepsis evaluation including cerebrospinal fluid analysis, received empiric antibiotics and were discharged home once the bacterial cultures were negative within 48-72 hours.

Only 9 (41%) patients presented with a respiratory illness, and 7 (32%) required respiratory support. Four patients needed mechanical ventilation; 2 of these patients had underlying pulmonary disease, a teenager with bronchiectasis and a 1 year old with chronic lung disease due to prematurity. Both progressed within 6-72 hours from high flow oxygen support to intensive care unit admission and intubation. Of the two other patients who required intubation, one had cerebral palsy and status epilepticus and the second child was otherwise healthy and presented in cardiac arrest.

Most patients with respiratory illness were managed with supportive therapy and antibiotics as indicated. However, three patients admitted to the pediatric intensive care unit and on mechanical ventilation qualified for compassionate use of Remdesivir. The drug was only available for patients with documented infection and respiratory deterioration requiring

mechanical ventilation without concomitant liver or kidney disease. All three of the patients treated with Remdesivir were eventually extubated.

Two patients had neurological abnormalities: an 11-year-old healthy boy presented with fever, headache, confusion and seizure. His cerebrospinal fluid (CSF) showed mild pleocytosis (WBC 16, RBC 921) protein 92 mg/dl, glucose 97 mg/dl, the CSF PCR panel was negative and he had an abnormal EEG (diffuse cerebral dysfunction); he improved, without short-term sequelae, within 48 hours. A second patient, a 12-year-old girl with cerebral palsy, developed new onset seizures after several days of fever and cough, requiring mechanical ventilation. She improved to baseline after 18 days in the hospital.

Three patients with malignancies were hospitalized. One presented with mild sore throat and fever, the second was asymptomatic and admitted for routine chemotherapy. The third patient, a teenager, had bilateral pneumonitis and hypoxia and required oxygen therapy for 3 days.

In terms of laboratory abnormalities, lymphopenia was noted in 32%, and an elevated procalcitonin or C-reactive protein were present in the majority of patients in whom the tests were performed. Abnormal chest x-ray findings, with bilateral opacities, were noted in 5/11 patients (Table). Viral co-infection was detected in 2/7 tested for other viruses.

During the second half of the study period, a positive PCR was noted in 7 patients (32%) who were hospitalized for non-COVID related symptoms. Four patients had documented bacterial infections and one was diagnosed with appendicitis (Table). The other two presented with illnesses of unclear etiology. One had inflammation of the forearm muscles with no abscess formation but fever and elevated inflammatory markers, was treated with antibiotics and did well. A third patient, a 6 months old boy, presented after cardiac arrest at home with no known

underlying diseases; his echocardiogram showed severely depressed ventricular function and his chest x-ray at the time of admission was normal.

Two patients were completely asymptomatic at the time of admission but were positive by PCR, one was admitted for social reasons and the other for routine chemotherapy as mentioned above.

## Discussion

In our study, hospitalized pediatric patients with COVID-19 had a wide spectrum of presentation and few displayed the classic respiratory symptoms associated with this disease in the adult population; only 41% of admitted children had respiratory tract illness. These findings differ from the description of the disease in several initial studies out of China where the major presentation was a respiratory illness of varying severity (4-6), but are similar to findings from a more recent meta-analysis (7). Almost half of our cohort was under age 1 year, and half of those were under 6 weeks of age presenting with fever alone, necessitating an evaluation for sepsis. Our findings again show differences between the reports from China, where in one large study of 171 children only 18% were under age 1 year and the median age of presentation was 6.7 years (5).

Our initial testing strategy was according to the federal and local guidelines that recommended PCR testing for the symptoms of fever, cough and shortness of breath, or travel to certain countries or close contact with a confirmed case. With the implementation of our universal screening strategy of all admitted pediatric patients, we identified 9 (41%) patients with COVID-19 that would have been missed, as they did not meet the then-recommended criteria for testing. For the patients admitted with alternate diagnoses it is not clear if and how significant a role

SARS-CoV-2 had in their illness. Two patients presented with encephalitis with no alternative etiology; it is possible that SARS-CoV-2 was the cause in both cases.

Our strategy also led to documenting asymptomatic infection in 2 patients, one of whom was immunocompromised and needed chemotherapy to be postponed based on the test result. Finally, the youngest infant in our cohort, an 11-day-old, was born to a mother who was well and family members were asymptomatic, suggestive of asymptomatic transmission in the home. Only a minority of our patients (28%) had documented confirmed viral exposure, highlighting that the infection rates at a given time in a particular city should drive the strategies of pediatric testing, rather than confirmed contact alone. This finding also is unexpected as several of the reports from China (3-5) describe the vast majority of transmission in children from family clusters.

In conclusion, early experience at our hospital shows that most hospitalized pediatric patients did not present with the classic symptoms attributed to COVID-19 and the majority did not have household exposure to the infection thereby presenting atypically from what is seen in adults and the reported pediatric experience from China. Guidelines to test pediatric patients need to be broadened and take into account that patients presenting with other illnesses may also be positive for COVID-19. Testing of all hospitalized patients will not only identify cases early in the course of their admission process, but will also help prevent inadvertent exposure of other patients and health care workers, assist in cohorting infected patients and aid in conservation of personal protective equipment.



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Table: Characteristics of hospitalized pediatric patients with COVID-19

Characteristic (N=22)	No.	(%)
<b>Sex</b>		
Male	12	55%
Female	10	45%
<b>Age (years)</b>		
Distribution- no. (%)		
< 1	10	45%
1-6	4	18%
7-12	3	14%
13-18	5	23%
<b>Presenting symptoms</b>		
Fever	15	68%
Any respiratory symptom	9	41%
- Difficulty breathing	6	27%
- Nasal Congestion	5	23%
- Cough	4	18%
Fatigue	6	27%
Seizures	2	9%
Headache	1	4%
<b>Duration of symptoms prior to admission (days)</b>		
Asymptomatic	2	9%
< 1	3	14%
1-3	13	59%
> 3 days	4	18%
<b>Known COVID contact</b>		
At home	3	14%
Outside of home	3	14%
None known	16	72%
<b>Underlying medical conditions</b>	<b>6</b>	<b>27%</b>
<b>Other admitting diagnosis and COVID positivity</b>	<b>7</b>	<b>32%</b>
<b>Respiratory support</b>		
Non-invasive Ventilation	3	14%
Mechanical Ventilation	4	18%
None	15	68%
<b>Viral co-infection/Total tested</b>	<b>2/7</b>	<b>29%</b>
<b>Chest x-ray abnormalities/Total imaged</b>	<b>5/11</b>	<b>45%</b>
<b>Laboratory abnormalities/Total tested</b>		
CRP >1mg/L	8/10	80%*
Procalcitonin > 0.5ng/ml	6/7	86%**
Absolute lymphocytes < 1500/uL	7/22	32%
Transaminitis	2/7	29%
<b>Note:</b>		
<b>*4/8 with co-diagnoses</b>		
<b>**3/7 with underlying medical condition</b>		

**Underlying medical conditions:** Malignancy -3, Bronchiectasis -1, Cardiac (PDA-closed VSD) -1, Prematurity/chronic lung disease -1

**Other admitting diagnosis:** 1 each of Perforated appendix, urinary tract infection, cellulitis, septic arthritis, cardiac arrest, purulent otorrhea, myositis. **Patient also tested positive for SARS-CoV-2**

**Viral co-infection:** Both positive for entero/rhinovirus

**Respiratory support (Non-invasive ventilation)-** includes nasal canula, high flow oxygen, BiPAP

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