



Secondary household transmission of SARS-CoV-2 among children and adolescents: Clinical and epidemiological aspects

Eliane T. Afonso PhD¹ | Solomar M. Marques PhD¹ | Lusmaia D. C. Costa PhD¹ |
 Patrícia M. Fortes PhD¹ | Fernanda Peixoto PhD¹ | Danielli C. Bichuetti-Silva PhD¹ |
 Natália D. A. Aredes PhD² | Claci F. W. Rosso PhD² | Faétilla dos S. Oliveira MSc² |
 Fabíola S. Fiaccadori PhD³ | Menira B. de L. D. e Souza PhD³ |
 Elisângela de P. Silveira-Lacerda PhD⁴ | Gabriela S. Bazilio PhD⁵ |
 Clayton L. Borges PhD⁶  | Juliana A. P. Rocha PhD⁶ |
 Alessandra V. Naghettini PhD¹ | Paulo S. S. da Costa PhD¹ | Rafael A. Guimarães PhD² 

¹Department of Pediatrics, Faculty of Medicine, Federal University of Goiás, Goiânia, Goiás, Brazil

²Faculty of Nursing, Federal University of Goiás, Goiânia, Goiás, Brazil

³Virology and Cell Culture Laboratory, Institute of Tropical Pathology and Public Health, Federal University of Goiás, Goiânia, Goiás, Brazil

⁴Department of Genetics, Institute of Biological Sciences, Federal University of Goiás, Goiânia, Goiás, Brazil

⁵Laboratory of Clinical Analysis of Higher Education, Institute of Biological Sciences, Federal University of Goiás, Goiânia, Brazil

⁶Department of Biochemistry and Molecular Biology, Institute of Biological Sciences, Federal University of Goiás, Goiânia, Goiás, Brazil

Correspondence

Rafael A. Guimarães, PhD, Faculty of Nursing, Federal University of Goiás, Goiânia 74605-080, Goiás, Brazil.

Email: rafaelalves@ufg.br

Funding information

Ministério da Educação do Brasil

Abstract

Objective: To evaluate the secondary attack rate (SAR) in children and adolescents, contacts of essential activities workers who were infected by SARS-CoV-2; and to describe associated clinical and epidemiological data.

Methods: A cross-sectional study conducted in children and adolescents aged 5 to 19 years of age, that were household contacts of parents and other relatives who were infected by SARS-CoV-2 in the city of Goiânia, Central Brazil, from March to October 2020. Sociodemographic and clinical data were collected from all participants. Nasopharyngeal and oropharyngeal swabs were collected and tested for SARS-CoV-2 RNA using real-time reverse transcription polymerase chain reaction (RT-PCR). Factors associated with SARS-CoV-2 infection and SAR were analyzed using Poisson regression.

Results: A total of 267 children and adolescents were investigated. The prevalence of SARS-CoV-2 RNA by the real-time RT-PCR test and/or the presence of COVID-19 associated symptoms (anosmia/ageusia and flu syndrome) was 25.1% (95.0% Confidence Interval [95.0% CI] = 20.3-30.6). More than half (55.1%) of the participants had signs and symptoms. The most prevalent signs and symptoms in positive individuals were nasal congestion (62.7%), headache (55.2%), cough (50.8%), myalgia (47.8%), runny nose (47.8%), and anosmia (47.8%). The Poisson model showed that the following signs or symptoms were associated with SARS-CoV-2 infection: fever, nasal congestion, decreased appetite, nausea, anosmia, and ageusia. Families that had more than one infected adult, in addition to the index case, presented greater transmissibility to children and adolescents.

Conclusions: Our results contribute to the hypothesis that children and adolescents are not important sources of transmission of SARS-CoV-2 in the home environment during a period of social distancing and school closure; even though they are susceptible to infection in the household (around ¼ of our study population).

KEYWORDS

adolescents, children, household infections, COVID-19, epidemiology, SARS-CoV-2

1 | INTRODUCTION

The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), remains among the greatest public health challenges in the world, contributing to a high morbidity and mortality burden in different age groups, in addition to economic and social costs for the affected countries. The pandemic character of COVID-19 was recognized by the World Health Organization (WHO) in March 2020.¹ Since then, more than a year later, there are still, increasing numbers of daily transmissions of the virus and deaths by COVID-19 in low, medium, and high-income countries.²

In the global scenario, Brazil emerged as one of the countries that has suffered the highest impact of COVID-19 in the world; the emergence of new variants of the virus among other factors, such as low testing and failure to comply with measures of social distancing, have contributed to its rapid dispersion in all major regions of the country. It is currently the second country with the highest record of accumulated cases (14,122,795) and deaths (400,000) in the world.²

The urgent need to understand the different aspects of COVID-19 and its natural history has quickly resulted in numerous published studies on the topic with substantial contributions about the disease, the management of patients, as well as the development of vaccines in record time. Specificities in the clinical presentations of COVID-19 and the transmissibility of SARS-CoV-2 were found in different populations and age groups.^{3,4} Despite advances, some questions related to the clinical and epidemiological aspects of COVID-19 continue to require evidence in the pediatric population, especially in children and adolescents who did not require hospitalization.

Studies show that in children and adolescents, SARS-CoV-2 infection ranges from asymptomatic presentation to severe clinical symptoms with a greater predominance of mild to moderate conditions.⁵ The most common clinical manifestations of COVID-19 in the pediatric population have been a variety of signs and symptoms related to acute upper respiratory tract infection such as fever, fatigue, cough, sore throat, nasal congestion, and shortness of breath.⁶ In more severe cases, patients may progress to respiratory failure, kidney injury, shock, and coagulation dysfunction, requiring mechanical ventilation and admission to the intensive care unit (ICU).⁷ However, some particularities in the clinical manifestations of COVID-19 in children have drawn attention as cases associated with multisystemic inflammatory syndrome and Kawasaki syndrome that have been reported in the pediatric population.^{8,9}

Estimates by the Centers for Disease Control and Prevention, during the first months of the pandemic in 2020, show that 1.7% of the total reported cases of COVID-19 occurred in children

under 18 years old, and 5.6% of the children who developed symptoms evolved in need of hospitalization.¹⁰ Later, data from May to December 2020 in the United States of America showed an important trend of increasing COVID-19 numbers in this age group with 1,222,023 confirmed cases among children and adolescents from 0 to 17 years of age, and most of them evolved with the presence of signs and symptoms (91.9%).¹¹

At the beginning of the pandemic, epidemiological data of SARS-CoV-2 infection in the pediatric population in Brazil revealed a profile of patients with mild manifestations, with few reports of hospitalizations and fatal outcomes. A profile that was different from that of adults, especially those over 60 years of age. With the pandemic advancing in the country in 2021, COVID-19 continued to affect children and adolescents, with an increase in cases of severe acute respiratory syndrome in the pediatric population.¹²

In the search COVID-19 control, understanding the dynamics of SARS-CoV-2 virus transmissibility in different groups of individuals in the community assumes an important role that can contribute to strategies to reduce viral dissemination and the emergence of new cases. Transmission of SARS-CoV-2 in households during periods of suspension from school activities in the pandemic has been little described in the literature. Some studies on the possible routes of infection of children and adolescents have shown secondary attack rate (SAR) that vary widely depending on the methodology, region, and population.^{4,13,14} The transmission of SARS-CoV-2 in the home environment and the role of children and adolescents in this dynamic are not clear and need to be better understood.

In Wuhan, the first epicenter of COVID-19 in the world, children, and adolescents aged 6–19 were susceptible to infection by the SARS-CoV-2 in their household, in the presence of a primary case; with a SAR of 10.8% for the assessed period.¹³ A study in Singapore reported secondary transmission of SARS-CoV-2 from an adult to a household contact child in 5.2% of evaluated families.¹⁴ In Brazil, a multicenter study found that 39% of the 79 children admitted to an ICU because of COVID-19 had contact with a suspected case, with 87% of cases from the home environment.¹⁵

The increasing number of illness cases among essential activities workers, such as those in the health field, has been one of the relevant aspects in the epidemiology of COVID-19 and makes the occupational risk of infection by SARS-CoV-2 evident. The concern with the occurrence of secondary transmission from these professionals to other people in the community, including their family nuclei, became the object of study in different places during the pandemic.¹⁶

In this context, the objective of this study was to estimate the rate of secondary attack in children and adolescents, home contacts of workers in essential activities, who were diagnosed with COVID-19, and to describe clinical and epidemiological aspects in this population.

2 | METHODS

2.1 | Study design

This is a cross-sectional and analytical study that investigated the secondary transmission of SARS-CoV-2 in children and adolescents, household contacts of essential activities workers which had been positive for SARS-CoV-2 RNA by molecular testing.

2.2 | Setting

The study was carried out in the city of Goiânia, capital of the state of Goiás (Midwest Region of Brazil), a city with approximately 1,536,097 inhabitants, 298,043 of whom are between 5 and 19 years old.¹⁷ Currently, Goiânia is a regional and national reference of the Brazilian Unified Health System (SUS) Care Network for the care of patients with COVID-19. The number of confirmed accumulated COVID-19 cases in Goiânia at the beginning of the study (June 2020) was 3,452, with 6.0% among those under 19 years old. At the end of the study (October 2020), the total number of COVID-19 cases expanded to 67,871 with an increase in cases (8.0%) among children/adolescents under 19 years old.¹⁸

Some restrictive government measures to control the progress of the pandemic in the state of Goiás were adopted as of March 2020, with the suspension of nonessential activities. In-person school activities were suspended within the public and private education sectors and were only partially resumed in January 2021.

2.3 | Study population

This study was carried out between June 15 and October 28, 2020, and it had as its starting point the identification of workers of essential activities diagnosed with COVID-19, and confirmed by RT-PCR, designated index cases. The workers in essential activities within the index cases group were: (i) health care workers (HCWs) (68.9%) such as doctors, nurses, nursing technicians, physiotherapists, among others, (ii) public security workers (PSWs) (5.6%), such as police and security guards, (iii) university-level education workers, including administrative workers, teachers, and technicians (13.1%); and (iv) others workers as urban cleaning professionals and others (12.4%). Recruitment took place at the research center structured for the development of the study. An announcement about the objectives, target audience and methods was released by the official media and websites. The attendance of the index cases occurred by appointment, and all were tested at the research center. The base sampling of recruitment of index cases was of the non-probabilistic type.

Based on the identification of the index cases, an investigation was carried out aiming at the analysis of the secondary transmission of SARS-CoV-2 to children and adolescents, who presented or not COVID-19 symptoms, in their household.

In the present study, the following inclusion criteria were adopted: (i) being aged 5–19 years and (ii) living in the same household as the index case, regardless of the degree of kinship. There was no restriction on the

number of children and adolescents per household. However, only one index case per household was considered for the study.

Children and adolescents were recruited via phone calls and text messages to the adult index case) who had tested positive for SARS-CoV-2 RNA within 10 days of identification of index cases. Clarifications about the research were made available with the scheduling of the clinical sample collection and attendance of the participants within 24–48 h after telephone contact.

2.4 | Data collection

The research data collection was performed by experienced and previously trained professionals and researchers. On the day of each participant's attendance at the sample collection site, an interview was conducted with the legal guardian to obtain sociodemographic data and potential factors associated with SARS-CoV-2 infection. Variables related to clinical signs or symptoms, housing conditions, and care related to the prevention of COVID-19 adopted at home were part of these instruments.

Nasopharyngeal and oropharyngeal swabs were obtained from each child/adolescent participant on the same day of the research interview. Clinical sample collection was carried out following the protocol, for carrying out diagnostic tests for SARS-CoV-2 and other respiratory viruses, recommended by the Brazilian Ministry of Health.¹⁹ Samples were stored at 4–8°C and processed within 24–72 hours. All samples collected were tested for SARS-CoV-2 RNA detection using RT-PCR.²⁰ The swabs were collected by trained pediatric doctors, nurses, and physiotherapists and only once in each child or adolescent, even when the result of the RT-PCR was undetermined. To estimate viral loads, children were categorized into three groups, based on the PCR amplification cycle threshold (Ct) values of their samples, as high, moderate, or low viral load (Ct < 25, 25–30, or >30, respectively), as previously suggested.²¹

2.5 | Definition and monitoring of confirmed cases of SARS-COV-2 infection by and COVID-19

The definition of confirmed cases of SARS-CoV-2 infection included laboratory and clinical-epidemiological criteria in line with the recommendations of the Ministry of Health of Brazil¹⁹ and the WHO.²²

Symptomatic or asymptomatic children and adolescents were considered positive by laboratory confirmation using the RT-PCR method, using probes and primers targeting two coronavirus regions (N1 and N2) and the human RNase P gene (internal control) (IDT). Reaction system and amplification conditions were performed according to the manufacturer's specifications in a 7500 Fast Dx Real Time PCR System (Life Technologies). The result was considered valid only when the cycle threshold (Ct) value of the reference gene was 38 or less. The result was considered positive when the Ct value of the viral genes was 38 or less and negative when it was greater than 38.

A confirmed case of COVID-19, by clinical-epidemiological criteria, was defined as an individual with nondetectable SARS-CoV-2 RNA by RT-PCR in nasopharyngeal and oropharyngeal swab but that presented the following criteria: Flu Syndrome or Severe Acute Respiratory Syndrome associated with anosmia (olfactory dysfunction) or ageusia (gustatory dysfunction) without any other previous cause; in addition to a history of home contact with an index case.¹⁹

Recommendations and guidelines from the Ministry of Health of Brazil were used as a theoretical reference for the classification of clinical presentations of COVID-19 in Flu Syndrome mild, moderate or Severe Acute Respiratory Syndrome.¹⁹ The presence of rash and conjunctivitis were considered as possible atypical signs of COVID-19. Cases not clinically classified as Flu Syndrome, Severe Acute Respiratory Syndrome, or atypical were classified in the category of "other" clinical presentations. The individuals classified as asymptomatic were those with no report or finding of any clinical sign or symptom surveyed on the day of the appointment despite having tested positive for SARS-CoV-2 RNA by RT-PCR.

Essential activity workers with COVID-19, confirmed by the RT-PCR, were considered the primary case (index cases) at their households. Their respective infected household contacts were defined as secondary case or secondary transmission cases.

The clinical evolution of children and adolescents was monitored for 14 days from the date of clinical material collection for laboratory testing. A telephone monitoring service and a checklist with targeted questions were organized for this purpose. The contact was made on the 7th and on the 14th day of follow-up when monitoring ended. Questions related to the presence or absence of signs and symptoms, occurrence of hospitalization, complications, and death were recorded.

2.6 | Clinical signs and symptoms

For analysis purposes, the clinical signs and symptoms reported by home contacts, on the swab collection date, were grouped into categories: (i) systemic: fever, myalgia, fatigue, arthralgia, and hypoxia; (ii) high respiratory: sore throat, runny nose, nasal congestion; (iii) low respiratory: cough, dyspnea, chest pain; (iv) neurological: headache, anosmia, ageusia; (v) digestive: abdominal pain, nausea, vomiting, and diarrhea; (vi) rash and conjunctivitis.

2.7 | Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences software, 25.0 version. The Kolmogorov-Smirnov normality test with Lilliefors correction was used to evaluate the normality of the variable age. Initially, an exploratory analysis of the main demographic, clinical, and laboratory characteristics of the study participants was carried out. Quantitative variables were described as the median and interquartile range (IQR) due to the absence of normality. Qualitative variables were described as absolute (n) and relative (%) frequencies.

Then, the two groups (positive or negative for SARS-CoV-2) were compared using Fisher's exact test (qualitative variables) or Mann-Whitney U test (quantitative variables). Variables related to signs and symptoms with, sex and, age (quantitative variable) of children and adolescents were included in the regression model (p -value $< .20$) with robust variance, to verify the signs and symptoms associated with SARS-CoV-2 infection. The results of the regression model were presented with aPR (adjusted prevalence ratio), 95.0% Confidence Interval (95.0% CI), regression coefficient (β), and p value. Statistical significance was established using the Wald test. The sensitivity analysis of the signs and symptoms associated with SARS-CoV-2 infection was also conducted including positivity as a dependent variable only by laboratory confirmation.

Also, confirmed cases of SARS-COV-2 infection were grouped into symptomatic and asymptomatic groups and compared concerning the variables sex, age (quantitative variable and age group), race/skin color, comorbidities, and viral load (quantitative variable and viral load group) using Mann-Whitney U test or Fisher's exact test.

The SAR was calculated for households with a single primary case and was defined as the proportion of secondary infections detected among all household children and adolescents participating in the study. Individuals who lived in the same household were not distinguished in the analysis. Bivariate Poisson regression was used to obtain the rate ratio (RR) and 95.0% IC between the SAR according to categories of variables related to cases index (sex, profession group, number of adults living in house—group, number of rooms in house—group, economic class, bond with children and adolescent, and additional infected adult in the family) and variables of children and adolescents (sex, age group, race/skin color, presence of signs and symptoms, and comorbidities).

The variables of the index cases were categorized into: sex (male or female), profession group (HCWs, PSWs, Education workers and, others), number of adults living in house (≤ 2 or > 2), Number of rooms in house (≤ 6 or >6), economic class (A/B [\geq U\$\$ 2,280.00] or C/D/E [$<$ U\$\$ 2,280.00], bond (mother, father or others) and, another infected adult in the family (no or yes). Quantitative variables were categorized according to the median, except for the economic class in which the Brazilian Institute of Geography and Statistics classification was used. The variables of children and adolescents were categorized into: sex (male or female), age group (5-9 years, 10-14 years or 15-19 years), race/skin color (white, mixed race/black and others [Asian or native American], presence of signs and symptoms (symptomatic or asymptomatic), comorbidity (absent or present), and Ct as mentioned earlier.

In all analyzes, variables with a p -value < 0.05 were considered statistically significant.

2.8 | Ethics and consent

This study was approved by the Research Ethics Committee of the Clinical Hospital, Federal University of Goiás, protocol n. 4.173.690/2020. Verbal assent was obtained by all children and adolescents

included in the study. Also, verbal consent was obtained by the legal guardian of all participants. Only verbal consent was obtained with two researchers serving as witnesses, because of the risk of infection by SARS-CoV-2 due to contact with possibly contaminated surfaces and objects.

3 | RESULTS

3.1 | Selection of participants

Figure S1 summarizes the participants' selection flowchart. Of the 825 patients suspected of COVID-19, 18 (2.2%) refused to go through nasopharyngeal and oropharyngeal swab collection for the real-time RT-PCR test. Of the potentially eligible patients ($n = 807$), 421 (52.2%) were positive for SARS-CoV-2 RNA by real-time RT-PCR and, of these, 187 (44.4%) were included as index cases in the study. Lastly, 267 children and adolescents, household contacts of index cases were investigated for SARS-CoV-2 RNA.

3.2 | Prevalence of SARS-CoV-2

The prevalence of SARS-CoV-2, assessed by real-time RT-PCR test, in children and adolescents was 19.9% (95.0% CI = 15.5–25.1; 53/267). In addition, 5.2% (14/267) of the children tested negative for the SARS-CoV-2 RNA. However, they presented anosmia/ageusia and flu syndrome, being therefore considered confirmed cases of SARS-CoV-2 infection by clinical diagnosis, which resulted in an overall prevalence of 25.1% (95.0% CI = 20.3–30.6; 67/267) (Figure 1).

3.3 | Factors associated with SARS-CoV-2 infection

Table 1 shows the descriptive and comparative analysis of the demographic and clinical characteristics of case index and children and adolescents positive and negative for SARS-CoV-2.

The index cases were predominantly female (53.25), HCWs (68.9%) and belonged to economic class C/D/E (93.6%). The most frequent family link was the mother (57.7%) and in 33.0% additional adult in the family was infected with SARS-CoV-2. The median age of the children and adolescents was 11 years old (IQR = 8) and the majority (64.8%) were teenagers aged 10–19 years old (28.8% between 10 and 14 years old and 36.0% between 15 and 19 years old); 48.3% were self-declared to be black/brown. The majority (55.1%) of the participants had symptoms of SARS-CoV-2 infection. Of the total, 17.7% of the participants had at least one type of comorbidity. Asthma was the most prevalent comorbidity in the sample (10.1%) (Table 1).

The positive and negative groups for SARS-CoV-2 were similar regarding the characteristics of the index and family cases (p -value $\geq .05$). However, there was a greater proportion of positive children and adolescents in families that another adult was positive, in addition to the index case when compared to negative (55.2% vs. 25.5%; p -value $< .001$).

In the bivariate analysis of the comparison between positive and negative SARS-CoV-2 groups, there was no statistical difference between the groups regarding age, sex, and race/skin color of children and adolescents (p -value $\geq .05$). In the group of individuals with SARS-CoV-2, 10 participants (14.9%) had no signs and symptoms of COVID-19. On the other hand, among those that did not have detectable SARS-CoV-2 infection, 87 (43.5%) reported some symptoms

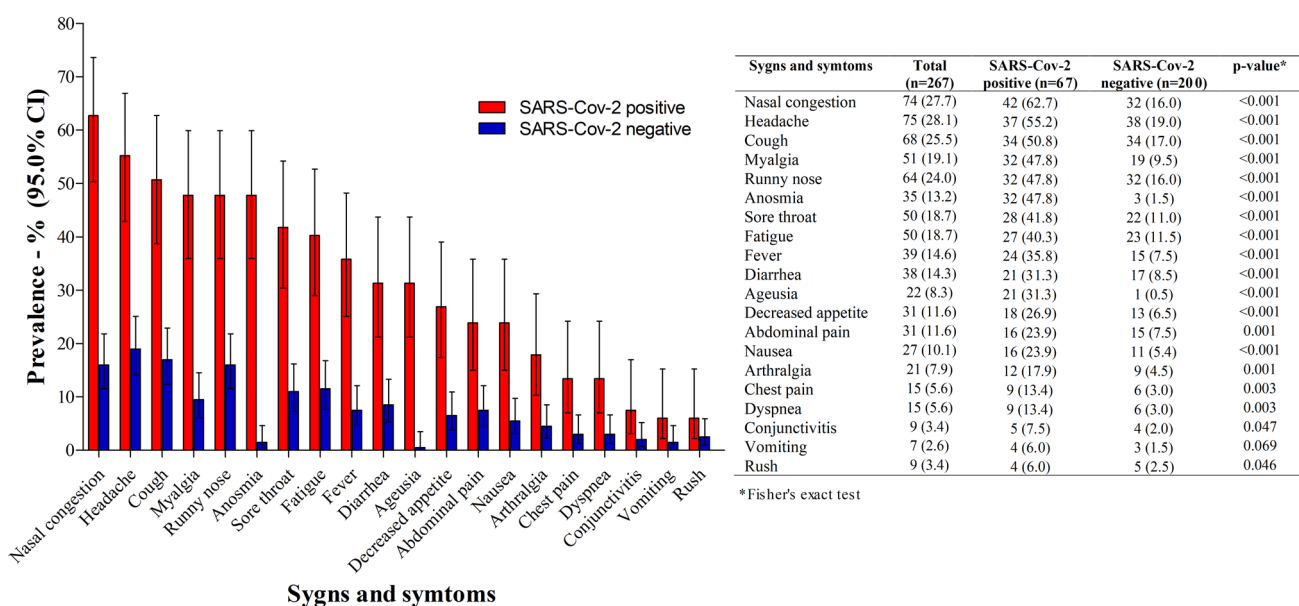


FIGURE 1 Comparative analysis of the signs and symptoms presented by children and adolescents (household contacts of index cases) between positive and negative for SARS-CoV-2

TABLE 1 Demographic and clinical characteristics of index cases and children and adolescents (household contacts) in the positive and negative SARS-CoV-2-groups

Variables	Total (n = 267)	SARS-CoV-2 positive (n = 67)	SARS-CoV-2 negative (n = 200)	p value
Index cases				
Sex, n (%)				
Male	125 (46.8)	30 (44.8)	95 (47.5)	.778*
Female	142 (53.2)	37 (55.2)	105 (52.3)	
Profession group, n (%)				
HCWs	184 (68.9)	40 (59.7)	144 (72.0)	.168*
PSWs	15 (5.6)	4 (6.6)	11 (5.5)	
Education workers	35 (13.1)	10 (14.9)	25 (12.5)	
Others	33 (12.4)	13 (19.4)	20 (10.0)	
Number of adults living in house, median (IQR)	2 (1)	2 (1)	2 (1)	.394 [†]
Number of adults living in house—group, n (%)				
≤2	183 (68.5)	42 (62.7)	141 (70.5)	.287*
>2	84 (31.5)	25 (37.3)	59 (29.5)	
Number of rooms in house, median (IQR)	6 (3)	6 (3)	6 (3)	.064 [†]
Number of rooms in house—group, n (%)				
≤6	150 (56.2)	41 (61.2)	109 (54.5)	.384*
>6	117 (43.8)	26 (38.8)	91 (45.5)	
Income family (US\$), median (IQR)	1140.0 (722.6)	950.0 (798.6)	1292.6 (722.6)	.072 [†]
Economic class, n (%)				
A/B	17 (6.4)	6 (9.0)	11 (5.5)	.384*
C/D/E	250 (93.6)	61 (91.0)	189 (94.5)	
Bond with children and adolescent, n (%)				
Mother	154 (57.7)	38 (56.7)	116 (58.0)	.835*
Father	71 (26.6)	17 (25.4)	54 (27.0)	
Others	42 (15.7)	12 (17.9)	30 (15.0)	
Additional infected adult in the family, n (%)				
No	179 (67.0)	30 (44.8)	149 (74.5)	<.001*
Yes	88 (33.0)	37 (55.2)	51 (25.5)	
Children and adolescents				
Sex, n (%)				
Male	125 (46.8)	30 (44.8)	95 (47.5)	.778*
Female	142 (53.2)	37 (55.2)	105 (52.5)	
Age (years), median (IQR)	11 (8)	13 (8)	11 (7)	.058 [†]
Age group (years), n (%)				
5–9	94 (35.2)	18 (26.9)	76 (38.0)	.250*
10–14	77 (28.8)	21 (31.3)	56 (28.0)	
15–19	96 (36.0)	28 (41.8)	68 (34.0)	

(Continues)

TABLE 1 (Continued)

Variables	Total (n = 267)	SARS-CoV-2 positive (n = 67)	SARS-CoV-2 negative (n = 200)	p value
Race/skin color, n (%)				
White	123 (46.1)	28 (41.8)	95 (47.5)	.736*
Mixed race/black	129 (48.3)	35 (52.3)	95 (47.0)	
Others	15 (5.6)	4 (6.0)	11 (5.5)	
Presence of signs and symptoms, n (%)				
Symptomatic	144 (53.9)	57 (85.1)	87 (43.5)	<.001*
Asymptomatic	123 (46.1)	10 (14.9)	113 (56.5)	
Comorbidity, n (%)				
Absent	221 (82.8)	51 (76.1)	170 (85.0)	.133*
Present	46 (17.2)	16 (23.9)	30 (15.0)	
Type of comorbidity, [‡] n (%)				
Asthma	27 (10.1)	10 (14.9)	17 (8.5)	.159*
Chronic gastrointestinal disease	6 (2.2)	2 (3.0)	4 (2.0)	.643*
Congenital cardiopathic	4 (1.5)	1 (1.5)	3 (1.5)	1.000*
Chronic kidney disease	4 (1.5)	-	4 (2.0)	.575*
Chronic neurological disease	4 (1.5)	2 (3.0)	2 (1.0)	.263*
CPD	3 (1.1)	1 (1.5)	2 (1.0)	1.000*
Diabetes mellitus	2 (0.7)	1 (1.5)	1 (0.5)	.440*
Hypertension	1 (0.4)	-	1 (0.5)	1.000*
Chronic liver disease	1 (0.4)	-	1 (0.5)	1.000*
Asplenia	1 (0.4)	-	1 (0.5)	1.000*
Cancer	1 (0.4)	1 (1.5)	-	.251*
Chronic hematological disease	-	-	-	-
HIV/AIDS	-	-	-	-

Abbreviations: AIDS, acquired immunodeficiency syndrome; CPD, chronic pulmonary disease; HCW, health care workers; HIV, human immunodeficiency virus; IQR, interquartile range; PSW, public security worker.

*Fisher's exact test.

†Mann-Whitney *U* test.

‡Variable with multiple responses.

of COVID-19. As expected, there was a higher proportion of symptomatic patients in the positive than negative SARS-CoV-2 RNA group (85.1% vs. 45.5%; *p*-value < .001) (Table 1).

Figure 1 shows the comparison of symptoms, considering the two study groups (SARS-CoV-2 RNA positive and SARS-CoV-2 RNA negative). The results showed a significant difference (*p*-value < .05) between the groups regarding all signs and symptoms investigated, except for vomiting (*p* = .069). The most prevalent symptoms in positive individuals were nasal congestion (62.7%), headache (55.2%), cough (50.8%), myalgia (47.8%), runny nose (47.8%), and anosmia (47.8%). The least frequent were conjunctivitis (7.5%), vomiting (6.0%), and skin rash (6.0%).

When patients with SARS-CoV-2 infection were evaluated by age group, the observed frequencies of concomitant anosmia and ageusia were 15.8%, 26.3%, and 57.9%, in the 5 to 9 years group, 10 to 14 years group, and in the 15 to 19 years group, respectively. In the negative SARS-CoV-2 RNA group, only one patient presented these dysfunctions simultaneously (data not shown).

Table 2 shows the group of signs and symptoms and clinical manifestation in the positive and negative SARS-CoV-2 groups. There was a higher prevalence of systemic, upper respiratory, lower respiratory, neurological, and gastrointestinal manifestations in the group of individuals with detectable SARS-CoV-2 RNA when compared to the negative SARS-CoV-2 group (*p*-value < .001).

TABLE 2 Symptomatology and clinical presentation of children and adolescents (household contacts of index cases) that were positive or negative for SARS-CoV-2

Variables	Total (n = 267)	SARS-CoV-2 positive (n = 67)	SARS-CoV-2 negative (n = 200)	p value
Signs and Symptoms groups, [†] n (%)				
Systemic	76 (28.5)	41 (61.2)	35 (17.5)	<.001*
Upper respiratory	91 (34.1)	45 (67.2)	46 (23.0)	<.001*
Lower respiratory	73 (27.3)	35 (52.2)	38 (19.0)	<.001*
Neurological	84 (31.5)	45 (67.2)	39 (19.5)	<.001*
Gastrointestinal	59 (22.1)	32 (47.8)	27 (13.5)	<.001*
Clinical presentation, n (%)				
Asymptomatic	123 (46.1)	10 (14.9)	113 (56.5)	<.001*
Mild flu syndrome	106 (39.7)	47 (70.1)	59 (29.5)	
Moderate flu syndrome	6 (2.2)	6 (9.0)	-	
Severe flu syndrome**	-	-	-	
Atypical	10 (3.7)	1 (1.5)	9 (4.5)	
Others	22 (8.2)	3 (4.5)	19 (9.5)	

*Fisher's exact test.

[†]Variable with multiple responses.

**There were no cases of hospitalization or deaths recorded during follow up period—up to 14 days after clinical sample collection).

As for the clinical presentation, 70.1% of the positive cases had mild flu syndrome, 9.0% moderate flu syndrome, 1.5% atypical symptoms, and 4.5% other clinical manifestations. There were no hospitalizations or deaths in the 14-day follow-up of the positive and negative SARS-CoV-2 RNA groups. In addition, 29.5% of the participants negative for SARS-CoV-2 had mild flu syndrome (Table 2). There was a statistical difference regarding the clinical presentation forms between the groups (p -value < .001).

Table 3 summarizes the results of the multiple Poisson regression analysis of signs and symptoms associated with SARS-CoV-2 infection in children and adolescents. The adjusted model showed that the following factors were associated with SARS-CoV-2 infection: fever (aPR: 1.86; 95.0% CI: 1.08–3.21), nasal congestion (aPR: 2.96; 95.0% CI: 1.77–4.96), decreased appetite (aPR: 2.00; 95.0% CI: 1.37–2.92), nausea (aPR: 1.92; 95.0% CI: 1.16–3.19), anosmia (aPR: 3.09; 95.0% CI: 1.95–4.90) and ageusia (aPR: 1.80; 95.0% CI: 1.15–2.81). The adjusted model showed an excellent fit: $\chi^2 = 1117.3773$, $p = 1.000$; $R^2 = 0.211$).

3.4 | Sensitivity analysis

The sensitivity analysis of factors associated with SARS-CoV-2 was conducted, including in the regression model the positivity for SARS-CoV-2 RNA by real-time RT-PCR as the dependent variable (real-time RT-PCR: 214 vs. real-time RT-PCR+: 53). The Poisson regression model showed that the following factors were associated with SARS-CoV-2 infection: fever (aPR: 1.85; 95.0% CI: 1.05–3.25), nasal

TABLE 3 Multiple regression analysis of the signs and symptoms associated with SARS-CoV-2 infection in children and adolescents (household contacts of index cases)

Variables	aPR	95.0% CI	β	p value*
Fever	1.86	1.08–3.21	0.62	.025
Nasal congestion	2.96	1.77–4.96	1.09	<.001
Decreased appetite	2.00	1.37–2.92	0.69	<.001
Nausea	1.92	1.16–3.19	0.65	<.001
Anosmia	3.09	1.95–4.90	1.13	<.001
Ageusia	1.80	1.15–2.81	0.59	.009

Note: Model adjusted for sex and age of children and adolescents and all signs and symptoms for COVID-19 investigated.

Abbreviations: β , regression coefficient; aPR, adjusted prevalence ratio; 95.0% CI, 95.0% confidence interval.

*Wald statistic.

congestion (aPR: 2.66; 95.0% CI: 1.50–4.73), decreased appetite (aPR: 2.04; 95.0% CI: 1.34–3.10), diarrhea (aPR: 1.60; 95.0% CI: 1.35–3.58), nausea (aPR: 2.19; 95.0% CI: 1.35–3.58) and anosmia (aPR: 2.95; 95.0% CI: 1.79–4.84). The models were similar in terms of the associated factors, except for diarrhea associated only with the positivity for SARS-CoV-2 RNA by real-time RT-PCR; and loss of statistical significance of ageusia in this model. The adjusted model showed an excellent fit: $\chi^2 = 121.1826$, $p = 1.000$; $R^2 = 0.191$) (Table S1).

3.5 | Comparison between symptomatic and asymptomatic SARS-CoV-2 infection

Table 4 summarizes the characteristics of children and adolescents according to the presence or absence of signs and symptoms associated with SARS-CoV-2 infection. There was no significant difference considering age group, race/skin color, comorbidity, and viral load (Ct) between the symptomatic and asymptomatic groups (p -value $\geq .05$). However, the median age was statistically higher in symptomatic individuals when compared to asymptomatic individuals (14 years vs. 10 years; p -value = .022). Regarding viral loads, we found a median Ct of 31 (IQR = 11). We also observed that 52.1% of the children had what was considered low viral loads. We did not find a significant median difference in viral loads between symptomatic and asymptomatic patients (p -value = .280).

3.6 | Secondary attack rate

Table 5 summarizes the SAR in the study sample. There was no relationship between SAR and sex, age group, race/color, and

comorbidity of children and adolescents, as well as among the characteristics of the index cases (p -value $\geq .05$). However, it was observed that the SAR in families that had more than one infected adult, in addition to the index case, it was 1.50 times higher than those without this feature (RR: 1.50; 95.0% CI: 1.55–4.06). Also, it was observed that the SAR in symptomatic contacts was 4.87 times higher when compared to that of the nonsymptomatic group (RR: 4.87; 95.0% CI: 2.49–9.53).

4 | DISCUSSION

This study revealed considerable transmissibility of SARS-CoV-2 in a sample of children and adolescents that were household contacts of essential activities workers, diagnosed with COVID-19 in Goiânia, Central Brazil. The general SAR showed that a quarter of the sample was infected, confirming the risk and the susceptibility of this group to household infection. Unlike most of the investigations available in the literature, the study population consisted of children and adolescents who were not hospitalized, and that were asymptomatic or symptomatic for COVID-19. This will certainly contribute to a better

Variables	Total (n = 67)	Symptomatic (n = 57)	Asymptomatic (n = 10)	p value
Sex, n (%)				
Male	30 (44.8)	27 (47.4)	3 (30.0)	.493*
Female	37 (55.2)	30 (52.6)	7 (70.0)	
Age (years), median (IQR)	13 (8)	14 (8)	10 (4)	.022 [†]
Age group (years), n (%)				
5–9	18 (26.9)	13 (22.8)	5 (50.0)	.169*
10–14	21 (31.3)	18 (31.6)	3 (50.0)	
15–19	28 (41.8)	26 (45.6)	2 (20.0)	
Race/skin color, n (%)				
White	28 (41.8)	25 (43.9)	3 (30.0)	.630*
Mixed race/black	35 (52.2)	28 (49.1)	7 (70.0)	
Others	4 (6.0)	4 (7.0)	-	
Comorbidity, n (%)				
Absent	51 (76.1)	45 (79.0)	6 (60.0)	.234*
Present	16 (23.9)	12 (21.1)	4 (40.0)	
Viral load (Ct), median (IQR)	31 (11)	30 (12)	34 (9)	.280 [†]
Viral load—group, n (%) [‡]				.514*
High	14 (29.2)	13 (32.5)	1 (12.5)	
Intermediate	9 (18.8)	8 (20.0)	1 (12.5)	
Low	25 (52.0)	19 (47.5)	6 (75.0)	

TABLE 4 Characteristics of symptomatic and asymptomatic children and adolescents positive for SARS-CoV-2 (household contacts of index cases)

Abbreviations: Ct, cycle threshold; IQR, interquartile range.

*Fisher's exact test.

[†]Mann-Whitney *U* test.

[‡]Of 48 children for whom the cycle thresholds were available.

TABLE 5 Characteristics of secondary transmission of SARS-CoV-2 among children and adolescents (household contacts of index cases)

Variables	Secondary cases (n = 67)	Total household contacts (n = 267)	SAR	RR (95.0% CI)	p value*
Index cases					
Sex					
Male	30	125	24.0	1.00	
Female	37	142	26.1	1.05 (0.63–1.73)	.863
Profession group					
HCWs	40	184	21.7	1.00	
PSWs	4	4	26.7	1.23 (0.44–3.43)	.697
Education workers	10	10	28.6	1.31 (0.66–2.63)	.440
Others	13	13	39.4	1.81 (0.97–3.39)	.063
Number of adults living in house–group					
≤2	42	183	23.0	1.00	
>2	25	84	29.8	1.30 (0.79–2.13)	.304
Number of rooms in house–group					
≤6	41	150	27.3	1.00	
>6	26	117	22.2	0.81 (0.50–1.33)	.409
Economic class					
A/B	6	17	35.3	1.00	
C/D/E	61	250	24.4	0.69 (0.30–1.60)	.388
Bond with children and adolescent					
Mother	38	154	24.7	1.00	
Father	17	71	23.9	0.97 (0.55–1.72)	.918
Others	12	42	28.6	1.16 (0.60–2.22)	.658
Additional infected adult in the family					
No	30	179	26.8	1.00	
Yes	37	88	42.0	2.50 (1.55–4.06)	<.001
Children and adolescents					
Sex					
Male	30	125	24.0	1.00	
Female	37	142	26.1	1.08 (0.67–1.76)	.738
Age group (years)					
5–9	18	94	19.2	1.00	
10–14	21	77	27.3	1.32 (0.76–2.67)	.271
15–19	28	96	29.2	1.52 (0.84–2.75)	.164
Race/skin color					
White	28	123	22.8	1.00	
Mixed race/black	35	129	27.1	1.19 (0.73–1.95)	.489
Others	4	15	26.7	1.17 (0.41–3.34)	.767
Presence of signs and symptoms					
Asymptomatic	10	123	8.1	1.00	
Symptomatic	57	144	39.6	4.87 (2.49–9.53)	<.001

(Continues)

TABLE 5 (Continued)

Variables	Secondary cases (n = 67)	Total household contacts (n = 267)	SAR	RR (95.0% CI)	p value*
Comorbidity					
Absent	51	221	23.1	1.00	
Present	16	46	34.8	1.50 (0.86–2.64)	.152
General	67	267	25.1	-	-

Abbreviations: 95.0% CI, 95.0% confidence interval; RR, rate ratio; SAR, secondary attack rate.

*Wald statistic.

understanding of transmissibility and potential of infection by SARS-CoV-2 among individuals with nonserious clinical presentations of COVID-19, in addition to supporting public management policies for clinical practice and epidemiological surveillance.

In general, since the beginning of the pandemic, the clinical presentation of COVID-19 in children has been less severe than in adults.⁵ For the group of adolescents, there are few reports in the literature.^{3,23} A study carried out in New York (USA) showed that the course of SARS-CoV-2 infection and the course of the immune response are different in adult and pediatric patients.²⁴ Children have fewer severe respiratory symptoms, but they can sometimes develop the life-threatening multisystemic inflammatory syndrome. This evidence possibly partially justifies the less severe outcome among children when compared to the adult population.

In the present study, although the majority of those infected with SARS-CoV-2 evolved with the presence of some sign and symptom (85.0%), the predominant clinical form was mild influenza syndrome, which corroborates previous investigations conducted in children and adolescents.^{7,9} Studies carried out on hospitalized children and adolescents suggest a higher index of severity and ICU admissions, especially in the 1st year of life and in the presence of comorbidities.^{7,25} In the 14 days of follow-up of the individuals included in the study, we did not find any case of severe flu syndrome and consequent hospitalization or death. This may be related to the fact that children less than five years of age were not included in the study; additionally, two-thirds of the participants that had detectable SARS-CoV-2 RNA did not have comorbidities as potential aggravating factors.

The presence of anosmia and ageusia in SARS-CoV-2 positive children has been poorly recorded in previous studies, possibly due to the difficulty in characterizing these symptoms in the pediatric population. Similar to what has been reported,^{26,27} we found a higher frequency of anosmia and ageusia in infected adolescents over 15 years old and a lower frequency in infected children between 5 and 9 years old. These symptoms are currently considered sentinels for the diagnosis of COVID-19 (sentinel symptoms).²² Our results showed a higher prevalence of anosmia and ageusia in the group of SARS-CoV-2 RNA-positive participants compared to that of SARS-CoV-2 RNA-negative, suggesting that the presence of these symptoms can be useful in the clinical diagnosis of SARS-CoV-2 infection in those over 5 years of age.

In our study, fever, nasal congestion, lack of appetite, and nausea were associated with infection by SARS-CoV-2 in multiple regression analysis. However, these signs and symptoms are frequently present in other respiratory virus infections that are common during childhood.^{28,29} Therefore, the similarity of these associated COVID-19 symptoms with those of different viral infections can prevent suspected cases of the disease from being recognized and contribute to an underestimated number of cases in this age group.

It has been indicated that fever and cough are the most prevalent signs and symptoms of COVID-19 in children and adolescents,^{7,15,25} and a meta-analysis study also revealed that the most common clinical signs and symptoms of COVID-19 in this population were fever and cough.³⁰

In our study sample, upper respiratory symptoms, especially nasal congestion; and neurological symptoms, especially headache, were the most prevalent in COVID-19 patients, as reported by other studies.^{7,9,11} It is important to note that these symptoms do not usually correlate with the severity of the disease. However, the presence of lower respiratory symptoms, mainly dyspnea and chest pain, are commonly associated with severity and hospitalization by COVID-19.^{7,15,31} The low frequency of these symptoms that signal severity in our study is justified since mild flu syndrome accounted for 70.1% of the clinical presentations of the study population. Fever, in particular, was present in only 35.8% of those positive for SARS-CoV-2 RNA; however, it was associated with infection by SARS-CoV-2 in multiple regression analysis.

To date, few studies have assessed secondary transmission of SARS-CoV-2 involving children and adolescents. A systematic review on the topic found wide variation in the values of the secondary household attack rates for SARS-CoV-2 in different countries and age groups.³² However, studies have reported rates of secondary general attack with values from 4.6% to 62.3%.^{32–34}

We showed that children and adolescents are susceptible to infection by SARS-CoV-2 within the household as a consequence of close contact with an infected adult living in the same home. A recent study conducted in Brazil also points out in this direction. Lugon et al.³⁵ found that 13.9% of children and adolescents less than 14 years of age living at home with infected adults tested positive for SARS-CoV-2 RNA by real-time RT-PCR. We report a higher rate of household transmission of SARS-CoV-2 to children and adolescents, which may have occurred due to methodological differences, such as

differences in the participants' age between studies, sample collection, and testing considering the time of contact, amongst others. We also included the epidemiological clinical criterion in the definition of a confirmed case, unlike previous studies that used only the laboratory criterion for diagnosis. In addition, a previous study showed that the heterogeneity in secondary domestic attack rates in different regions is probably due to differences in the compliance of prevention measures, surveillance practices, and lack of physical distancing among family members living in the same house.³⁰

It is known that the secondary transmission of SARS-CoV-2 can be related to several factors, including biological, behavioral, and contextual determinants.⁴ Our study showed that families that had more than one infected adult, in addition to the index case, presented greater transmissibility to children and adolescents. Among the multiple factors that may have influenced the SAR and that were not investigated is the lack of physical contact restriction, not wearing masks at home, and false beliefs related to disease prevention.³⁶ In the present study, the inevitability of domestic coexistence, especially in the family relationship with children, who demand daily care, may have contributed to the overall SAR verified. In addition, although the index cases in this investigation are mostly HCWs, with supposed knowledge about measures to prevent the spread of SARS-CoV-2, the transmission may have occurred early on, during the presymptomatic stage of these cases³⁷ and preceding the adoption of stricter preventive measures. Aspects related to social vulnerability and socioeconomic impact of protection measures may also influence family behaviors, and, therefore, increase transmission.³⁸

Our results contribute to the growing hypothesis throughout the pandemic that children and adolescents are not important sources of transmission of SARS-CoV-2 in the home environment during a period of social distancing and suspended school activities. In line with this hypothesis, a study in India showed a low rate of secondary attack (1.7%) for adults from children as index cases.³⁹ Also in this direction, a meta-analysis on the home transmission of SARS-CoV-2 identified children as a source of contagion at home in only 4.0% of the detected cases of secondary infection. In turn, adults, when identified as index cases, accounted for 97.8% of cases of secondary infection that occurred in the home environment.⁴⁰

Viral load was higher in symptomatic individuals when compared to the loads from those without symptoms, although without statistical difference. We found that about 15% of children and adolescents infected with SARS-CoV-2 were asymptomatic and this group had lower viral loads. It has been suggested that children and adolescents may harbor the virus, but this may not translate into transmissibility and therefore, they play a minor role in transmission.⁴¹

Our study has some limitations. The cross-sectional nature of the investigation does not allow the establishment of a causal relationship between the independent variables analyzed and the SARS-CoV-2 infection with the SAR in children and adolescents. Also, the non-probabilistic sample employed does not allow the generalization of the obtained results for other children and adolescents in contact with people infected by SARS-CoV-2. The data relating to the comorbidities and signs and symptoms of COVID-19 were self-

reported, subject to memory, and response biased. Some variables, such as comorbidities, had low prevalence and therefore lacked statistical power to verify the differences between the SARS-CoV-2 RNA negative and SARS-CoV-2 RNA positive groups. The collected data made it impossible to analyze the sensitivity of risk factors for infection with SARS-CoV-2 in subgroups of children and adolescents. Furthermore, all children and adolescents were tested, regardless of the date, distance kept from the index case, and time of contact with the index cases (data not available), in addition to being tested only once and, in the case of symptomatic cases, we did not consider the date of onset of symptoms and also did not conduct serologic tests, which may have underestimated the magnitude of the verified rates.

However, our study has several strengths. A relatively robust sample was used, when compared to previously published investigations, especially from developing countries, to investigate factors associated with SARS-CoV-2 and the rate of a secondary attack. Our sample consisted of children and adolescents not hospitalized, unlike most studies reported in the literature. In the positivity estimate, we included cases that presented clinical-epidemiological evidence for confirmation of SARS-CoV-2 infection, in addition to the laboratory diagnosis criteria. We also assessed the prevalence of the main comorbidities in the group and their influence on positivity. Finally, we also investigated a large set of signs and symptoms of SARS-CoV-2, including symptoms of anosmia and ageusia in children and adolescents, little reported in previous studies in this population. We also analyzed the main signs and symptoms that predict SARS-CoV-2 infection in children and adolescents through multiple regression analysis.

Data presented showed that children and adolescents, even in situations of social withdrawal and with suspended school activities, are susceptible to infection by the SARS-CoV-2 virus in the home environment. We found that $\frac{1}{4}$ of the children and adolescents were infected with the SARS-CoV-2 virus. In this cohort, there was no record of hospitalization or death. The vast majority of clinical presentations were mild or even asymptomatic. Our data suggests that olfactory and taste disorders may be useful for clinical screening of COVID-19 in children over 5 years of age. These findings are useful for the establishment of COVID surveillance and control strategies and may support certain decision-making, such as the return to school activities. The dynamics of home transmission of the SARS-CoV-2 virus observed in the present study reinforces the need for continuous surveillance in this population.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Eliane T. Afonso: conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); project administration (equal); supervision (equal); validation (equal); visualization (equal); writing original draft (equal); writing review & editing (equal). **Solomar M. Marques:** conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); project administration (equal); supervision (equal); validation (equal); visualization (equal); writing original draft (equal). **Lusmaia D. C. Costa:**

conceptualization (equal); data curation (equal); investigation (equal); methodology (equal); validation (equal); visualization (equal); writing original draft (equal). **Patrícia M. Fortes**: conceptualization (equal); data curation (equal); investigation (equal); methodology (equal); writing original draft (equal). **Fernanda Peixoto**: conceptualization (equal); data curation (equal); investigation (equal); methodology (equal); writing original draft (equal). **Danielli C. Bichueti-Silva**: conceptualization (equal); data curation (equal); investigation (equal); methodology (equal). **Natália D. A. Aredes**: conceptualization (equal); investigation (equal); methodology (equal); writing original draft (equal). **Claci F. W. Rosso**: conceptualization (equal); investigation (equal); methodology (equal); project administration (equal); supervision (equal). **Faétila dos S. Oliveira**: conceptualization (equal); data curation (equal); investigation (equal); methodology (equal). **Fabiola S. Fiaccadori**: methodology (equal); writing review & editing (equal). **Menira B. de L. D. e Souza**: methodology (equal); writing review & editing (equal). **Elisângela de P. Silveira-Lacerda**: methodology (equal). **Clayton L. Borges**: conceptualization (equal); data curation (equal); methodology (equal). **Juliana A. P. Rocha**: conceptualization (equal); data curation (equal); methodology (equal). **Alessandra V. Naghettini**: conceptualization (equal); data curation (equal); investigation (equal); methodology (equal); project administration (equal); supervision (equal); validation (equal); visualization (equal); writing original draft (equal); writing review & editing (equal). **Paulo S. S. da Costa**: conceptualization (equal); data curation (equal); methodology (equal); writing original draft (equal); writing review & editing (equal). **Rafael A. Guimarães**: conceptualization (equal); formal analysis (equal); investigation (equal); methodology (equal); project administration (equal); supervision (equal); validation (equal); visualization (equal); writing original draft (equal); writing review & editing (equal).

DATA AVAILABILITY STATEMENT

The crude data generated in this study can be made available upon request and justification to the corresponding author considering the national and international guidelines of ethics in research with human beings.

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SUPPORTING INFORMATION

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

How to cite this article: Afonso ET, Marques SM, Costa LDC, et al. Secondary household transmission of SARS-CoV-2 among children and adolescents: Clinical and epidemiological aspects. *Pediatric Pulmonology*. 2022;57:162-175. doi:10.1002/ppul.25711