Received: 23 March 2020 | Accepted: 24 March 2020

DOI: 10.1111/apa.15271

ACTA PÆDIATRICA
NURTURING THE CHILD
WILEY

EDITORIAL

Why is COVID-19 so mild in children?

There is an urgent need to understand why the course of the coronavirus that started in late 2019 (COVID-19) is affecting different groups of individuals with varying severity during the ongoing global pandemic. Greater knowledge of the disease, which is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), will help us to prioritise our limited health resources. Because the virus is new, and no vaccine is yet available, everyone is naïve and susceptible to being infected with SARS-CoV2. The virus will continue to spread until an effective vaccine exists or sufficient members of our global population have been infected to establish herd immunity. At the moment, the best way to minimise loss of life and severe cases requiring intensive care is to try and shelter vulnerable groups of individuals and slow down the spread of the virus.

The Korean Center for Disease Control and Prevention has probably tested the most extensive and therefore the most representative population. It reported that, up to 20 March, 6.3% of all cases that tested positive for COVID-19 were children under 19 years of age. The data from Korea are frequently being updated.[1] It is still unclear how many of the population who have been tested belonged to the same age group, so enrichment of COVID-19 within this young adult age group is uncertain. However, a general pattern has been reported from multiple countries and that is that children who test positive for COVID-19 experience a mild form of the disease. This means that children and younger adults who do not have underlying conditions, such as impaired lung function or immunosuppression, have a much lower risk of severe forms of COVID-19 than other age groups. The reasons for this mild COVID-19 disease in children remain elusive, and multiple hypotheses exist. This editorial discusses some of those theories.

On a general note, the immune systems of children and adults are different, both with respect to their composition and functional responsiveness.[2] In addition, there are differences in the immune systems of very young children, preschool children and teenagers. During the first weeks of life, the human newborn infant is exposed to a range of novel environmental exposures and undergoes dramatic changes.[3] Another difference between newborn infants and older children is the presence of some maternal antibodies during the first months of life. These antibodies do not include novel viruses such as SARS-CoV2.[4] One possible explanation for the milder COVID-19 disease presentation in children is that children have a qualitatively different response to the SARS-CoV2 virus to adults. Another possibility is that the presence of other simultaneous viruses in the mucosa of lungs and airways, which are common in young children, could limit the growth of SARS-CoV2 by direct virus-to-virus interactions and competition.[5] This fits with emerging data from the current pandemic, which has indicated a link between the amount of viral copies and COVID-19 severity.[6] This could also explain some of the tragic deaths of healthcare workers, who have probably been exposed to large amounts of the SARS-Cov2 virus.

Another possible theory for the mild COVID-19 infections in children is related to differences in the expression of the angiotensin-converting enzyme (ACE) 2 receptor necessary for SARS-Cov2 binding and infection. This receptor is expressed in the airways, the lung and intestines, but not in the immune cells.[7] Treatment with ACE inhibitors or angiotensin receptor blockers induces expression of ACE2. Both therapies are common in adults with hypertension and much less common in children. This has led some to believe that elevated ACE2 expression could explain the worse outcomes in adults infected with SARS-Cov2, but others have reported protective effects of ACE2 during lung infections.[8]

Severe COVID-19 disease is characterised by three phases. The viral and pulmonary phases are followed by the final hyperinflammatory phase, which can lead to severe acute respiratory distress syndrome (ARDS), impaired cardiac function and death. Children are not less prone to developing ARDS during respiratory tract infections than adults.[9] In fact, during the H1N1 flu pandemic in 2009, being under the age of one year was a significant risk factor for developing a severe form of the infection and ARDS.[10] The reasons for the mild presentation in most children with COVID-19 are not clear at the moment, but several plausible mechanisms exist within the fields of immunology, anatomy and virology. Further studies will be required to test these hypotheses, but it is clear that understanding the milder COVID-19 disease in children will provide important information about the disease. It will also suggest important protective mechanisms and suggest targets for future therapies.

There is a final point that I would like to make, and that is that even though children tend to have mild forms of COVID-19, that does not mean that we should ignore those who have the disease. We still need to take measures to prevent them becoming infected if we are to mitigate the pandemic. Children can probably transmit viruses, and they have been found to harbour large amounts of virus, even without showing symptoms.[11] We also need to bear in mind that viruses can persist in faeces long after they are absent from nasopharyngeal secretions.

CONFLICTS OF INTEREST

The author has no conflicts of interest to declare.

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