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SARS-CoV-2 Infection Dynamics in Children and Household Contacts in a Slum in Rio de Janeiro

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abstract

OBJECTIVES: To investigate the dynamics of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in a vulnerable population of children and their household contacts.

METHODS: SARS-CoV-2 reverse transcription polymerase chain reaction assays and coronavirus disease 2019 (COVID-19) immunoglobulin G serology tests were performed in children and their household contacts after enrollment during primary health care clinic visits. Participants were followed prospectively with subsequent specimens collected through household visits in Manguinhos, an impoverished urban slum (a favela) in Rio de Janeiro at 1, 2, and 4 weeks and quarterly post study enrollment.

RESULTS: Six hundred sixty-seven participants from 259 households were enrolled from May to September 2020. This included 323 children (0–13 years), 54 adolescents (14–19 years), and 290 adults. Forty-five (13.9%) children had positive test results for SARS-CoV-2 polymerase chain reaction. SARS-CoV-2 infection was most frequent in children aged <1 year (25%) and children aged 11 to 13 years (21%). No child had severe COVID-19 symptoms. Asymptomatic infection was more prevalent in children aged <14 years than in those aged ≥14 years (74.3% and 51.1%, respectively). All children ($n = 45$) diagnosed with SARS-CoV-2 infection had an adult contact with evidence of recent infection.

CONCLUSIONS: In our setting, children do not seem to be the source of SARS-CoV-2 infection and most frequently acquire the virus from adults. Our findings suggest that, in settings such as ours, schools and child care potentially may be reopened safely if adequate COVID-19 mitigation measures are in place and staff are appropriately immunized.



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Drs Lugo and Brasil conducted a literature search, designed the data collection instruments, collected and interpreted data, and wrote the initial and final drafts of the manuscript; Drs Fuller and Nielsen-Saines contributed to the literature search, data interpretation, and the writing of the initial and final drafts of the manuscript; Drs Salgado and Abreu de Carvalho, Ms Damasceno, and Ms Fernandes designed the data collection instruments, collected data, and reviewed and revised the manuscript; Drs Calvet, Resende, Matos, Machado Fumian, Malta, Cruz, Bastos, Guaraldo, Whitworth, Smith, Siqueira, and Carvalho contributed to data analysis and reviewed the manuscript for important intellectual content; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

WHAT'S KNOWN ON THIS SUBJECT: Studies have reported that children and adolescents who attend summer camp and social events away from home can introduce the virus to their household contacts.

WHAT THIS STUDY ADDS: Children do not seem to be the source of infection within their households and most frequently acquire severe acute respiratory syndrome coronavirus 2 from adults.

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As of May 2021, >168 million confirmed cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been reported worldwide, 10% of which occurred in Brazil. Since the first report of coronavirus disease 2019 (COVID-19) in Brazil on February 26, 2020, >16 million confirmed cases and 454 000 deaths have been reported in the country, making Brazil second only to the United States in the absolute number of deaths due to COVID-19.¹ Rio de Janeiro has the highest number of COVID-19 deaths of any city in Brazil.² Because children are generally paucisymptomatic and tend to adhere less to hygiene and social distancing practices, they could potentially be a significantly underappreciated source of SARS-CoV-2 transmission. The concern about asymptomatic shedding of SARS-CoV-2 by children has also motivated many countries to close schools as one of the tools to halt the spread of infection.³

Studies involving family nuclei are an attractive means of investigating transmission of acute respiratory infections as well as clinical evolution of disease in individuals of different ages. The high frequency and intensity of contact between family members generates an environment conducive to transmission, particularly in dense, urban households. In some studies, researchers have investigated families to analyze the transmission of influenza,⁴⁻⁶ but few have explored SARS-CoV-2 infection and transmission.⁷

A better understanding of the role of children in transmission dynamics is of paramount importance for the development of guidelines for safely reopening schools⁸ and other public spaces and also for the development of immunization guidelines for pediatric populations. This is particularly salient in low socioeconomic status communities,

such as slums, where household density is high. As is the case in other low middle income countries, multigenerational dwellings are common in Brazil,⁹ potentially providing opportunities for transmission between the pediatric population and older age groups. Our main objective in this study was to investigate the dynamics of SARS-CoV-2 infection in children and their household contacts living in a vulnerable urban slum in Rio de Janeiro.

METHODS

We recruited and followed children aged <14 years who visited a primary health care facility for any reason (eg, immunization, routine consultation, emergency care, accompanying relatives to the clinic, etc) and additional children who shared the same residential address.

Recruitment took place at the Germano SINVAL Faria Health Center (GSFHC), a primary health care center located in the Northern sector of the city of Rio de Janeiro. GSFHC serves, on average, 21 000 children and adults per month, providing primary care and immunization services to the community of Manguinhos, an impoverished urban slum (a favela) that lacks public services such as sanitation and electricity. Residents are assigned to receive care at this clinic on the basis of their address in accordance with the policies of Brazil's public health care system. Manguinhos is traversed by 2 rivers and an aqueduct ~5 km long,¹⁰ referred to hereafter as "canals." The lowest-income households of the community are located along the canals, which are polluted with trash and sewage.¹¹

After enrollment, children and their household contacts received home visits from study personnel. Home visits occurred 1, 2, and 4 weeks

after enrollment, then quarterly. SARS-CoV-2 polymerase chain reaction (PCR) assays and immunoglobulin G (IgG) serology tests were performed on all children and their household contacts after written informed consent by the parent or legal guardian or the patient's own informed consent if they were aged ≥ 18 years. Children aged ≥ 6 years also provided written assent to study participation. Seroprevalence was defined as a positive serological result, which was counted once for each individual who tested positive, on the date of their first positive result. Nasopharyngeal swabs were tested by real-time reverse transcription polymerase chain reaction (RT-PCR) to amplify the *E* gene and the RdRp region of the *Orf1ab* gene of SARS-CoV-2 using the Charité protocol. Cycle thresholds (CTs) <40 were classified as positive. Rectal swabs were self-collected in the case of adults, collected by the study pediatrician for children aged <2 years, and collected by the mother for children aged >2 years. Rectal swabs were tested by real-time RT-PCR by using 2 sets of primers or probes targeting the virus nucleocapsid N gene (N₁ and N₂ region).⁷ SARS-CoV-2 serology testing (IgG) was performed by using a chemiluminescence immunoassay targeting the N gene (Abbott Laboratories, Abbott Park, IL). All assays were performed according to the manufacturer's instructions.

Adolescent and adult household contacts were tested for SARS-CoV-2 by RT-PCR, independent of the presence of symptoms. We classified a participant as having a positive test result if at least 1 of their serial samples collected during the study tested positive. In addition, children and household contacts completed a study questionnaire, which collected

sociodemographic variables, including number of residents and number of rooms and the proportion of children living with siblings, grandparents, and other family members. Targeted physical examinations of all children and symptomatic adults were performed concurrently. All data and laboratory results were recorded through a Research Electronic Data Capture tool (REDCap; Vanderbilt University, Nashville, TN).¹² Household size was defined as the number of residents per room.

The primary outcome was the frequency of SARS-CoV-2 infections (positive RT-PCR results and IgG antibodies) identified in the study population. We measured infection dynamics by assessing the percentage of children aged <14 years who had PCR-positive test results for SARS-CoV-2 and concurrently had an adult contact with positive SARS-CoV-2 IgG antibodies or history of past COVID-19. This was defined as the presence of a recent respiratory illness accompanied by anosmia or ageusia. We inferred that if SARS-CoV-2 transmissions were primarily from adults and adolescents to children, children who had positive PCR results would have an adult or adolescent contact who had positive IgG antibodies to SARS-CoV-2 or a clinical history suggestive of past COVID-19. In addition, we assessed the timing of peak SARS-CoV-2 IgG prevalence in children versus adults and adolescents. We hypothesized that, if transmission were primarily from adults and adolescents to children, the peak IgG prevalence in adults and adolescents would occur before peak IgG prevalence in children.

Before recruitment, the necessary sample size was determined. We calculated the sample size required to estimate the

prevalence of SARS-CoV-2 in children as the following:

$$n = \frac{NZ^2p(1-p)}{d^2(N-1) + Z^2p(1-p)}$$

where n is the number of children that must be sampled to estimate the prevalence of SARS-CoV-2 with 95% confidence. Z is the critical value of the standard normal distribution corresponding to this confidence level. We defined d , the allowable margin of error, as 5%. N is defined as the number of children treated at GSFHC. We obtained the number of children aged <14 years treated at the clinic in January, February, and March 2020.¹³ We defined N as 4040, which is the mean number of children treated over this 3-month period. p is defined as an initial estimate of the prevalence of SARS-CoV-2. New York City has a population density of 10 000 residents per kilometer squared and a SARS-CoV-2 seroprevalence of ~30%.¹⁴ Because Manguinhos has a similar population density,¹⁵ we defined p as 30%. Using these definitions to estimate the incidence of SARS-CoV-2 with 95% confidence and allowing for 5% loss to follow-up, we calculated that a sample size of 314 children was required. All tests were performed with Stata/IC 16.1 (Stata Corp, College Station, TX) and SAS 9.4 (SAS Institute, Inc, Cary, NC). Boschloo's test was used to compare the rate of positivity by PCR between spans of 3 weeks within the study period.

A geographic information system was created by assigning households to 1 of 9 neighborhoods within the slum based on the participant's home address. For each neighborhood, we calculated the length of roads as a proxy for access to public transportation, the length of open canals as a proxy for sanitation, and the distance from GSFHC. All calculations were performed in ArcGIS Desktop 10.6.1.

We calculated Spearman's correlation between these variables and the percentage of children from the neighborhood who tested positive for SARS-CoV-2 by RT-PCR.

The study was approved by the Brazilian National Ethics Committee under register number 30639420.0.0000.5262.

RESULTS

Recruitment and follow-up took place between May 18 and September 24, 2020. In total, 78.6% of individuals approached consented to study participation. We had 20.5% refusals within the pediatric age group. We enrolled 323 children aged <14 years, 54 adolescents aged 14 to 19 years, and 290 adults aged >19 years who were household contacts of participating children (Fig 1). A total of 259 households were studied. The median number of persons per household was 4 (interquartile range: 3–5).

Among 323 children, 41 had positive test results for SARS-CoV-2 by RT-PCR in their first visit and 4 had positive test results in the second visit, totaling 45 children with positive results identified during the study period (13.93%). Among children, the incidence of new cases identified by RT-PCR was higher in May than in July ($P = .022$), and it rose again from July to September (Fig 2), although the increase was not statistically significant ($P = .13$). This is similar to the temporal pattern of SARS-CoV-2 incidence in the city of Rio de Janeiro as a whole (Fig 3).¹⁶ With respect to SARS-CoV-2 antibody prevalence in the population, SARS-CoV-2 IgG seroprevalence declined from July to September in children and adults (Fig 2).

Among 342 contacts aged ≥ 14 years, 13.16% were infected with SARS-CoV-2, as measured by RT-PCR. The rate of SARS-CoV-2 infection was higher in

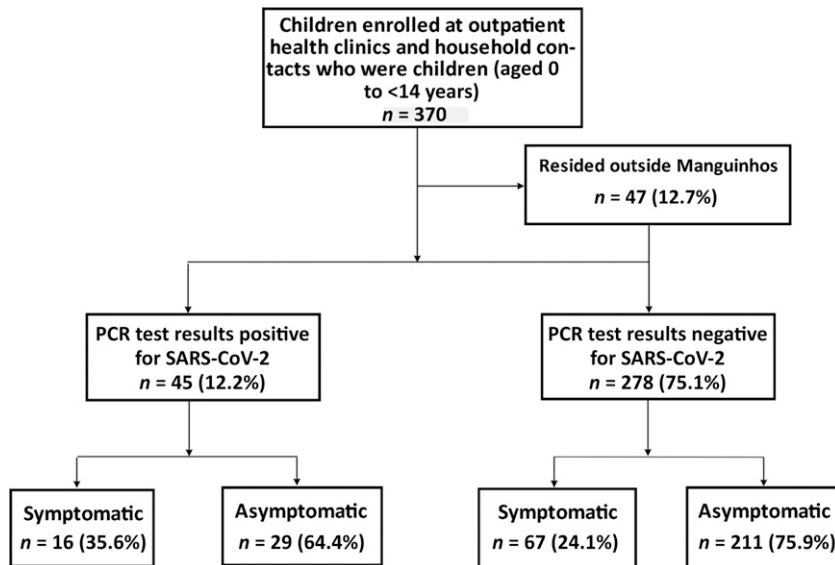


FIGURE 1
Flowchart of children enrolled in the study.

children aged <1 year (25%) and preadolescents aged 11 to 13 years (21%) (Fig 4A). The frequency of SARS-CoV-2 infection was also higher in the same age group when IgG results were considered (Fig 4B).

Eight participants in our study had persistently positive results for SARS-CoV-2 RNA for >14 days: 4 symptomatic adults and 4 children, 3

of whom were symptomatic. Three individuals who had persistently positive results had positive gastrointestinal and respiratory tract specimens. One additional individual with persistently positive results had positive gastrointestinal specimens.

A total of 32.5% (79 of 243) of children aged <14 years and 31.9% (72 of 222) of household contacts

had IgG-positive test results, indicating that they had already been exposed to SARS-CoV-2 by September 2020 (Fig 4). Of the 45 children who had PCR-positive test results, 26 had an adult contact who provided specimens for SARS-CoV-2 testing at the time of pediatric study enrollment. All 26 samples from concurrent adult household contacts tested positive either by PCR or chemiluminescence immunoassay. The 19 remaining adult contacts did not consent to provide a sample of their own. However, all 19 adults reported with symptoms of suspected COVID-19.

The number of persons per room was not significantly correlated with the percentage of household members with positive test results for SARS-CoV-2 by PCR or serology testing ($r = 0.06$, $P > .05$) (Fig 1). The proportion of children who lived with grandparent(s) (ie, multigenerational family households) was not significantly different among those who had positive test results for SARS-CoV-2 by PCR versus those who had negative results ($P = .13$). Furthermore, the proportion of

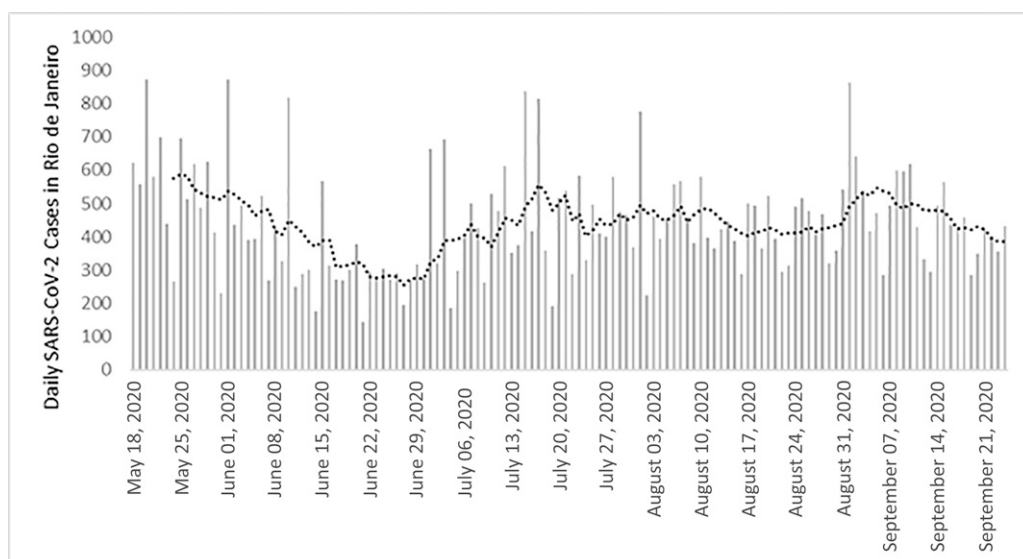


FIGURE 2
Daily SARS-CoV-2 cases in Rio de Janeiro, May 18 to September 28, 2020. Bars represent the confirmed number of cases based on the date of symptom onset. The dotted line is the 7-day moving average of cases (Fig S10 shows the dates of nonpharmaceutical interventions to control the epidemic).

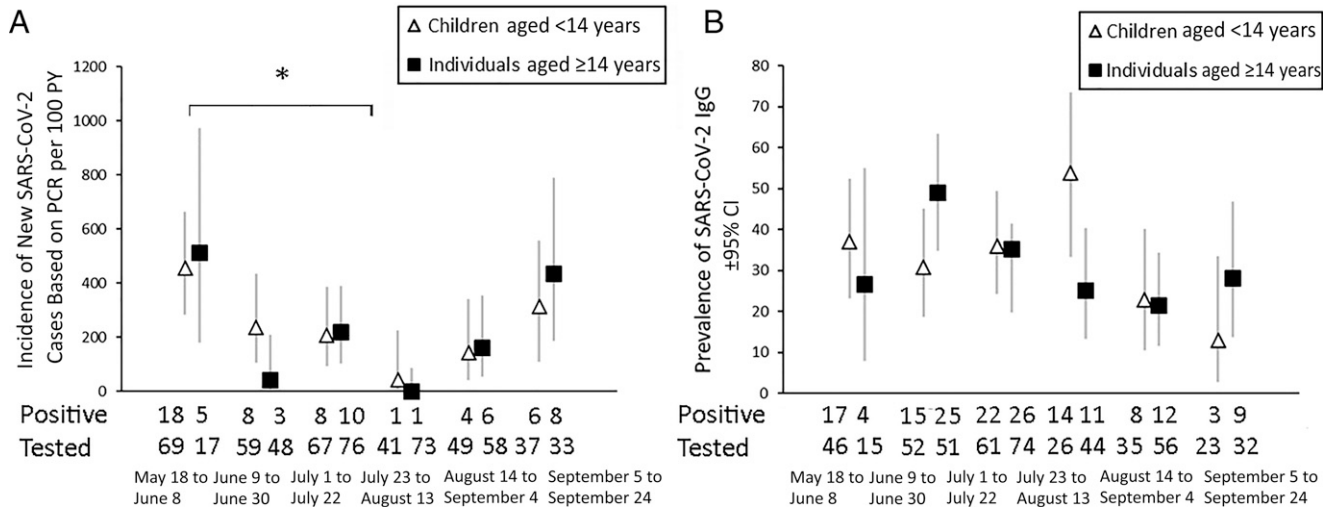


FIGURE 3 A, Incidence of SARS-CoV-2 based on RT-PCR per 100 person-years (PY). * $P < .05$. B, Prevalence of SARS-CoV-2 IgG antibodies. “Tested” denotes the number of children aged <14 or individuals aged ≥ 14 in each 3-week period. “Positive” denotes the number positive for SARS-CoV-2 by RT-PCR. CI, confidence interval.

children who lived with no siblings versus those with ≥ 1 sibling did not differ significantly between children

who had PCR-positive results or PCR-negative results ($P = .15$). No severe cases of COVID-19 were noted among

these children and their household contacts, including siblings. Differences in CT values among infected children were not significantly different, nor were differences in CT values by sample type, age, or household size (Figs 2–4).

A total of 39 of 45 children who tested positive by PCR (87%) and 286 of 323 (89%) children who had a PCR test result (either positive or negative) could be assigned to a neighborhood on the basis of home addresses. The percentage of children who tested positive for SARS-CoV-2 by RT-PCR per neighborhood varied from 0% to 33%. SARS-CoV-2 prevalence was highest in the neighborhoods of Higienópolis and Vila Turismo, in northwestern Manguinhos and also in the neighborhood of Mandela in southeastern Manguinhos (Fig 5). There was no significant correlation between percent positivity and road length ($P = .64$), canal length ($P = .59$), or proximity to the health clinic ($P = .74$).

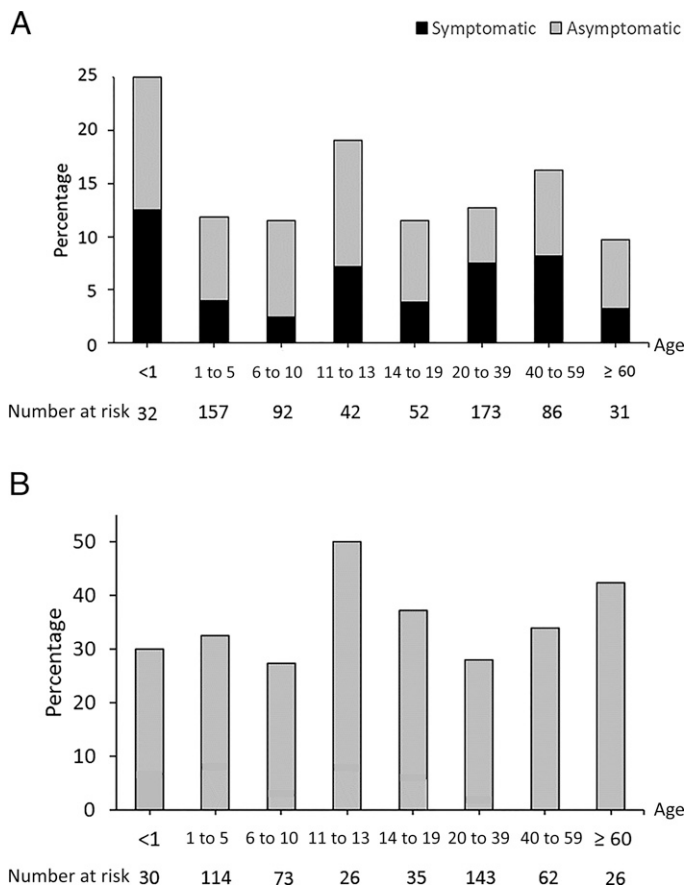


FIGURE 4 Frequency of SARS-CoV-2–positive test results by age group in Manguinhos. A, PCR. B, IgG.

DISCUSSION

In our study, all children with SARS-CoV-2 infection identified by RT-PCR had an adult or teenage household

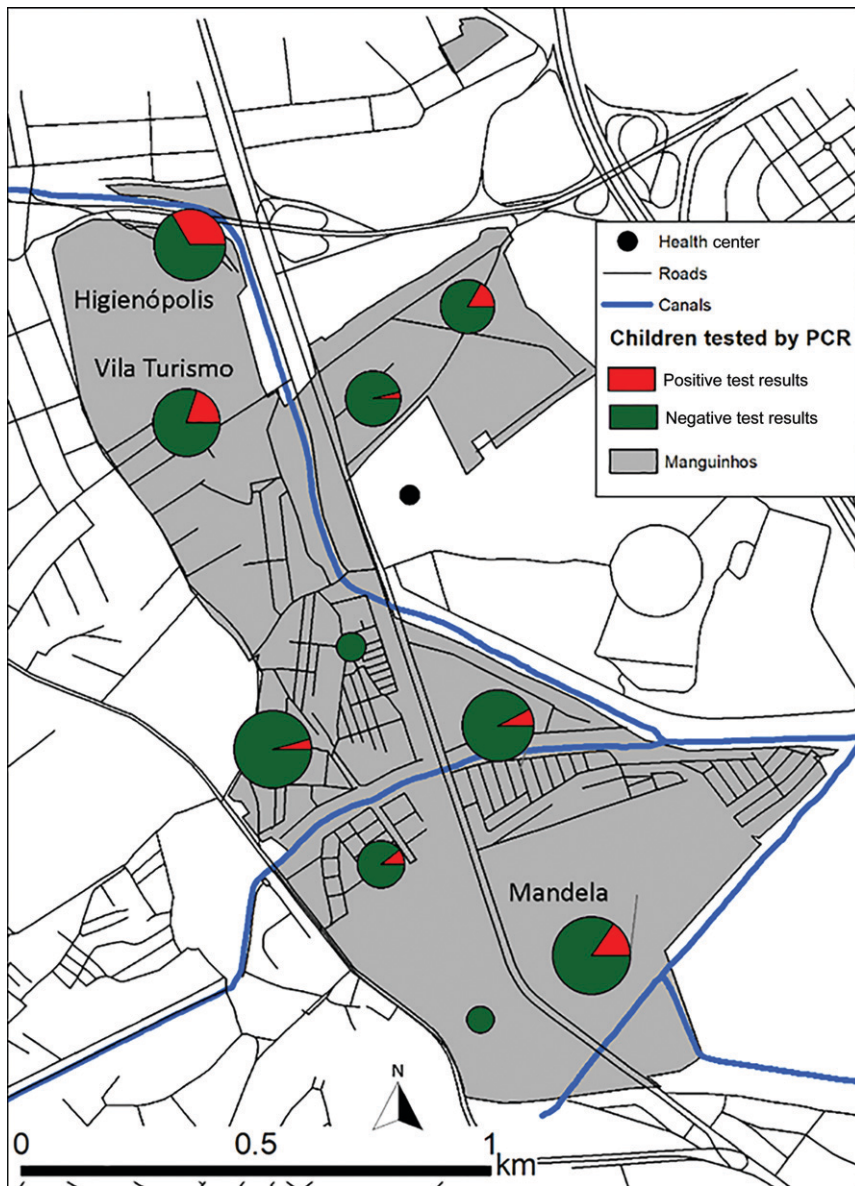


FIGURE 5 Distribution of SARS-CoV-2 in Manguinhos by neighborhood. The size of each pie chart is proportional to the number of children recruited from the neighborhood.

contact with suspected or confirmed SARS-CoV-2 before the child's diagnosis. Unless these children were long-term SARS-CoV-2 shedders, our results are compatible with the hypothesis that children were infected after or concurrent to household contacts, mostly their parents. To this extent, our preliminary results suggest that children do not seem to be the source of infection and most frequently acquire SARS-CoV-2 from

adults, rather than transmitting it to them, which is different from previous studies.^{17,18} A possible explanation for our findings would be that children are paucisymptomatic in most cases and, therefore, would disperse fewer droplets and aerosols in the environment. The risk that children could infect others depends on factors such as SARS-CoV-2 viral load (VL) in the nasal secretions and feces, which could vary by age.

However, comparisons of SARS-CoV-2 VL in younger and older children have yielded conflicting results, with one study reporting higher VL in the former,¹⁹ whereas others have found no effect of age.^{20,21} In our population, we observed that children aged <1 year and young teenagers tended to have the highest rates of infection and symptomatic disease. The former may be because of the close contact between children aged <1 year and their mothers and the latter because of the lower adherence to social distancing by young teenagers.

Adults might be more important spreaders because they have continued to work outside the home, whereas schools were closed early in the course of the pandemic and remained closed through the study. Indeed, these adults were more vulnerable to SARS-CoV-2 because they maintained their activities as frontline workers, being exposed to a large number of individuals throughout the pandemic. Although schools remained closed, in mid-August 2020, other social distancing rules were eased in Rio de Janeiro, most businesses reopened, and crowded public transportation resumed (Fig 2 and S10). Such reopening increased exposure among adults and increased their chance of being the real "vectors" of SARS-CoV-2 infection, as shown in the second wave of infections (Fig 3).

In the current study, we observed a higher proportion of infected children aged <1 year compared with other pediatric age groups, which may be attributable to direct contact with their mothers. A study in China reported a SARS-CoV-2 infection prevalence of 17% in children aged <1 year,²² whereas in our study the prevalence was ~30%. Ours is one of only a handful of studies to date in which SARS-CoV-2 infection in nonhospitalized children, all of whom resided in the

same community, was investigated. Because of factors such as the risk of urban violence in Manguinhos, children do not usually play outside alone until they are over 5 years of age. On the other hand, there is considerable variation among 5-to-12-year-old children regarding the time spent outside of the home. Children aged ≥ 13 years typically spend a substantial proportion of time outside their home.

Approximately one-third of household contacts in our study had IgG-positive test results, indicating that they had already been exposed to SARS-CoV-2 by August 2020, a higher prevalence of infection than that reported for the general population of Rio de Janeiro during that time period (7.5% [4.2–12.2] vs 33% [28.6–37.6]).²³ Although the duration of protection after infection remains unknown, in most immunization protocols, seropositive individuals are eligible to be vaccinated because this remains the principal manner of reducing severe forms of COVID-19. It is also hoped that immunization will reduce transmission. These results are important for planning the reopening of both schools and day care centers, which have remained closed since March, and also for the development of COVID-19 immunization strategies, such as prioritizing vaccination of teachers and child care professionals.

Our results underscore the importance of including children in vaccine trials. Furthermore, if adults are immunized and children are not, children may continue to perpetuate the epidemic, highlighting the difference between vaccination

strategies based on individual protection and vaccination strategies aimed at achieving herd immunity. If minimally 85% of susceptible individuals need to be immunized to curb the COVID-19 pandemic in high-incidence countries, this level of protection can only be achieved with the inclusion of children in immunization programs, especially in Brazil, where 25% of the population is aged < 18 years.²⁴

Study limitations included the logistic challenges of conducting home visits in this community because of the risk of violence toward study staff, resulting in variable adherence to study procedures, missed visits, and delays in the enrollment of families. The relaxation of social distancing measures also made it more difficult to recruit adults, especially men, who returned to work and thus became unavailable. We might have underestimated the number of past infections if we tested too soon after infection onset or too late after infection because of waning of antibodies. This was difficult to determine because the date of infection was largely unknown in children and household contacts, most of whom were asymptomatic. Furthermore, the absence of IgG antibodies could be explained by effective innate immunity, leading to robust cellular immune responses after exposure to SARS-CoV-2²⁵ with no subsequent antibody immune responses.

CONCLUSIONS

Children do not seem to be the source of SARS-CoV-2 infection in our setting. Our findings demonstrate that most frequently

children acquire infection from adults rather than transmitting it to them. Our results support the strategy of safely reopening schools and day care centers in our setting, particularly with strict COVID-19 mitigation measures and staff immunization. In low-resource settings such as ours, this is critical because access to online classes remains limited.

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ABBREVIATIONS

COVID-19: coronavirus disease 2019
CT: cycle threshold
GSFHC: Germano Sinval Faria Health Center
IgG: immunoglobulin G
PCR: polymerase chain reaction
RT-PCR: reverse transcription polymerase chain reaction
SARS-CoV-2: severe acute respiratory syndrome coronavirus 2
VL: viral load

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POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

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