Critically ill children in paediatric intensive care unit are no less susceptible to infectious diseases amid the COVID-19 pandemic

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With the lifting of various measures intended to limit the spread of coronavirus disease 2019 (COVID-19), paediatric cases have been on the rise, with approximately 2% to 6% of those infected becoming critically ill.[1-6] During the early phase of the pandemic, a review of 2135 paediatric cases in China revealed the proportion of severe and critical illness to be higher in the younger age-group, in particular infants.[5] In a separate report by the United States Centers for Disease Control and Prevention, 62% of those aged <1 year were hospitalised compared with 4.1% to 14% among those aged 1 to 17 years.[6] However as the pandemic evolves, the epidemiology seems to have changed and COVID-19 is now affecting older children more severely. In the latest report from the United States, critically ill children with COVID-19 were predominantly adolescents, had co-morbidities, and required some form of respiratory support.[7] In many cases, the presence of acute respiratory distress syndrome was associated with prolonged paediatric intensive care (PICU) and hospital stay.[8]

Recently there has been an emergence of paediatric hyperinflammatory and shock syndromes including paediatric inflammatory multisystem syndrome (PIMS), MIS-C (multisystem inflammatory syndrome in children), and PIMS-TS (paediatric inflammatory multisystem syndrome temporally associated with severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]).[9,10] These are systemic diseases involving persistent fever, inflammation and organ dysfunction associated with SARS-CoV-2; 80% of the patients with this new disease entity require intensive care support with a 2% fatality rate.[3,11-13] Furthermore, COVID-19 is associated with dysfunction across many organ systems as in PIMS as well as syndromes such as COVID stress syndrome and COVID toe syndrome.[14]

Unlike other respiratory viruses such as influenza and respiratory syncytial virus, there has fortunately been no paediatric mortality due to COVID-19 in Hong Kong. We reviewed all admissions to the Hong Kong Children's Hospital PICU with nasal pharyngeal swab/aspiration for SARS-CoV-2 between 1 February and 6 September 2020, and found that 22 (16.3%) of our admitted patients were tested and they were all negative for COVID-19 (Table 1). During the early stages of the COVID-19 epidemic in Hong Kong, screening for COVID-19 was not universal for all PICU admissions; only patients meeting set criteria were screened, primarily in-patients, patients acutely admitted, or patients transferred in who had not already been tested. Patients who had been tested negative elsewhere or in-patients with no exposure were not tested in the initial phase of the pandemic. During the same period, there were 441 (9%) of COVID-19 cases in Hong Kong were aged ≤18 years (Table 2[15]). In addition to SARS-CoV-2, various viral and bacterial pathogens were isolated in these paediatric patients with COVID-19. Viruses isolated include adenovirus, Epstein-Barr virus, and BK virus in blood samples; rhinovirus, enterovirus, and cytomegalovirus in respiratory specimens; and BK virus in urine samples. A wide variety of bacteria were also isolated, including a case of hyperinflammatory hemophagocytic lymphohistiocytosis syndrome due to *Orientia tsutsugamushi* instead of SARS-CoV-2. Compared with paediatric patients with SARS-CoV-2 in the community, viral and bacterial infections were present in 22.7% and 50% of SARS-CoV-2 negative patients in our PICU cohort, respectively (P<0.001). The COVID-19 screening criteria changed as the pandemic evolved and it is now mandatory to screen every patient admitted to the PICU for COVID-19.

In our opinion, it is unlikely that PICUs in

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TABLE 1. Patients admitted to Hong Kong Children's Hospital PICU, 1 February to 6 September 2020*

Total No. of PICU admissions	135
COVID-19 test on PICU admission	22 (16.3%)†
Negative COVID-19 test result	22 (100%)
Age, y	5.6 (1.6-10.2)
Sex, male:female	1:1.2
Fever	13 (59.1)
Lymphopenia	12 (54.5)
Contact history	0 (0)
Travel history	2 (9.1)
Respiratory symptoms	15 (68.2)
Viral infection	5 (22.7)‡
Bacterial infection	11 (50)§
Length of stay, d	7.7 (2.5-15.0)

Abbreviations: COVID-19 = coronavirus disease 2019; PICU = paediatric intensive care unit

* Data are presented as No. (%) or median (interquartile range), unless otherwise noted

† Excluding one COVID-19 test as a patient had two tests in the same episode of illness

‡ Viral infections: blood (adenovirus, Epstein–Barr virus, BK virus); respiratory (rhinovirus/enterovirus, cytomegalovirus); urine (BK virus)

§ Bacterial infections: blood (*Streptococcus mitis*, *Orientia tsutsugamushi*, *Staphylococcus aureus*); respiratory (*Streptococcus pneumonia*, methicillin-resistant *Staphylococcus* aureus, *Acinetobacter calcoaceticus*, *Acinetobacter baumannii* complex, *Stenotrophomonas maltophilia*); stool (*Citrobacter freundii*); soft tissue/body cavity/bone (*Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Escherichia coli*, *Haemophilus influenzae*)

TABLE 2. Cases of coronavirus disease 2019 in Hong Kong (n=4879), 1 February to 6 September 2020[16] *

Paediatric cases (age ≤18 y)	441 (9)
Age, y	11 (5-16)
Sex, male:female	1:0.86
Asymptomatic paediatric cases	190 (43.1)
Symptom onset to report delay, mo	2 (0-5)
Paediatric case imported or related to imported case	201 (45.6)

* Data are presented as No. (%) or median (interquartile range)

Hong Kong have missed any cases of COVID-19. During the pandemic, it is easy to overestimate the prevalence of COVID-19 due to cognitive bias, and assume all patients with fever are infected with COVID-19 until proven otherwise, leading to potential therapeutic errors.[16] However, our observations have concluded that critically ill children are susceptible to contracting a whole host of infectious diseases. Therefore, in addition to screening for COVID-19, physicians must also be vigilant of other pathogens that could affect critically ill children, and duly take antimicrobial and isolation precautions within healthcare environments. It appears that SARS-CoV-2 infection is generally an asymptomatic or very mild disease in children. In contrast, serious viral and bacterial infections are associated with critically ill children tested negative for SARS-CoV-2.

Author contributions

All authors contributed to the concept or design, acquisition of data, analysis or interpretation of data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

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