# Pediatric Critical Care and COVID-19

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Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2, disproportionally affects adults (children <5% in most reports).[1] Adult critical illness is characterized by acute hypoxemia, multiorgan failure, and high mortality.[2,3] Reported risk factors for severe illness include age, cardiorespiratory comorbidities, obesity, and laboratory findings (lymphopenia and elevated D-dimer).[2,4] Pediatric reports describe low infection rates and infrequent PICU admission.[5,6] The largest PICU report consists of 48 North American children.[7] It describes treatments and outcomes but not with adequate granularity to understand critical pediatric COVID-19. The Critical Coronavirus and Kids Epidemiology Study was designed to specifically investigate severe cases and provide detailed data. It involves >60 centers in nearly 20 countries from the Americas and Europe. In this report, we provide preliminary insights into our first 17 patients.

## METHODS

The Critical Coronavirus and Kids Epidemiology is a cohort study of children <19 years old with severe or critical COVID-19. The study period runs from April through December 2020. For this report, we included patients enrolled through April 23.

We defined critical COVID-19 as a positive severe acute respiratory syndrome coronavirus 2 test result and requiring ICU therapies (high-flow nasal cannula [HFNC], noninvasive ventilation [NIV], invasive mechanical ventilation [IMV], vasoactive support, continuous renal replacement therapy). Severe COVID-19 included those receiving mask or nasal oxygen exceeding the pediatric acute respiratory distress syndrome (ARDS) "at risk" threshold.[8]

Deidentified data were collected by using a modification of the International Severe Acute Respiratory and Emerging Infection Consortium form (https://isaric.tghn.org/COVID-19-CRF/). Local ethics approval was obtained with a waiver of need for consent.

## RESULTS

We enrolled 17 children from 10 PICUs in Chile, Colombia, Italy, Spain, and the United States. Detailed data are in the Supplemental Information. Most patients were male (65%), young (median 4 years; range 0.08–18 years), and without known COVID-19 exposure (14 of 17). Comorbidities (Table 1, Supplemental Table 3) were common (71%) but variable. Symptoms were heterogenous, with fever and cough being most frequent (Table 1, Supplemental Table 3). Most with gastrointestinal (GI) symptoms (4 of 6) were also diagnosed with myocarditis (Supplemental Table 4). All these were from Europe and without previous cardiovascular disease.

Patients had frequent laboratory testing (Table 1, Supplemental Table 5). Common findings included leukocytosis, lymphopenia, elevated inflammatory markers, D-dimer, and

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troponin I. Four had viral or bacterial respiratory coinfection.

Most subjects required respiratory support (Table 2, Supplemental Table 6), with nearly half requiring IMV. Five initially treated with HFNC needed no escalation; 2 were intubated. One initially treated with NIV was intubated. Pulmonary-specific adjuncts were uncommon. Most patients received antibiotics; fewer received antiviral agents (Table 2, Supplemental Table 6). Corticosteroids, hydroxychloroquine, and tocilizumab were each prescribed to nearly half. Intravenous immunoglobulin (IVIg) was prescribed exclusively for myocarditis.

Pneumonia and ARDS were common diagnoses (Table 2, Supplemental Table 6). Vasoactive infusions were frequent, including 3 of 4 with myocarditis. Other organ support or complications were uncommon. Outcomes (minimum 3 weeks data) are shown in Table 2 and Supplemental Table 6. As of submission, 3 patients remained hospitalized, 1 remained in the ICU, and 1 died.

## DISCUSSION

Our description exclusively about critical pediatric COVID-19 reveals an uncommon (17 patients, 60 centers) but heterogeneous disease. Children frequently had GI rather than respiratory symptoms after a brief illness and recovered quickly despite significant support. We found regional variability of diagnoses (myocarditis in Europe), treatments (remdesivir in North America), and age.

Our findings parallel recent studies describing frequent comorbidities but a short PICU stay and low mortality, contrasting with adults.[2,3,6,7] Compared to the North American series, our study was international, younger, included only severe disease, and revealed a wider range of common symptoms.[7] We also provide critical COVID-19 laboratory findings.

**TABLE 1** Demographics, Presenting Symptoms, and Selected Laboratory Findings

| Characteristic | Result |
|---|---|
| Days of symptoms preadmission, median (IQR) | 3.5 (2–5.8) |
| Days of symptoms before positive test, median (IQR) | 3.5 (2–6.8) |
| Comorbidities[a] | |
| None | 5 (29) |
| Respiratory | 1 (6) |
| Cardiac | 2 (12) |
| Cancer and/or immune | 2 (12) |
| Obesity | 2 (12) |
| Other[b] | 8 (47) |
| Symptoms at admission[a] | |
| Fever | 13 (76) |
| Cough | 9 (53) |
| Dyspnea | 6 (35) |
| Congestion | 6 (35) |
| GI | 6 (35) |
| Other | 5 (29) |
| Laboratory value on admission | |
| Leukocytosis, WBC count >11 000 per μL | 9 (53) |
| Elevated D-dimer >0.5 mg/μL | 7 (41) |
| Procalcitonin >2 ng/mL, at admission | 6 (35) |
| C-reactive protein >2 mg/L, at admission | 13 (76) |
| Laboratory value ever during hospitalization | |
| Leukocytosis | 12 (71) |
| Lymphopenia <1000 per μL | 8 (47) |
| Elevated D-dimer | 9 (53) |
| Ferritin >200 ng/mL | 7 (41) |
| Troponin I >1 ng/mL | 4 (25) |

Results are presented as *n* (%) unless otherwise noted. IQR, interquartile range; WBC, white blood cell.

[a] Total adds up to >100% because some had >1 comorbidity or symptom.

[b] Includes chronic GI disorders (3), chronic neurologic disorders (2), prematurity (1), trisomy 21 (1), and tracheomalacia (1).

**TABLE 2** ICU Therapies and Medications

| Treatment | Result |
|---|---|
| Respiratory support[a] | |
| None | 3 (18) |
| HFNC | 7 (41) |
| NIV | 4 (24) |
| IMV | 8 (47) |
| Vasoactive infusion | 9 (53) |
| Respiratory adjuncts[b] | 1 (6) |
| Medications | |
| Antibiotics | 15 (88) |
| Remdesivir | 4 (24) |
| Lopinavir and/or ritonavir | 1 (6) |
| Corticosteroids | 9 (53) |
| Tocilizumab | 7 (41) |
| Hydroxychloroquine | 8 (47) |
| Diagnosis and/or complication | |
| Pneumonia | 13 (76) |
| ARDS[c] | 8; 2 mild, 1 moderate, 3 severe (47) |
| Myocarditis | 4 (24) |
| Cardiac arrest | 3 (18) |
| AKI | 3 (18) |
| Outcome | |
| Died | 1 (6) |
| MV duration, d, median (IQR) | 6 (4–11) |
| ICU LOS, d, median (IQR) | 5.5 (4.3–8.5) |
| Hospital LOS, d, median (IQR) | 13 (6.8–15) |

Data are expressed as *n* (%) unless otherwise noted. AKI, acute kidney injury; IQR, interquartile range; LOS, length of stay; MV, mechanical ventilation.

[a] Percentage adds up to >100 because some patients received >1 modality.

[b] Includes inhaled nitric oxide, prone positioning, and neuromuscular blockade.

[c] Two were supported with NIV, so we were unable to classify severity.

We found that 3 children had peri-intubation arrest, markedly higher than expected.[9] At least 1 resulted from unfamiliar protective equipment and intubation processes. Clinicians must consider the risks before intubating these children. Pediatric COVID-19 myocarditis has not been previously reported, although adult cases are described.[10] It is unclear why myocarditis was only identified in Europe, but pediatric clinicians should consider cardiac involvement, particularly in those with the GI complaints common in our myocarditis patients.

This is a small case series and should be used to generate hypotheses for research rather than informing current treatment. Regional variations may limit our ability to identify outcome associations but do reveal regional differences. Finally, others use different definitions for COVID-19 severity, but their subjectivity could lead to patient misclassification.[6] Our definitions are simple, objective, and reflect clinically relevant distinctions.

## CONCLUSIONS

We provide early clinical and laboratory data about critical pediatric COVID-19, which suggest a variable disease but generally good outcomes compared with adults. Targets for research include the course of organ failure in pediatric critical COVID-19, laboratory findings for predicting illness course or complications, the inflammatory response and its role in pathophysiology, best treatments, and specific organ involvement, such as myocarditis.


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## ABBREVIATIONS

ARDS: acute respiratory distress syndrome
COVID-19: coronavirus disease 2019
GI: gastrointestinal
HFNC: high-flow nasal cannula
IMV: invasive mechanical ventilation
IVIg: intravenous immunoglobulin
NIV: noninvasive ventilation


Drs González-Dambrauskas and Vásquez-Hoyos designed the study, oversaw data collection and analysis, and participated in drafting and editing the manuscript; Dr Karsies designed the study, supervised data collection and analysis, conducted statistical analysis, and participated in drafting and editing the manuscript; Dr Shein designed the study, participated in data analysis and interpretation, and participated in drafting and editing the manuscript; Drs Camporesi, Díaz-Rubio, Piñeres-Olave, Fernández-Sarmiento, Gertz, Harwayne-Gidansky, Pietroboni, Urbano, Wegner, and Zemanate participated in creation of the study concept and data interpretation and were involved in data acquisition and drafting and editing the manuscript; and all authors had final approval of the manuscript, approved the final manuscript as submitted, and agree to be accountable for all aspects of the work.

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