Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Potential dual outbreak of COVID-19 and HFMD among children in Asia-Pacific countries in the HFMD-endemic area

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In the era of the pandemic of coronavirus disease 2019 (COVID-19), the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infects infants and children with mild or atypical symptoms [1,2]. The new variations in SARS-CoV-2 recently found in the United Kingdom greatly increased the risk of infection among children [3]. Although previous evidence showed that children rarely developed severe symptoms from COVID-19, the hospitalization rate was 24.5% and the ICU admission rate was 2.5% among children in the United States [4]. Further, there is a lack of evidence regarding the influence of the recently appeared SARS-CoV-2 variations. Thus, it is of great significance to monitor and track the COVID-19 infection among children.

As of December 22, 2020, a total of 1,006,682 cases had been reported in Western Pacific countries, including 18,895 deaths reported [5]. Evidence showed that COVID-19 targeted strategies as city lockdown and social distancing had made an essential contribution to this disease's constraint and some other communicable diseases, including hand, foot, and mouth disease (HFMD) and influenza, etc. HFMD inflicts harm, most commonly among children under five years old, which has caused 96,900 (40,600–259,000) annual losses on DALYs (number of years lost due to specific disease) in Asian Pacific countries [6].

Although daily numbers of infections have greatly declined, small outbreaks of COVID-19 still happens in Asian countries. The coming season is most alarmingly the peak incidence of HFMD in many Asia-Pacific countries [6]. In light of the growing concern over the consequences of combined HFMD and COVID-19 epidemics, it is of great significance to consider and devise prevention strategies against the two viruses.

Based on the evidence from the outbreaks over the past years, most probably the HFMD cases would increase and develop the similar pattern in the coming season as people returning to work and children returning to school or daycare settings. Although the pandemic of COVID-19 in Asian countries have been brought under control, given the risk of the outbreaks caused by imported cases in Asian Pacific countries in the HFMD-endemic area, it is indispensable to consider the possibility of dual attack of COVID-19 and HFMD in the coming season. We assumed that the outbreak of COVID-19 mainly occurred from January to March, while the previous studies indicated that the HFMD cases substantially increased during February and May [6]. It is highly possible that there may exist the co-infection with SARS-CoV-2 and enterovirus in the spring. Additionally, the COVID-19 and HFMD shared some of the pathways, including respiratory droplets and hands-oral pathway. Further, our previous studies have shown that, the highest incidence of HFMD occur among children aged one year and younger [7]. In China, the reported mean annual severe illness rate was 11.8 (95% CI: 11.7–11.8) per one million person-years, with the yearly mortality rate as 0.308 (95% CI: 0.307–0.310) per one million person-years [8]. HFMD causes a substantial disease burden in young children. During the early stages of the COVID-19 outbreak, children were considered to be rarely infected by SARS-CoV-2 due to the lower exposure [9]. However, the recent new virus variation increased the risk of infection among children [3]. Further, infants and young children develop a relatively more severe illness than older children [10]. Hence it raises concern on treatment and management of children co-infected with enterovirus and SARS-CoV-2. So far, there has no report about co-infection with enterovirus and SARS-CoV-2, dengue virus and SARS-CoV-2 [11], or SARS-CoV-2 and influenza virus [12], alerting us that children may be simultaneously infected with both SARS-CoV-2 and enterovirus, particularly infant and young children who may develop severe symptoms and signs. The proportion of asymptomatic SARS-CoV-2 infection among children reached up to 35%. Children with asymptomatic infection usually have high viral loads of SARS-CoV-2 with prolonged fecal-shedding that causing nosocomial infection or pandemic to happen among the hospitalized severe HFMD cases [13]. Besides, the household transmission is another subject of concern regarding HFMD or COVID-19 infections. It is critical to block this transmission route.

In summary, it is challenging to prevent HFMD during the COVID-19 pandemic. Many healthcare staff has been redistributed to fight for the COVID-19 epidemics, leading to a shortage of public health and medical

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resources. Furthermore, the fear of SARS-CoV-2 infection in the hospital may hinder the early visits to the medical settings, thus increase the severity of the illness. The co-infection of enterovirus and SARS-CoV-2 would be more severe in aggravating the burden of healthcare systems. Other than measures as social distancing with timely treatment, regular cleaning, and disinfection, and prevention of the shared pathways (mask wearing, hands wash, etc.) to prevent HFMD and COVID-19, we also strongly recommend using more accurate, rapid, and accessible diagnostic techniques include real-time reverse transcription-polymerase chain reaction assays to identify SARS-CoV-2 patients with asymptomatic infection at the early stage. Specific guidelines for diagnosing and treating COVID-19 and HFMD co-infection, as well as COVID-19 and influenza con-infection, are expected to be in place soon.Considering the well-control of COVID-19 in some Asia-Pacific countries, it is suggestive for the countries that still under the influence of COVID-19 to consider the risk and prevention of COVID-19 and HFMD infection, as well as that of influenza and COVID-19.

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Conflict of interest statement

The authors declare that there are no conflicts of interest.

Author contributions

Lina Jiang and Jing Wang: Data Curation, Writing - Original Draft. **Bin Yu**: Writing - Review & Editing. **Chuanyi Ning**: Funding Acquisition, Visualization and Supervision. **Yi Tan**: Conceptualization and Validation.

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