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Short communication

Assessment of SARS-CoV-2 testing in children during a low prevalence period (VIGIL study 1)



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ABSTRACT

Objectives: SARS-CoV-2 induces a broad spectrum of clinical manifestations, which overlap with other viral infections very common in children. We aimed to describe the percentage of positive SARS-CoV-2 RT-PCR tests in symptomatic and asymptomatic ambulatory children and to determine the predictive factors for positivity.

Patients and Methods: From June 1 to July 31, 2020, we conducted a cross-sectional prospective, multi-center study (13 hospital emergency units and 59 ambulatory pediatricians) throughout France. Children under 15 years of age with a prescription of nasopharyngeal SARS-CoV-2 RT-PCR test were enrolled.

Results: Among the 1,553 RT-PCR tests, 22 were positive (1.4%; 95%CI [0.9; 2.1]). In both univariate and multivariate analyses, the predictive factors for positivity were age below 2 years (OR: 4.5 [1.6; 12.7]) and history of contact (OR: 12.3 [4.6; 32.8]).

Conclusions: In an epidemic stage with low SARS-CoV-2 circulation, sampling of children with nonspecific symptoms and without known contact could be questioned.

1. Introduction

Since the beginning of the pandemic in China, it was observed that children experienced fewer severe forms of COVID-19. Children are also less likely to be hospitalized in conventional wards or intensive care units, and deaths are rare [1]. Since then, several studies have suggested that children are also less often infected than adults [2]. The rate of SARS-CoV-2-positive real-time reverse transcription-polymerase chain reaction (RT-PCR) tests in children was more frequently lower than in adults, even if the dynamics of the curve for children followed that of adults. Thus, the rate of positivity during periods of high viral circulation, at the time of

the epidemic peak in March 2020 in France, was always lower in children (maximum 11%) than in adults (29%) [3,4].

Although many studies suggested that children are less likely to spread the virus, the question of their role as silent contaminators remains debated [5,6]. This doubt explains the recommendations to not only test case contact children but also those with mild symptoms. The aim of screening children is to prevent the spread of COVID-19 through intra-familial and school transmission [7].

SARS-CoV-2 induces a broad spectrum of clinical manifestations (fever, rhinitis, cough, diarrhea, vomiting, etc.), which overlap with many other respiratory and digestive viral infections very common in children [8]. However, even during a pandemic period, many other viruses circulate notably during the winter season, and especially in infants and toddlers. Reinforced hygiene measures promoted by public health interventions and aimed at reducing the risk of SARS-CoV-2 transmission were also successful in reducing the incidence of these other diseases [9,10]. These measures

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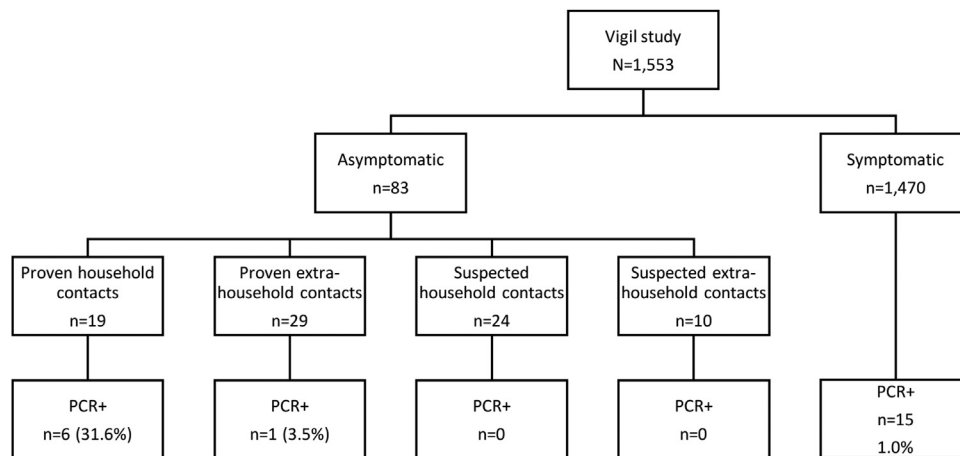


Fig. 1. Distribution of children according to the presence or absence of symptoms, contacts, and SARS-CoV-2 PCR test results.

also have a strong impact on the transmission of numerous infectious diseases, more specifically on viral or viral-induced pediatric diseases [11].

Various countries recommended performing RT-PCR testing on symptomatic patients, including children. Thus, if each child has to be tested at each viral episode, it will represent a very large number of performed tests per child and per season with its set of inconvenience and cost. Indeed, nasopharyngeal specimen collection is uncomfortable, and young children are often uncooperative during the procedure, thus increasing the risk of nasal trauma.

Although children are often unable to produce saliva specimens spontaneously, buccal swabs have been suggested to obtain saliva for testing. Buccal swabs are less invasive and cause less discomfort for children. However, buccal specimens yielded substantially lower viral loads and had poor sensitivity compared with nasopharyngeal specimens. The major overall cost of repeating these tests would still remain.

In France, the first lockdown took place from March 17 to May 11, 2020, followed by a gradual reopening of nurseries and schools. This study started on June 1, three weeks after the end of the first lockdown, and on this date more than 80% of elementary schools had reopened. The aim of our study was to describe the percentage of SARS-CoV-2-positive RT-PCR tests in symptomatic and asymptomatic ambulatory children and to determine the predictive factors for SARS-CoV-2 RT-PCR positivity.

2. Patients and Methods

From June 1 to July 31, 2020, with the Clinical and therapeutic pediatric association of the Val de Marne (French acronym ACTIV), the French Association of Ambulatory Pediatrics (French acronym AFPA) and the Pediatric Infectious Disease Group (French acronym GPIP) network research units, we conducted a cross-sectional prospective, multicenter study. Throughout France, 73 centers (13 hospital emergency units and 60 pediatricians in ambulatory settings) enrolled all children under 15 years of age for whom a SARS-CoV-2 RT-PCR test was performed on nasopharyngeal swab. Ambulatory and hospital virology laboratories performed the RT-PCR analysis for SARS-CoV-2.

After informing the parents of participating children, an electronic case report form (eCRF) was prospectively completed by the pediatrician on a secure database. The following data were recorded: socio-demographic data, day care attendance modalities for the past 15 days (the strategy of closing schools decided by the French government started on March 17 and ended on May 11, 2020), contact with a person confirmed or suspected of

COVID-19, presence or absence of symptoms and signs. The following were considered symptoms or signs compatible with SARS CoV-2 infection: fever, cough, rhinorrhea, wheezing, dyspnea, diarrhea, vomiting, cutaneous signs, anosmia and ageusia, and fever chills.

Data were entered by using the eCRF (PHP/MySQL) and analyzed using Stata/SE v15 (StataCorp, College Station, TX, USA). Quantitative data were compared by Student's *t* test and categorical data by Chi² or Fisher's exact test. We used a logistic regression model for analysis of factors associated with SARS-CoV-2 RT-PCR positivity. Variables (age, suspected or confirmed COVID-19 contact, and day-care attendance modalities during the last 15 days) with $P < 0.20$ on univariate analysis were included in the multivariable model, estimating odds ratios (ORs) and 95% CIs. Only significant variables ($P < 0.05$) were kept in the final model. All tests were 2-sided and were considered significant at $P < 0.05$. The study protocol was approved by an ethics committee (Centre Hospitalier Intercommunal de Créteil, France). The study was registered at ClinicalTrials.gov NCT04412317.

3. Results

From June 1 to July 31, 2020, 1,553 children underwent SARS-CoV-2 RT-PCR testing; 820 (52.9%) in emergency units and 733 (47.1%) in ambulatory settings. Mean age was 3.5 ± 3.6 years (min 1 month, max 15 years old) and median age was 2.0 years. Infants below 3 months accounted for 2.8% of the 1,553 children. Among the 1,553 SARS-CoV-2 RT-PCR tests, 22 were positive (1.4%; 95%CI [0.9; 2.1]).

The rates of positive RT-PCR tests were 1.0% (14/1,384, 95%CI [0.6; 1.7]) among patients without known contact and 8.4% (7/83, 95%CI [3.5; 16.6]) among those with a history of contact. Among children with known contact ($n = 83$), 19 (22.9%) were family contacts (Fig. 1).

Children under 2 years of age accounted for 44.6% of the cohort and 71.4% of the positive RT-PCR tests (15/21) ($P = 0.013$)

In both univariate and multivariate analyses, the predictive factors for positive RT-PCR tests were age below 2 years (OR: 4.5 [1.6; 12.7]) and history of SARS-CoV-2 contact (OR: 12.3 [4.6; 32.8]).

4. Discussion

To our knowledge, this is the first ambulatory study conducted in hospital emergency units and pediatric ambulatory settings at the French national level with a cohort of more than 1500 symptomatic and asymptomatic patients under 15 years of age. The

percentage of positive RT-PCR tests in children was low (1.4%) but the study started three weeks after the end of the first lockdown while schools were slowly reopening (more than 1,8 million of children were back to school). During the same period according to the French epidemiological data records, the rate of positive tests was around 3% in the general population. Despite that, we sampled symptomatic and asymptomatic ambulatory children with or without contact. The rates of positive RT-PCR tests were low in our study (1.4%). These results speak in favor of a lower rate of infections in children. In our study, the main risk factor identified was a contact with a COVID-19-positive person, especially within the family ($P < 0.0001$).

Our study has several limitations. First, the period during which the study was conducted:

- it was indeed conducted three weeks after the end of the first lockdown when the viral circulation of SARS-CoV-2 was lower. Our results can therefore only be extrapolated at a similar moment with low viral circulation;
- it was also conducted in the early summer period, when the rate of pediatric visits for digestive or respiratory diseases suggesting an infectious cause was lower than in the winter period, particularly after the lockdown which led to a decrease in contagious infectious diseases.

Overall, these findings raise major concerns about a screening strategy only based on symptoms when the circulation of SARS-CoV-2 is low. The value of routine swab in children with common winter symptoms such as fever, cough, diarrhea, or vomiting must be questioned. The low efficiency of the sampling and their repetition represent a major cost and inconvenience.

During periods of increased viral circulation, this study deserves to be repeated to better determine the risk factors for contamination of children, and to better approach their role in transmission. Indeed, in epidemic stages with low SARS-CoV-2 circulation, sampling of children with nonspecific symptoms and without known contacts could be questioned.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments.

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Author contributions

RC, CL, CJ designed the study. RC, CL, EE, SB analyzed and interpreted the data and drafted the article. CL and SB performed the statistical analysis. All authors revised and approved the article.

Disclosure of interest

The authors declare that they have no competing interest.

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