Pediatric COVID-19: what disease is this?

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The coronavirus disease 2019 (COVID-19) pandemic spares no nations or cities causing escalating incidence and mortality. Royalty, prime ministers, celebrities and high government officials alike have been affected by the disease. For peculiar reasons, children and infants have generally been spared in Hong Kong, China until recently, when returning students from affected cities with the virus who largely presented with mild symptoms. In fact, several countries have reported on pediatric COVID-19.

According to the data gathered by the Centre for Health Protection, as of May 22, there have been 111 confirmed pediatric cases of COVID-19 in Hong Kong, China consisting of 62 males and 49 females, aged between 0 and 18 years old. All cases have been reported to be either mild or asymptomatic, with no pediatric intensive care unit (PICU) admissions and fortunately no deaths [1]. Most of the pediatric cases were imported cases (90%), and the remaining were mostly epidemiologically linked with local/possible local cases (7.2%), followed by those epidemiologically linked with imported cases (1.8%) and local cases (1%). The mean age for the imported cases is much higher than that of the non-imported cases (15.1 versus 6.5 years, \( P < 0.05 \)). When comparing the local proportion of COVID-19 infections in the 0–19 years age group in Hong Kong, China with other countries (most of these countries use 19-years as their upper age limit), the percentage (14.3%) is very high (Table 1). This can be explained by the aforementioned group of overseas students that have been imported to our city. Most of the local imported cases were travelers returning from the UK and the USA [1]. With over 1064 confirmed cases and four deaths, 10.4% of the infected patients were children (\( \leq 18 \) years old). The infection is generally very mild in children, and 39.6% were asymptomatic. This phenomenon is consistent with our experience with SARS 17 years ago, when most of the infected children also had mild clinical manifestations [10, 11]. The Chinese mainland also has reported mortality and morbidity of pediatric COVID-19 cases and has concluded that the disease was generally mild [10, 12]. Mortality is very low in children, and most of the known cases were teenagers [13–16]. Similarly, low mortality and morbidity among children infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or middle east respiratory syndrome coronavirus or SARS-CoV had been observed in the literature [12, 17]. Hence, it is reassuring that children are less likely to be adversely affected by COVID-19. In contrast, mortality appears to be higher in the local adult population at approximately 0.4% and even higher (3.7%) in the US [1, 5, 6].

Reports of children with confirmed COVID-19 in mainland China have described mild cold-like with/without gastrointestinal symptoms and suggest that severe complications (e.g., acute respiratory distress syndrome, septic shock) appear to be uncommon. However, as with other respiratory illnesses, certain populations of children with underlying health conditions may be at increased risk of severe infection. One report stated that the detection of human-CoV alone or in co-infection with rhinovirus-C was independently associated with pediatric intensive care unit admission in young children hospitalized for lower respiratory infection [18].

The virus does not pass from pregnant women to fetuses during pregnancy. It appears that transmission does not include vertical routes, such as amniotic fluid, cord blood, or breast milk [19]. Approved or clinically proven antiviral drugs recommended for COVID-19 in children do not exist. Clinical management includes prompt implementation of recommended infection prevention and control measures in healthcare settings and supportive management of complications [12]. Children should engage in the usual preventive actions to avoid infection, including cleaning hands often using soap and water or alcohol-based hand sanitizer, avoiding contact with others who are sick, and staying up to date on vaccinations, including influenza vaccine.
It is still unclear why coronavirus disease is milder in the pediatric population, similar to other respiratory viral illnesses. Mortality and morbidity of coronavirus disease are postulated to be due to the exaggerated cytokine storm that results in self-destruction of the lung parenchyma and other organ systems [20, 21]. Similar to other respiratory viral diseases, such as the seasonal influenza, two demographic groups seem to have a higher propensity to die from the disease, namely frail elderly people with chronic disease and seemingly healthy adults with exacerbated autoinflammatory responses with cytokine storm syndromes [10, 21, 22]. In contrast, two groups of patients seem to survive epidemics of coronavirus infections with very mild symptoms, namely the children and infants [17]. Our pediatric experience concurs with global data and allows us to reassure anxious parents of the benign nature of coronavirus among children and young people. Nevertheless, from a public health perspective, our current imperative is to contain these imported cases and to prevent onward transmissions, especially from children and young people to the elderly and vulnerable patients with co-morbidities. Coronavirus in mild or asymptomatic adolescent returners, like soldiers in the Trojan Horse, have to be contained. Universal masking, vigilant contact tracing, surveillance programs for testing suspected cases and social distancing are proven effective non-pharmaceutical interventions that are indispensable for containing the epidemic. The global battle against the coronavirus continues.

The latest enigma associated with pediatric COVID-19 is a novel multisystem inflammatory syndrome (MIS) of hyperinflammation resembling toxic shock syndrome, atypical Kawasaki disease (KD) or the Kawasaki disease shock syndrome (KDSS) [23–27]. Another novel acronym, PIM-TS is coined which stands for pediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 [26]. Although controversial, common respiratory viruses including adenovirus, enterovirus, rhinovirus, coronavirus and respiratory syncytial viral have long been reported to be associated with KD. We postulate that SARS-CoV-2 may behave like any respiratory virus that can occasion-ally cause MIS, KDSS or the multi-organ dysfunction syndrome so familiar to the intensivists. Perhaps, we do not need another acronym.

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Table 1 Comparison of COVID-19 cases in the 0–19 years old of different cities/countries

| Variables                                      | Hong Kong, China [1] | Mainland China [2] | Singapore [3] | Korea [4] | USA [5, 6] | Italy [7] | United Kingdom [8] | Spain [9] |
|------------------------------------------------|----------------------|--------------------|---------------|-----------|------------|-----------|---------------------|----------|
| Total COVID-19 cases in the study population   | 1064                 | 72,314b            | 802           | 9037      | 671,485    | 20,686    | 145,808             | 198,863  |
| Infection in the 0–19 y, n (%)                 | 153 (14.3)           | 965 (1.3)b         | 38 (4.7)      | 573 (6.3) | 12,791 (1.9)c| 268 (1.3) | 2365 (1.6)          | 950 (0.5)d|

Demographics and case characteristics

| Age (y), median (IQR)                           | 18 (15–19)           | No data            | 18 (5.8–19)   | No data   | No data    | No data   | No data             | No data |
| Male:female                                     | 1:0.76               | No data            | 1:1.38        | No data   | No data    | No data   | No data             | No data |
| Asymptomatic, n (%)                             | 53 (34.6)            | No data            | No data       | No data   | No data    | No data   | No data             | No data |
| Import, n (%)                                   | 141 (92.2)           | No data            | 27 (71.1)     | No data   | No data    | No data   | No data             | No data |
| Symptoms onset to diagnosis (d), median (IQR)  | 2 (0–5)              | No data            | No data       | No data   | No data    | No data   | No data             | No data |
| Mortality                                       | 0                    | 0                  | 0             | 0         | 3          | 0         | 16                  | 2§       |

COVID-19 coronavirus disease 2019, IQR interquartile range. aPatients up to 19 years old were included as most cities/countries report data with this age range; bInclude suspected COVID-19 cases; cInclude patients < 18 years old only; dInclude patients < 15 years old only.
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