

How lethal is SARS-CoV-2 pneumonia when compared with respiratory syncytial virus and influenza in young children?

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Background and objective

SARS-CoV-2 is known to cause milder disease in children when compared with adults, but the extent of this is unclear. The aim of this article is to estimate the case fatality rate (CFR) for SARS-CoV-2 infection and SARS-CoV-2 pneumonia in young children aged <5 years, and compare this with estimated CFRs for respiratory syncytial virus (RSV) and influenza.

Methods

This article reviews published case series of SARS-CoV-2 infection in the paediatric population and epidemiological data on COVID-19 published on official government websites internationally and in Australia.

Results

The CFR of SARS-CoV-2 pneumonia in children aged <5 years is estimated to be 0.15–1.35%, which is lower than the estimated CFR of RSV pneumonia of 0.3–2.1%, but higher than the estimated CFR of influenza pneumonia of 0.14–0.45%.

Discussion

SARS-CoV-2 infection is likely to be less lethal than RSV in children aged <5 years, but more lethal than influenza.

AS AT 16 APRIL 2020, the COVID-19 pandemic, caused by the SARS-CoV-2 virus, is known to cause milder disease in children when compared with adults, based on a systematic review of epidemiological studies published to date.¹ Nevertheless, children aged <5 years, and particularly those aged <1 year, are more vulnerable to severe disease.²

Overall, respiratory viral infections in young children have significant morbidity and mortality. In 2002, respiratory infections accounted for 18% of mortality for children aged <5 years. Morbidity is significant in this age group, accounting for 22% of hospitalisations and 59% of general practice consults in the UK.³

Methods

This review of the relevant literature and published epidemiological data from 18 March 2020 to 16 April 2020 aims to bring some clarity to the case fatality rates (CFRs) of SARS-CoV-2 infection and SARS-CoV-2 pneumonia in the paediatric population when compared with influenza, respiratory syncytial virus (RSV) and other serious vaccine-preventable pathogens.

This knowledge is especially relevant to general practitioners (GPs), as they are at the forefront of national childhood vaccination programs and play a critical part in promoting these programs.

Definitions

In this article, CFR is defined as the proportion of cases that are fatal within a specified time, in line with the definition from *A dictionary of epidemiology*.⁴ Cases are defined as total cases (confirmed cases).

Results

Estimating the CFR of SARS-CoV-2 infection in the paediatric population

Data from China

In a case series of 2143 children aged <18 years, one death was recorded (an adolescent aged 14 years).² As at 16 April 2020, this is the largest case series of a paediatric population to date, based on nationwide data from the Chinese Center for Disease Control and Prevention.

In another case series, which had a sample size of 171 children aged <16 years, one death was recorded (an infant aged 10 months).⁵ In this particular study, 1391 children who were close contacts of confirmed and suspected cases were tested, with 171 positive cases. This study was based at Wuhan Children's Hospital, the only centre assigned by the central government for treating infected children aged <16 years in Wuhan.

Data from Italy

Based on a sample of 2341 children between the ages of zero and 18 years, one

death of a child between the ages of zero and nine years was recorded.⁶ This equates to a crude CFR of 0.043%. These data are based on information published online daily by the Istituto Superiore di Sanità.

Data from the USA

In a sample of 2572 children aged <18 years, three deaths were recorded.⁷ There was no information on the exact ages of these children. This was based on information published by the Centers for Disease Control and Prevention in their weekly Morbidity and Mortality Report.

Summary of the estimated CFR of SARS-CoV-2 infection in the paediatric population

Based on the best available epidemiological information available in the paediatric population (Table 1), the CFR of SARS-CoV-2 infection may range from 0.043% to 0.58% among a paediatric population aged 0–18 years (Table 2).

The CFR of SARS-CoV-2 pneumonia may range from 0.10% to 0.90% in a paediatric population aged <18 years.

In the case series of 2143 children, the percentage of children aged <5 years with severe and critical disease was 8.71%, while the percentage of children aged <18 years with severe and critical disease was 5.83%.² Children aged <5 years are therefore 1.5 times more likely than children aged <18 years to have severe and critical disease.

Assuming that children who have severe and critical disease are more likely to die from COVID-19, it may be possible to derive a very crude estimate of the CFR of SARS-CoV-2 infection and SARS-CoV-2

pneumonia in children aged <5 years (Table 3).

Estimating the CFR of RSV infection in the paediatric population

RSV is the most common cause of death in childhood from pneumonia after *Pneumococcus* and *Haemophilus influenzae* type b. It accounts for 22% of all episodes of pneumonia in young children.⁸

A systematic review and meta-analysis of the global burden of disease in young children due to RSV estimated that globally in 2005:⁸

- in developed countries, the CFR of RSV pneumonia of children aged <1 year was 0.7%, while the CFR of children aged <5 years was 0.3%
- in developing countries, the CFR of RSV pneumonia was 2.1% for both children aged <1 year and those aged <5 years.

Summary of the estimated CFR of RSV pneumonia in the paediatric population

In the literature, the CFR of RSV is not available as most published articles focus only on RSV pneumonia or hospitalised patients with RSV.

Depending on age and geographical location, RSV pneumonia CFR may range from 0.3% to 2.1% in children aged <5 years (Table 2).

Estimating the CFR of influenza infection in the paediatric population

Influenza accounted for 7% of all severe paediatric pneumonia episodes in 2008.⁹ It is the second most common pathogen in children with pneumonia,⁹ with the most common pathogen being RSV.

Based on information published by the Centers for Disease Control and Prevention (2017–18 influenza season)¹⁰ and a systematic review and meta-analysis⁹ of influenza's global burden of disease of children (2008):

- the CFR of influenza infection may range from 0.0031% to 0.030% among a paediatric population aged <5 years
- the CFR of influenza-associated pneumonia may range from 0.14% to 0.45% in children aged <5 years (Table 2).

Discussion

In almost all epidemiological datasets available, a disproportionately low number of paediatric cases (aged <18 years) are reported. USA's Centers for Disease Control and Prevention reports 1.7%;⁷ China reports 9%;¹¹ Italy reports 1.6%;⁶ Korea reports 6.3%;¹² and Australia reports 3.22%.¹³

Interestingly, a study on transmission dynamics in Shenzhen, China, found that children were as likely as adults to be infected, with rates of infection in children aged <10 years being 7.4%, while the population average was 7.9%.¹⁴ The study looked at 391 positive cases and 1286 of their close contacts.¹⁴ Unfortunately, the study did not look specifically at the symptoms of the cases. Nevertheless, it is not uncommon for children with SARS-CoV-2 pneumonia to be asymptomatic.^{4,15}

If it is true that the infection rate of children is similar to that of adults, the fact that they are disproportionately underrepresented in epidemiological studies may suggest that there are more

Table 1. Epidemiological data of the paediatric population from three different geographical locations

Country	Data source	Sample size	Age range	CFR (SARS-CoV-2)	CFR (SARS-CoV-2 pneumonia)
China ²	Case series	2,143	<18 years	0.047%	0.10%
China ⁵	Case series	171	<16 years	0.58%	0.90%
Italy ⁶	Epidemiological data	2,341	0–18 years	0.043%	Not available
USA ⁷	Epidemiological data	2,572	<18 years	0.12%	Not available

CFR, case fatality rate

cases of infected children who are undiagnosed than adults.

This may indicate that the true CFR of SARS-CoV-2 infection and SARS-CoV-2 pneumonia in children is much lower than what is suggested in this article.

Nevertheless, based on the estimates presented in Table 2, RSV pneumonia is more fatal than SARS-CoV-2 pneumonia and influenza-associated pneumonia.

There is no vaccine available for RSV, although it is likely to be more fatal than SARS-CoV-2 in children aged <5 years. Palivizumab, a monoclonal antibody that has been shown to reduce hospitalisation rates, is available for high-risk children in Australia.¹⁶

While more epidemiological studies are required, this article will hopefully provide impetus for further research to more accurately quantify the lethality of SARS-CoV-2 pneumonia in young children, and spur efforts towards an RSV vaccine. Fortunately, there is already a widely available vaccine against invasive pneumococcal disease, which has a CFR of 5.6% in children aged <5 years,¹⁷ and *H. influenzae* type b, which has a CFR of 4.56% in a similar age group.¹⁸

Limitations

As a result of the limited availability of data and different testing criteria and preparedness of health systems in various countries, estimating the true CFR is challenging. As such, data from different countries are presented.

Data from government epidemiological sources are more likely to be underestimations of the CFR, as the numerator at the early phase of the pandemic is likely to be underestimated. Conversely, data from case series are more likely to be overestimations of the CFR, as the denominator is likely to be an underestimate of the true number of cases.

These are very crude estimates of the CFR of SARS-CoV-2 infection in children, based on the best available data.

Unfortunately, the US Centers for Disease Control and Prevention data and Italian data do not provide sufficient information on the number of infected children with COVID-19 pneumonia. As such, the CFR of SARS-CoV-2 pneumonia is only estimated using data from China.

Additionally, each case series or epidemiological dataset referenced had

a different age cut-off. As such, it is not possible to provide accurate CFR estimates for children aged <5 years with SARS-CoV-2 for a direct comparison with the systematic reviews and meta-analyses available for RSV and influenza in young children.

Data on comorbidities of the children were unavailable from all sources, hence it is not possible to ascertain CFRs based on pre-existing risk factors.

Conclusion

There are early indications that SARS-CoV-2 pneumonia in children aged <5 years may be more lethal than influenza, but not as lethal as RSV. Invasive pneumococcal disease and *H. influenzae*, both vaccine-preventable diseases, are at least twice as lethal as RSV.

This highlights the importance of early childhood vaccination programs and influenza vaccination in the midst of the COVID-19 pandemic. Parents should not avoid bringing their young children to general practice clinics, local council or pharmacies for vaccinations for fear of COVID-19, as many of these vaccinations protect their children from diseases more severe and deadly than COVID-19.

High-quality epidemiological studies, particularly in the paediatric population, will be vital to develop better estimates of the CFR of SARS-CoV-2 infection and pneumonia in young children.

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Table 2. Comparison of estimated case fatality rate of SARS-CoV-2, respiratory syncytial virus and influenza in the paediatric population

	SARS-CoV-2	Respiratory syncytial virus	Influenza
Case fatality rate	0.043–0.58%	Not available	0.0031–0.030%
Case fatality rate (pneumonia)	0.10–0.90%	0.3–2.1%	0.14–0.45%
Age range	0–18 years	<5 years	<5 years

Table 3. Comparison of estimated case fatality rate of SARS-CoV-2, respiratory syncytial virus and influenza in children aged <5 years

	SARS-CoV-2	Respiratory syncytial virus	Influenza
Case fatality rate	0.065–0.87%*	Not available	0.0031–0.030%
Case fatality rate (pneumonia)	0.15–1.35%*	0.3–2.1%	0.14–0.45%
Age range	<5 years	<5 years	<5 years

*These figures have been obtained by multiplying those in Table 2 by 1.5.

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