

COVID-19: A UK Children's Hospital Experience

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OBJECTIVES: Reports from China relating to coronavirus disease (COVID-19) in children indicate a milder disease course compared with adults. Although a few pediatric COVID-19 reports from other parts of the world exist, there are none from the United Kingdom. We describe the clinical characteristics of children with COVID-19 admitted to a specialist children's hospital in United Kingdom.

METHODS: Retrospective case-series of inpatients with a positive polymerase chain reaction test for severe acute respiratory syndrome coronavirus 2, during a 6-week period from March 14 to April 24, 2020.

RESULTS: Forty-five children tested positive for severe acute respiratory syndrome coronavirus 2 during the study period. Median (interquartile range) age was 3.5 (0.7–12) years, and 31 (69%) were male. Children with comorbidities constituted 64% (29 of 45) of the study population, including 44% (20 of 45) who were considered “extremely vulnerable.” Fever (67%) and cough (55%) were the most common symptoms. High C-reactive protein (>10 mg/L) was observed in 68% (19 of 28). Lymphopenia (<1.2 × 10⁹/L) was observed in 23% (9 of 40) of children, but it was related to coexisting medical conditions in 6 children. Nine children required supplemental oxygen, two of whom received high-flow nasal cannula oxygen; one needed noninvasive ventilation and one child required invasive mechanical ventilation. Median length of stay of children with an admission outcome (*n* = 42, 93%) was 3 (2–7) days. There were no COVID-19-related deaths.

CONCLUSIONS: COVID-19 had a relatively mild course of illness in majority of the hospitalized children that included a subgroup of vulnerable children with significant comorbidities. Confirmation of this in larger nationwide studies of children is required.

ABSTRACT

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Deidentified individual participant data will not be made available.

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Coronavirus disease 2019 (COVID-19) due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus was declared a pandemic in March 2020.¹ Since then, COVID-19 has affected >3 million people worldwide and has been associated with >200 000 deaths worldwide.² Recent COVID-19 literature from China, including a pediatric systematic review, revealed that many children experienced a milder course of illness and better prognosis than adults.^{3,4} The review highlighted the lack of clinical or epidemiological data in children from Europe and America. There have been a few subsequent publications but no pediatric data from the United Kingdom,⁵⁻⁸ one of the worst affected countries worldwide with >25 000 fatalities.²

We describe clinical characteristics of children with COVID-19 admitted to a large regional specialist children's hospital in the West Midlands, United Kingdom. The hospital provides tertiary and quaternary specialist pediatric services, with an emergency department, with ≥ 300 pediatric inpatient beds, including a 31-bedded PICU.

METHODS

We performed a retrospective review of hospital inpatients with a positive test for SARS-CoV-2 during a 6-week period (March 14th–April 24th, 2020). Data related to demographic, clinical, laboratory, and radiologic features were obtained from hospital databases. Institutional research governance approval was obtained for waiver of ethics application, as an observational study using routinely collected data. Criteria for performing SARS-CoV-2 testing evolved during the study period but predominantly required a febrile respiratory illness (ie, temperature $\geq 37.8^{\circ}\text{C}$ and cough, coryza, shortness of breath, hoarseness, wheeze, sneezing, or respiratory distress). Testing criteria subsequently included atypical symptoms (acute abdominal pain, diarrhea, respiratory symptoms or signs without fever), especially in those requiring PICU admission, where the history was unclear or unavailable (eg admission after major trauma or burns), and immunocompromised children. Children

with a previous negative test for SARS-CoV-2 were retested if there was clinical deterioration, unexplained by an alternative diagnosis. In our study, we included children admitted from the community via the emergency department, those transferred from other hospitals, and inpatients admitted for other indications who subsequently developed symptoms meeting the above testing criteria. SARS-CoV-2 testing was performed by using real-time reverse transcriptase polymerase chain reaction from an upper airway sample (eg, combined nose and throat swabs) but occasionally from the lower respiratory tract via tracheal aspiration, if intubated. Other investigations and clinical management were performed as per relevant clinicians' discretion. Those children categorized as "extremely vulnerable" met the Public Health England UK criteria.⁹ Briefly, this includes children with various malignancies receiving chemotherapy, immunotherapy, or radiotherapy; children with recent stem cell transplant; children with respiratory conditions (eg, cystic fibrosis, severe asthma); children with rare diseases including inborn errors of metabolism; and children receiving immunosuppressive medications.⁹ Data about other underlying chronic medical conditions (eg, cerebral palsy, Down syndrome) were also recorded. Data analyses was performed by using Microsoft Excel (Microsoft Corporation, Redmond, WA), and results are presented as numbers (percentages) or median (interquartile ranges [IQRs]) as appropriate.

RESULTS

Forty-five of the 389 (12%) children tested were positive for SARS-CoV-2 antigen during the study period. Thirty-one (69%) were male. The median age of the children with COVID-19 was 3.5 (IQR: 0.7–12) years; 15 (33%) were infants (<1 year), and 14 (31%) were aged ≥ 10 years. Of those with known ethnicity data ($n = 39$): 41% were white, 28% were Asian, 13% were black, and 18% belonged to other ethnicities. Twenty-three (50%) children tested positive for SARS-CoV-2 during the third week of the study period. Clinical features of the cohort are described

in Table 1. All 3 children presenting with seizures had a previous seizure history (1 with confirmed epilepsy) and recovered rapidly with no residual neurologic deficits. A total of 64% (29 of 45) of the children in this study had at least one preexisting chronic medical condition, with 44% (20 of 45) meeting the "extremely vulnerable" Public Health England definition.

High C-reactive protein (CRP; >10 mg/L) in 68% (19 of 28) and lymphopenia ($<1.2 \times 10^9/\text{L}$) in 23% (9 of 40) were found in those children having the test performed. Of these, 8 children with elevated CRP had either coinfections, sickle cell crisis, or a recent operation or procedure, whereas 6 children with lymphopenia had malignancy-related bone marrow suppression. When children with other causes mentioned above were removed, a high CRP was observed in 55% (11 of 20) and lymphopenia was observed in 9% (3 of 34).

None of the 45 children had features of multisystem hyperinflammation or Kawasaki disease, hypotension, or shock. No specific COVID-19 drug treatments, such as immunomodulators or antiviral agents, were used in any of the study population. Three children (including 2 infants), 2 of whom had comorbidities, required high-flow nasal cannula oxygen ($n = 2$) or noninvasive continuous positive airway pressure (CPAP) ($n = 1$). One infant, with preexisting congenital heart disease, required PICU admission for invasive mechanical ventilation.

Forty-two of the 45 patients (93%) were discharged alive, and the 3 remaining hospital inpatients are there for treatment of underlying comorbidity rather than COVID-19. Median length of stay of children with an admission outcome was 3 (IQR: 2–7) days. There were no COVID-19–related deaths.

DISCUSSION

With our data, we describe a relatively mild course of COVID-19 in the vast majority of pediatric hospital inpatients. Only 20% required supplemental oxygen, and only 2 children needed any form of mechanical ventilation. Our study cohort included 44% of children within the high-risk category,

TABLE 1 Clinical Characteristics of COVID-19 in Children

Clinical Characteristics	No. (%) or Median (IQR)
Symptoms at presentation, ^a <i>n</i> (%)	
Fever	30 (67)
Cough	25 (55)
Shortness of breath	15 (33)
Gastrointestinal symptoms	13 (29)
Seizure	3 (7)
Comorbidities, ^a <i>n</i> (%)	
Hematology or oncology	10 (22)
Chromosomal or genetic disorder	9 (20)
Respiratory	6 (13)
Cardiac	4 (9)
Neurologic	4 (9)
Renal	3 (7)
Inherited metabolic disorders	1 (2)
None	16 (36)
Investigations, median (IQR)	
CRP (<i>n</i> = 28), mg/L	41.5 (2–70)
CRP (<i>n</i> = 20, excluding children with coexisting conditions), mg/L	15.5 (1–50)
Lymphocytes (<i>n</i> = 40), × 10 ⁹ /L	2.2 (1.2–4.1)
Lymphocytes (<i>n</i> = 34, excluding children with coexisting conditions), × 10 ⁹ /L	2.5 (1.6–4.8)
Chest radiograph findings (<i>n</i> = 18), <i>n</i> (%)	
Perihilar bronchial wall thickening	5 (28)
Consolidation	3 (17)
Lobar collapse	2 (11)
Respiratory support, <i>n</i> (%)	
Any supplemental oxygen	9 (20)
High-flow oxygen therapy or CPAP	3 (7)
Invasive ventilation	1 (2)

^a Children may have had multiple symptoms and/or comorbidities.

seizures) may be unrelated to COVID-19. Only 41% were white, consistent with local authority ethnicity data.¹⁴

Lymphopenia was observed in 23%, comparable to the 3.5% to 31% reported elsewhere.^{10,11} We observed elevated CRP >10 mg/L in 68%, compared with 10% to 20% in other studies,^{10,11} and although researchers of 1 study have reported ≤35% of children with elevated CRP, this used a lower CRP cutoff (>3 mg/L).¹³ Some of our study population had preexisting chronic medical conditions that potentially invalidate direct comparisons of these blood tests. After children with coexisting conditions were excluded, median CRP was only 15 (IQR: 1–50) mg/L. Moreover, only 40 of 45 had lymphocytes measured and 28 of 45 children had a CRP measurement, which may also reflect selection bias. Similarly, only 40% of children had a radiologic investigation, with most chest radiograph findings nonspecific and concurring with other similar reports.⁸ Median length of stay in this study was significantly lower than the reported mean of 12.9 days; however, discharge criteria may not be comparable, and the mean may have been skewed by a small number of long-stay patients.¹³

It is noteworthy that although only one child in our study population required intensive care support, during the same study period, >800 adults required ICU admission in the same region, demonstrating the difference in illness severity between adults and children.¹⁵

This is a retrospective report with specific inclusion criteria of pediatric inpatients positive for SARS-CoV-2 at a single UK children's hospital. Therefore, our findings are not necessarily generalizable or representative of pediatric COVID-19 in the community or, indeed, in nonspecialist hospitals. Given the relatively narrow testing criteria, asymptomatic children and children with atypical signs and symptoms may undoubtedly have been missed. We did not undertake contact tracing or ascertain the epidemiology of acquisition of COVID-19 in our study population. Nonetheless, this report represents the early experience of the clinical spectrum of COVID-19 in a

and it is reassuring that no children within this group had severe COVID-19 illness requiring PICU admission for either ventilatory or vasopressor support. The clinical course in those with underlying chronic medical conditions was similar to those without any underlying chronic medical condition, namely a mild, self-limiting illness and a short COVID-19-related inpatient stay.

Children aged 1 month to 17 years were represented in this study, as with other large-scale epidemiological studies from China, the United States, and Italy.^{3,6,8} It is reported that younger infants may be more at risk for severe illness.³ Although this current report is limited by the small

numbers of children with severe illness requiring respiratory support, 3 of the 4 requiring either high-flow nasal cannula, CPAP, or invasive ventilation were infants <1 year. In this study, 67% of children were febrile and 55% had cough, but this may reflect the testing criteria for SARS-CoV-2 in the hospital rather than the true symptomatic prevalence among children with COVID-19. Reports from China and the United States, where testing criteria included asymptomatic contacts, show 36% to 60% of children with fever and 19% to 65% had cough.^{6,8,10–13} It is possible that some children in our series could be asymptomatic carriers of SARS-CoV-2 and that their presenting symptoms (eg

pediatric cohort including complex and high-risk patients at a stand-alone children's hospital with multiple subspecialties. This is the first UK report of its kind, and although the sample size is modest, there is only one other larger cohort in the COVID-19 systematic review in children.⁴

CONCLUSIONS

We observed a relatively mild course of illness in the majority of children with COVID-19, including in those with significant comorbidities and those considered clinically extremely vulnerable. The clinical course was unaffected, despite relatively higher numbers of patients with an elevated CRP level. Most patients had prompt improvement in clinical signs and symptoms as reflected by the relatively short hospital inpatient stay. Further large-scale nationwide clinical characterization studies on COVID-19 are underway and will hopefully shed more light on this emerging illness.

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