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ORIGINAL ARTICLE

A very low prevalence of SARS-CoV-2 infection but a high prevalence of other respiratory virus infections in children admitted to paediatric emergency departments

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Abstract

Aim: To investigate the prevalence of infections by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and other respiratory viruses among children admitted to paediatric emergency departments (PEDs).

Methods: From April to July 2020, a prospective, multicentre cohort study was conducted in the PEDs of eight French university hospitals. Regardless of the reason for admission, a nasopharyngeal swab sample from each child was screened using reverse transcription polymerase chain reaction tests for SARS-CoV-2 and other respiratory viruses. We determined the prevalence of SARS-CoV-2 and other respiratory viruses and identified risk factors associated with a positive test.

Results: Of the 924 included children (median [interquartile range] age: 4 years [1–9]; boys: 55%), 908 (98.3%) were tested for SARS-CoV-2. Only three samples were positive (0.3%; 95% confidence interval: 0.1–1) and none of these children had symptoms

Abbreviations: ACE2, Angiotensin Conversion Enzyme 2; CI, Confidence interval; COVID-19, Coronavirus Disease 2019; IQR, Interquartile range; OR, Odds ratio; PEDs, Paediatric emergency departments; RNA, Ribonucleic acid; RSVs, Respiratory syncytial viruses; RT-PCR, Reverse-transcriptase polymerase chain reaction; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2.

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of coronavirus disease 2019. Of the 836 samples (90%) tested for other viruses, 129 (15.4%) were positive (primarily rhinovirus). Respiratory viruses were significantly more common in young children and in children with respiratory tract symptoms and fever.

Conclusion: The prevalence of SARS-CoV-2 among children admitted to emergency departments was low. In contrast, and despite social distancing and other protective measures, the prevalence of other respiratory viruses detection was high.

KEYWORDS
children, COVID-19, prevalence, respiratory virus, SARS-CoV-2

1 | INTRODUCTION

Children have been considered as possible vectors for the dissemination of the new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2),[1] as for other viral respiratory diseases. These assumptions prompted most governments to close schools during periods of lockdown in 2020.[2]

Children with suggestive symptoms were less likely to be infected by the SARS-CoV-2 than adults during the first epidemic waves in China, Europe and the United States.[3–6] However, the estimated proportion of asymptomatic cases of COVID-19 among children in initial reports ranged from 9% to 16%.[7,8] Children with mild or asymptomatic disease were suspected to be vectors for SARS-CoV-2. Data on paediatric SARS-CoV-2 infection and transmission rates are often pooled and thus do not take account of the children's specific features and differences between age groups. The true prevalence of SARS-CoV-2 infection among children is therefore still subject to debate.[9] We assessed this prevalence among children admitted to paediatric emergency departments (PEDs). The prevalence of infections with other respiratory viruses was assessed for comparative data.

Key notes

- Children infected by SARS-CoV-2 often have only mild symptoms or no symptoms, but they are considered as possible significant SARS-CoV-2 vectors.
- Of 924 children admitted at eight paediatric emergency departments, 20% with suggestive symptoms of a SARS-CoV-2 infection, the SARS-CoV-2 prevalence was 0.3%.
- Of 836 children tested for other respiratory viruses, the detection of these was high (15.4%), despite distancing.

2 | METHODS

2.1 | Design and objectives

We conducted a prospective, multicentre cohort study in the PEDs at eight university hospitals in France: Lille, Nancy, Nantes, Nice, Paris-Colombes, Saint-Etienne, Toulouse and Tours. The study ran from April 15th to July 13th, 2020. The study was approved by an independent ethics committee (RCB-2020-A00811-38) and registered by the French National Data Protection Commission (DEC20-092). The primary objective was to determine the prevalence of SARS-CoV-2 detection in children. Secondary objectives were to determine the prevalence of SARS-CoV-2 and other viruses in children depending on the presence or not of suggestive symptoms of a SARS-CoV-2 infection, including respiratory tract symptoms.

2.2 | Inclusion criteria, outcomes and study procedure

The main inclusion criteria were age under 18, admission to one of the eight PEDs during office hours (regardless of the reason) and the provision of written informed consent for children over the age of 6 and from at least one parent. The main exclusion criteria were admission outside office hours, clotting disorders, absence of social security coverage or inability to communicate easily. The primary endpoint was a positive reverse transcriptase polymerase chain reaction (RT-PCR) test for SARS-CoV-2 in the child's nasopharyngeal swab. Secondary endpoints were a positive RT-PCR test for SARS-CoV-2 or other respiratory viruses among children without or with symptoms suggestive of SARS-CoV-2 infection.

A standardised questionnaire was filled out. Nasopharyngeal samples were collected using flocked swabs in 3 ml of viral transport medium (Yocon) and sent to the laboratory. The sample was either tested immediately, in cases of urgent result needed, or stored at −80°C. A follow-up phone call was made on days 7, 14 and 28 post-admission.

2.3 | Laboratory tests

Immediately before RT-PCR, the specimens were thawed and heat inactivated for 30 min at 60°C. The Institut Pasteur Paris protocol

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(https://www.who.int/docs/default-source/coronaviruse/real-time-rt-pcr-assays-for-the-detection-of-sars-cov-2-institut-pasteur-paris.pdf?sfvrsn=3662fcb6_2) was used with various commercial RT-PCR assays to detect SARS-CoV-2 ribonucleic acid (RNA) (Table S1). For the detection of other respiratory viruses, RNA was extracted with the StarMag 96 Extraction Kit (Seegene Inc.) on a Microlab Nimbus instrument. The Allplex™ RP1, RP2, RP3 assays (Seegene Inc.) were used according to the manufacturer's instructions to detect RNA from influenza viruses A and B, respiratory syncytial viruses (RSVs) A and B, adenovirus, enterovirus, parainfluenza viruses 1, 2, 3 and 4, metapneumovirus, bocavirus, rhinovirus, and coronaviruses NL63, 229E and OC43.

2.4 | Statistics

Our sample size calculation was based on the precision of the estimated prevalence and its 95% confidence interval (CI), using the Clopper–Pearson exact method. We chose an absolute precision of 2%. Considering the highest reported prevalence of SARS-CoV-2 infection in children of 10%[10,11] [8.1–12.1], 914 children were required.

Categorical variables were expressed as the frequency (percentage). Prevalence data were expressed as a percentage (95%CI). Quantitative variables were expressed as median and interquartile range (IQR). A chi-squared test was used for intergroup comparisons of categorical variables, with calculation of the odds ratio and its 95%CI. A nonparametric Mann–Whitney test was used to compare values of continuous variables. The threshold for statistical significance was set to $p < 0.05$. All statistical analyses were performed with Epi-Info 6.04fr software (Centers for Disease Control and Prevention).

3 | RESULTS

Of the 924 patients included, 913 provided a nasopharyngeal sample, with 908 samples (98%) tested for SARS-CoV-2 and 836 (90%) tested for other respiratory viruses (Figure 1). The characteristics of the study population (median [IQR] age: 4 years [1–9]; boys: 55%) are summarised in Table S2.

The main reasons for the PED visit were possible COVID-19 symptoms (47% of the patients), with fever (30%), respiratory tract symptoms (11%) and digestive tract symptoms (27%). After a clinical examination, 185 children were classified by the physician as suspected cases of COVID-19 (20%). For the SARS-CoV-2 RT-PCR tests, 900 were negative, three were positive (0.3%; 95%CI: 0.1–1) and five had a technically uninterpretable result. The three children positive for SARS-CoV-2 were 3, 8 and 14 years old (Table S3). They did not have any symptom of COVID-19 the week before admission or on admission and did not develop any symptom or require hospital admission during the following 28 days.

Of the 836 PCR tests for other respiratory viruses, 129 were positive (15.4%; 95%CI: 13.1–18.0): 104 for one virus, 20 for two viruses and five for three viruses (Table 1). The most frequently detected virus was rhinovirus. When comparing the characteristics of children with and without a positive RT-PCR test for other respiratory viruses, those with a positive test were significantly younger and significantly more likely to have a history of fever and respiratory tract symptoms (Table S4).

4 | DISCUSSION

Only 0.3% of the 908 tested children were positive for SARS-CoV-2, and all were asymptomatic. Other respiratory viruses were found in

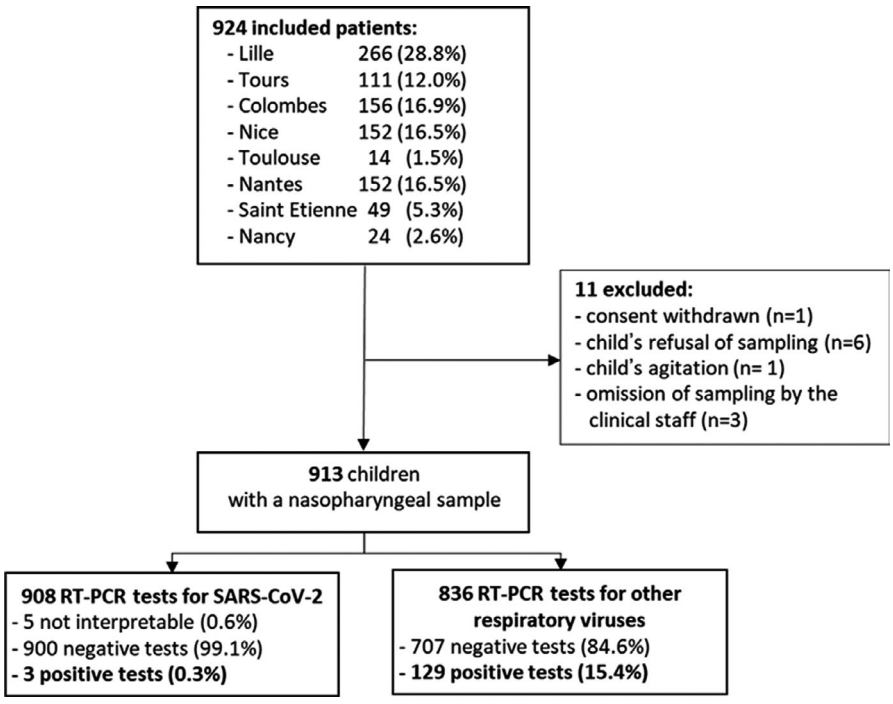

FIGURE 1 Study flow chart

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TABLE 1 Viruses identified in the 129 children with a positive multiplex reverse-transcriptase polymerase chain reaction

Virus	*n*	(%)	Symptomatic	Asymptomatic
Rhinovirus	68	(42.8%)	38	30
Adenovirus	31	(19.5%)	23	8
Bocavirus	30	(18.9%)	19	11
Enterovirus	12	(7.5%)	5	7
Rhinovirus/Enterovirus	7	(4.4%)	2	5
Myxovirus parainfluenzae 1, 2, 4	5	(3.1%)	3	2
Coronavirus N229 or NL63	4	(2.5%)	1	3
Respiratory syncytial virus A/B	2	(1.3%)	1	1
Total	159	(100.0%)	92 (58%)	67 (42%)

15.4%. A number of studies performed during the same period have found a low prevalence of SARS-CoV-2 among children. In a multicentre study performed in the United States, among asymptomatic children tested the pooled prevalence of SARS-CoV-2 infection was 0.65%.[12] In a German study among children aged 0–10 years recruited through public announcements, 0.04% had a positive RT-PCR test for SARS-CoV-2.[13] In Iceland, none of the 848 under-10 children in a screening population were positive.[14] Lastly, in a study of children in Poland from March to May 2020, 3.3% of symptomatic and none of asymptomatic children were positive for SARS-CoV-2.[15] Our results confirm the particularly low prevalence of SARS-CoV-2 detection in children.

Of the 145 children with suspected COVID-19 after a clinical examination, 23% had a positive RT-PCR test for another virus, mainly the rhinovirus and no cases of influenza virus infection. This contrasts with the RT-PCR results of the Polish study, where 16% of 37 symptomatic children were tested positive for RSV and 10% of 49 symptomatic children tested positive for influenza A/B.[15] The prevalence of infection with other respiratory viruses appears to be lower in adults. One study reported a prevalence of 10.3% for other respiratory pathogens in a population of symptomatic patients with a suspected SARS-CoV-2 infection.[16] As in our study, the rhinovirus was predominant (31%). SARS-CoV-2 co-infections with other respiratory viruses were rare, in less than 3% of patients.[16,17]

The strength of our study was its prospective, multicentre design; this enabled us to screen children for both SARS-CoV-2 and other respiratory viruses, which has rarely been done before. The study was performed during and just after France's first period of lockdown in 2020, which can explain the low prevalence of the SARS-CoV-2 detection in our population.[18] At the time of the study, the prevalence rate was between 5% and 10% in the general population and then declined to a prevalence still over 1%.[19] Missing data was low for the required primary and secondary endpoints.

The low surface level of Angiotensin Conversion Enzyme-2 receptors for SARS-CoV-2 on the child's respiratory mucosa is probably one explication for the low infection and dissemination rates.[20] But this low prevalence may vary with a poor level of protective measures and the emergence of more contagious variants. In contrast, other respiratory viruses can easily colonise the respiratory tract in children. However, the transmission of all these viruses was reduced by social distancing measures.[21] Although the presence of influenza and coronavirus in respiratory droplets was dramatically reduced by the use of a surgical mask, rhinovirus could still be detected.[22] The social distancing measures might explain why the influenza epidemic was reduced in the northern hemisphere and did not occur in the southern hemispheres in 2020,[23] whereas epidemics of rhinovirus infections and RSV bronchiolitis did occur.[24] The absence of effective protective measures in young children is likely to result in the persistent circulation of seasonal respiratory viruses in this population. We expect the prevalence of these infections to vary with the extent and intensity of the protective measures that adults and older children will continue to apply.

5 | CONCLUSION

Our study showed a low detection of SARS-CoV-2 in children admitted to the PEDs during and after the first lockdown in France. However, despite distancing measures applied during this period, the detection of other respiratory viruses remained high, especially in young children with fever and respiratory tract symptoms. Similar studies will be required to follow the detection of SARS-CoV-2 in children with the emergence of new variants.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare with regard to this research.

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REFERENCES

1. Cauchemez S, Valleron A-J, Boëlle P-Y, Flahault A, Ferguson NM. Estimating the impact of school closure on influenza transmission from Sentinel data. Nature. 2008;452:750-754.
2. Viner RM, Russell SJ, Croker H, et al. School closure and management practices during coronavirus outbreaks including COVID-19: a rapid systematic review. Lancet Child Adolesc Health. 2020;4:397-404.
3. Levy C, Basmaci R, Bensaid P, et al. Changes in reverse transcription polymerase chain reaction–positive severe acute respiratory

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syndrome coronavirus 2 rates in adults and children according to the epidemic stages. Pediatr Infect Dis J. 2020;39:369-371.
4. Livingston E, Bucher K. Coronavirus disease 2019 (COVID-19) in Italy. JAMA. 2020;323:1335.
5. CDC COVID-19 Response Team. Coronavirus disease 2019 in children – United States, February 12-April 2, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:422–426.
6. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in china: Summary of a report of 72 314 cases from the Chinese center for disease control and prevention. JAMA. 2020;323:1239-1242.
7. Wei M, Yuan J, Liu Y, Fu T, Yu X, Zhang Z-J. Novel Coronavirus infection in hospitalized infants under 1 year of age in China. JAMA. 2020;323(13):1313-1314.
8. Lu X, Zhang L, Du H, et al. SARS-CoV-2 infection in children. N Engl J Med. 2020;387:1663-1665.
9. Kelvin AA, Halperin S. COVID-19 in children: the link in the transmission chain. Lancet Infect Dis. 2020;20:633-634.
10. Davis BM, Foxman B, Monto AS, et al. Human coronaviruses and other respiratory infections in young adults on a university campus: prevalence, symptoms, and shedding. Influenza Other Respir Viruses. 2018;12:582-590.
11. Bailey LC, Razzaghi H, Burrows EK, et al. Assessment of 135 794 pediatric patients tested for severe acute respiratory syndrome coronavirus 2 across the United States. JAMA Pediatr. 2021;175:176-184.
12. Sola AM, David AP, Rosbe KW, Baba A, Ramirez-Avila L, Chan DK. Prevalence of SARS-CoV-2 infection in children without symptoms of coronavirus disease 2019. JAMA Pediatr. 2021;175:198-201.
13. Tönshoff B, Müller B, Elling R, et al. Prevalence of SARS-CoV-2 infection in children and their parents in southwest Germany. JAMA Pediatr. 2021;175:586-593.
14. Gudbjartsson DF, Helgason A, Jonsson H, et al. Spread of SARS-CoV-2 in the Icelandic population. N Engl J Med. 2020;382:2302-2315.
15. Kuchar E, Załęski A, Wronowski M, et al. Children were less frequently infected with SARS-CoV-2 than adults during 2020 COVID-19 pandemic in Warsaw, Poland. Eur J Clin Microbiol Infect Dis. 2021;40:541-547.
16. Si Y, Zhao Z, Chen R, et al. Epidemiological surveillance of common respiratory viruses in patients with suspected COVID-19 in Southwest China. BMC Infect Dis. 2020;20:688.
17. Burrel S, Hausfater P, Dres M, et al. Co-infection of SARS-CoV-2 with other respiratory viruses and performance of lower respiratory tract samples for the diagnosis of COVID-19. Int J Infect Dis. 2021;102:10-13.
18. Carrat F, Touvier M, Severi G, et al. Incidence and risk factors of COVID-19-like symptoms in the French general population during the lockdown period: a multi-cohort study. BMC Infect Dis. 2021;21:169.
19. Santé Publique France. COVID-19: point épidémiologique hebdomadaire du 2 juillet 2020. Available at: www.santepubliquefrance.fr/maladies-et-traumatismes/maladies-et-infections-respiratoires/infection-a-coronavirus/documents/bulletin-national/covid-19-point-epidemiologique-du-2-juillet-2020. Accessed 6th December, 2021.
20. Bunyavanich S, Do A, Vicencio A. Nasal gene expression of angiotensin-converting enzyme 2 in children and adults. JAMA. 2020;323:2427-2429.
21. Redlberger-Fritz M, Kundi M, Aberle SW, Puchhammer-Stöckl E. Significant impact of nationwide SARS-CoV-2 lockdown measures on the circulation of other respiratory virus infections in Austria. J Clin Virol. 2021;137:104795.
22. Leung NHL, Chu DKW, Shiu EYC, et al. Respiratory virus shedding in exhaled breath and efficacy of face masks. Nat Med. 2020;26:676-680.
23. Sullivan SG, Carlson S, Cheng AC, et al. Where has all the influenza gone? The impact of COVID-19 on the circulation of influenza and other respiratory viruses, Australia, March to September 2020. Euro Surveill. 2020;25:2001847.
24. Foley DA, Yeoh DK, Minney-Smith CA, et al. The interseasonal resurgence of Respiratory Syncytial Virus in Australian children following the reduction of coronavirus disease 2019-related public health measures. Clin Infect Dis. 2021;73:e2829-e2830.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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