Which should we fear more in preschoolers and infants: SARS-CoV-2 or respiratory syncytial virus?

In late December 2019, the first pneumonia cases caused by the novel SARS-CoV-2 were identified in Wuhan, China.[1] Initially, epidemiological data and clinical characteristics of SARS-CoV-2 across age ranges were largely unknown. Although the clinical spectrum of SARS-CoV-2 disease (COVID-19) continues to be defined, nowadays studies show that children under 19 years of age comprise a small proportion (1%–10%) of the total reported cases with a lower risk of developing critical illness compared with adults.[1 2] On the other hand, children at an average age of 9 years have been impacted by multisystem inflammatory syndrome. Fortunately, the currently observed mortality caused by this multisystem inflammatory syndrome is extremely low.[3] Research suggests that the lowered susceptibility in children is likely due to the scarcity of the SARS-CoV angiotensin-converting enzyme 2 (ACE2) receptor in the respiratory tract in children, meaning that the virus has less receptors to bind to and take hold within a child's respiratory tract. It is also hypothesised that higher rates of prior infection with other human coronavirus in children may provide protection against severe SARS-CoV-2 infection in children.[4]

Reported risk factors for severe disease among children include age, viral load and presence of comorbidities. A U-shaped curve for severity has been demonstrated in children diagnosed with COVID-19, with infants under 1 year of age and adolescents 10–14 years of age at higher risk of developing severe disease.[2] In a recent meta-analysis on the epidemiology of SARS-CoV-2 infection in children under 5 years of age, half of the COVID-19 were infants. It reported that 50% of young children under 5 years old required hospitalisation, while 5% of them were admitted to the intensive care unit. Only 0.8% of the studied cases died. The authors state that it is likely that many COVID-19 infections in young children requiring hospital admission were in fact mild disease, as those reported to have hospital admission were due to isolation requirements only, not necessarily due to severity of clinical conditions.[4]

In contrast, respiratory syncytial virus (RSV) has long been recognised as a major public health problem burden worldwide in Paediatrics. In a meta-analysis that included studies from 32 countries, the global estimated incidence rate of RSV acute respiratory infection hospitalisation for children under 5 years of age was 4.37 per 1000 children per year. Among preterm children under 1 year of age not receiving RSV immunoprophylaxis with palivizumab, hospitalisation rate reached 63.85. The global case fatality per 1000 children was 6.21 in children under 5 years of age. In addition to severe acute disease, evidence also suggest that children who had severe RSV infection early in life are more likely to develop subsequent wheezing during early childhood and hyperreactive airways and asthma later in life.[5]

Besides the above-mentioned long-term outcome, respiratory RSV infections may cause neurological complications in about 2% of cases. The most frequent are central apnea, seizure, lethargy, swallowing alteration, strabismus, hypotonia and encephalopathy. More recently, it was demonstrated that severe RSV respiratory infection suffered before 6 months of age impairs language learning during early infancy.[6] Considering that infancy is a delicate and fundamental period of life, impaired acquisition of developmental milestones in this phase has the potential to affect later stages of life. Neurological sequelae of COVID-19 have been reported in scarce studies in children. Sleep disturbances and headache are the most frequent symptoms when assessed around 6 months after a positive test for SARS-CoV-2. Adolescents and school-aged children, irrespective of the disease severity, represent the most affected group.[7 8] Prospective and controlled studies are needed to better define the far-reaching effects of the disease.

The rapid worldwide spread of SARS-CoV-2 infection and the severity of some cases of COVID-19 justified the global effort to identify effective preventive strategies and optimal medical management, including the implementation of targeted therapies and vaccine development.[1] To date, there are several vaccines available for clinical use in adults. In a situation where the COVID-19 vaccination is not available for children, maternal immunisation could be a viable preventive approach to protect infants.[4]

On the other hand, there is currently no licensed RSV vaccine. Researchers have been trying to develop an RSV vaccine since the mid-1960s. A number of studies have been conducted using RSV vaccines for infants and children, with encouraging results. The World Health Organization has predicted an effective RSV vaccine will come in the next 5–10 years. In contrast, there is no promising vaccine for maternal vaccination at the present time.[9] Although there is currently no vaccine available to prevent RSV infection, passive prophylaxis has been available with palivizumab since 1998. Palivizumab is a humanised murine monoclonal antibody administered monthly as an intramuscular injection and has shown a significant reduction in the overall rate of hospitalisation due to RSV infection. However, because of a greater cost, palivizumab prophylaxis for RSV can be considered cost-effective only in certain subgroup of children, such as preterm infants, and toddlers with certain congenital heart diseases.[10]

SARS-CoV-2 will likely remain endemic and co-circulate in the population together with RSV and other respiratory viruses. Consequently, the report of coinfection of RSV and SARS-CoV-2 should become increasingly more frequent over the next months. Coexistent infection is of particular interest, as it has the potential to worsen the clinical manifestations of the disease. Patient outcomes related to coinfection can be expressed by higher proportion of patients needing oxygen supplementation, higher rates of admission to intensive care unit and death. Until more data on the consequences of concomitant RSV and SARS-CoV-2 infection are available, we should drive our attention to results of single infections.

RSV is deemed to be one of the most important public healthcare issues in young children.[9] To date, considering the lack of immediate availability of vaccination against RSV, together with the expressive hospitalisation and lethality rates, and the long-term impact on child's health, it is perfectly understandable that RSV represents a relevant threat to the health of children. Therefore, RSV deserves at least the same level of attention as SARS-CoV-2. Health institutions, hospital administrators, healthcare providers and families around the world hope that the coming RSV vaccines will provide the necessary protection to reduce illness severity and deaths worldwide.

Valentina Coutinho Baldoto Gava Chakr [1,2]

[1]Pediatrics, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil
[2]Pediatrics, Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil

Correspondence to Dr Valentina Coutinho Baldoto Gava Chakr, Pediatrics, Universidade Federal do Rio Grande do Sul, Porto Alegre 90035-002, Brazil; vchakr@hcpa.edu.br

Contributors VCBGC conceived the presented idea, performed Medline search for evidence collection and wrote the manuscript.

Funding The author has not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

To cite Coutinho Baldoto Gava Chakr V. *Postgrad Med J* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/postgradmedj-2021-141012

Accepted 29 September 2021

Postgrad Med J 2021;**0**:1–2. doi:10.1136/postgradmedj-2021-141012

ORCID iD

Valentina Coutinho Baldoto Gava Chakr http://orcid.org/0000-0002-2550-733X

REFERENCES

1 Castagnoli R, Votto M, Licari A, *et al*. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review. *JAMA Pediatr* 2020;174:882–9.
2 Irfan O, Muttalib F, Tang K, *et al*. Clinical characteristics, treatment and outcomes of paediatric COVID-19: a systematic review and meta-analysis. *Arch Dis Child* 2021;106:440–8.
3 Zou H, Lu J, Liu J, *et al*. Characteristics of pediatric multi-system inflammatory syndrome (PMIS) associated with COVID-19: a meta-analysis and insights into pathogenesis. *Int J Infect Dis* 2021;102:319–26.
4 Bhuiyan MU, Stiboy E, Hassan MZ, *et al*. Epidemiology of COVID-19 infection in young children under five years: a systematic review and meta-analysis. *Vaccine* 2021;39:667–77.
5 Stein RT, Bont LJ, Zar H, *et al*. Respiratory syncytial virus hospitalization and mortality: systematic review and meta-analysis. *Pediatr Pulmonol* 2017;52:556–69.
6 Peña M, Jara C, Flores JC, *et al*. Severe respiratory disease caused by human respiratory syncytial virus impairs language learning during early infancy. *Sci Rep* 2020;10:22356.
7 Radtke T, Ulyte A, Puhan MA, *et al*. Long-term symptoms after SARS-CoV-2 infection in children and adolescents. *JAMA* 2021;326:869–71.
8 Buonsenso D, Munblit D, De Rose C, *et al*. Preliminary evidence on long COVID in children. *Acta Paediatr* 2021;110:2208–11.
9 Shan J, Britton PN, King CL, *et al*. The immunogenicity and safety of respiratory syncytial virus vaccines in development: a systematic review. *Influenza Other Respir Viruses* 2021;15:539–51.
10 Mac S, Sumner A, Duchesne-Belanger S, *et al*. Cost-effectiveness of Palivizumab for respiratory syncytial virus: a systematic review. *Pediatrics* 2019;143:e20184064.