Clinical Characterization, Transmissibility, and Seroconversion of SARS-CoV-2 Infection in Children (before the Start of Vaccination) in the Barcelona Metropolitan Region (Spain)

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Abstract

Objective Analyzing the clinical and microbiological characteristics of coronavirus disease 2019 (COVID-19) infection in children seems essential to determine their role in the etiopathogenesis of the disease.

Methods A prospective, longitudinal, and observational study, including children with severe acute respiratory syndrome coronavirus-2 infection, in the Barcelona Metropolitan Region (Spain), was performed. The recruitment pathways were: (1) children who attended a summer school and were included in an active surveillance study and (2) children who were visited in the Emergency Department of Hospital Sant Joan de Déu with symptoms. Close contacts with positive polymerase chain reaction (PCR) results were also included. The children recruited were followed up for 5 weeks.

Keywords
- SARS-CoV-2
- children
- RNA persistence
- serological response
- antibodies
- infectivity

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Evaluation of participants included a questionnaire for COVID-19 symptoms, nasopharyngeal swabbing for real-time PCR at 0, 7, and 14 days (weekly repeated up to week 5 if it resulted positive at 14 days), and serology testing at the recruitment and at the fifth week of follow-up.

Results A total of 90 children were recruited, of which 32% were asymptomatic. Transmission was studied in 70/90 children, and in 12 cases (17%), transmission to other children or adults was observed. No clinical or epidemiological differences were found between children who transmitted and those who did not. At the end of the follow-up, 11% of nasopharyngeal PCR remained positive. The serological response was studied in 73/90 children, and 80.82% of children seroconverted.

Conclusion No differences in epidemiological characteristics were found between children who transmitted and those who did not. PCR can be persistently positive for more than 5 weeks. The majority of patients who suffer from the disease produce antibodies against it.

Introduction

The rapid and global spread of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has triggered a pandemic that, during the past 3 years, caused significant disease and death globally. At the time of writing, >770 million cases have been reported, resulting in over 6.9 million deaths.[1]

At the beginning of the coronavirus infectious disease 2019 (COVID-19) pandemic, efforts were focused on studying the effect of COVID-19 on the adult population.[2]

To date, multiple studies have shown that the disease affects pediatric and adult populations differently, being less severe in children.[3] The reasons underlying the different outcomes of infections in children compared with adults are still not well understood.

Most of the infected children are either asymptomatic (up to 20% of the cases[4,5]) or have mild clinical manifestations, with fever and cough being the predominant clinical features at presentation.[3] Symptoms are usually similar to other viral respiratory infections with a good prognosis and a very low mortality rate[6]; thus, only a small proportion of children require hospitalization and intensive care.

Moreover, infectivity and serological response in children have not been sufficiently well characterized and could shed some light on the transmission potential of the disease according to age group. As already described in the literature, it seems that pediatric patients are less efficient at transmitting the infection to other children and adults.[7,8]

Vaccination in the adult population in Spain started in December 2020 and, a year later, vaccination in children began (Pfizer BNT162b2 and Moderna mRNA 1273 from 12 years of age and Pfizer BioNTech from 5 years of age). Initially, the decision to vaccinate children universally was controversial, given that most children have mild symptomatology (except SARS-CoV-2-associated pediatric multisystemic inflammatory syndrome), and after several studies showed that they do not appear to act as a major reservoir of infection.[9] In the year 2022 in Spain, vaccination against SARS-CoV-2 was indicated for children over 5 years of age, while in the latter year (2023–2024) it was indicated only for children with risk factors.

This study aims to describe the clinical manifestations of SARS-CoV-2 infection in children, analyze clinical and epidemiological factors associated with the infection transmission, and explore the microbiological dynamics, including RNA persistence and seroconversion. It should be noted that the present study was conducted before the initiation of vaccination and therefore provides interesting data on the natural history of SARS-CoV-2 infection in children.

Materials and Methods

This is a prospective, longitudinal, and observational study, including children with SARS-CoV-2 infection, in the Barcelona Metropolitan Region (Spain). The recruitment period spanned 3 months, from June to August 2020, coinciding with the first 3 months after which children were finally allowed to leave their households after a very strict lockdown (corresponding to the first wave of COVID-19).

Children aged 7 days old to 18 years old (both included) with positive detection of RNA SARS-CoV-2 by real-time polymerase chain reaction (RT-PCR) either in the nasopharynx or saliva were included and followed up. Participants who were unwilling to ensure adequate follow-up or whose parents did not provide consent were excluded.

Children with positive RT-PCR results from saliva or nasopharyngeal (NP) swabs were considered potential primary cases during the study. Subsequently, all children who were close contacts of the primary case were also asked to participate in the study, and those with positive RT-PCR were included. Evaluation of participants also included a questionnaire for COVID-19 symptoms, NP swabbing for RT-PCR at 0, 7, and 14 days (weekly repeated up to week 5 if it resulted positive at 14 days), and serology testing at the recruitment and the fifth week of follow-up.

The recruitment pathways (RP) were as follows:

1) Children with positive RT-PCR from saliva or NP swabs who attended a summer school and visited outpatient clinics in Hospital Sant Joan de Déu (HSJD) (RP1) because they were previously included in an active surveillance study.[7]
2) Children who were visited in the Emergency Department (ED) of HSJD with symptoms had a positive test and then agreed to participate in this study (RP2).

Information on transmissibility was obtained differently depending on the RP of each child. In children recruited from the summer schools' study, transmissibility was studied based on PCR and serial serology of close contacts performed in that study.[7,10] In the case of children recruited from the ED, contacts under 18 years of age with positive PCR were included in the study but adult contacts were not studied. In this case, information on transmissibility was obtained from the weekly anamnesis to the family. Since at the time of the study PCR was performed on everyone with symptoms, it was possible to obtain reliable information from most of the close contacts.

Definitions

A primary SARS-CoV-2 case was defined as a child with a positive RT-PCR for SARS-CoV-2 in saliva or NP swabs in the absence of SARS-CoV-2 IgG antibodies, with or without clinical symptoms. All household members (children and adults) were considered close contacts. In the case of children who attended summer school, all the people (children and adults) in the same stable group with whom primary cases did all summer activities were also considered close contacts. However, only children were included in this study.

Secondary SARS-CoV-2 infections were incident infections among close contacts of a primary case, as defined by (1) negative RT-PCR and negative IgG serology tests at enrolment followed by a positive test at 7 or 14 days, irrespective of the onset or presence of symptoms; (2) a positive RT-PCR at enrolment with onset of COVID-19 symptoms later than the primary case; or (3) evidence of seroconversion by week 5.

The primary outcome was to characterize the SARS-COV-2 children's presentation (being patients with a disease pattern classified as asymptomatic or symptomatic), to define how long SARS-CoV-2 remained positive in NP swabs and if it was associated with the disease severity and, finally, to determine the time taken to seroconversion.

The secondary outcome was to analyze clinical and epidemiological risk factors for transmission to other children or adults.

NP swabs or saliva were collected and introduced into micronic tubes with 750 µL of Zymo DNA/RNA Shield Lysis Buffer (Zymo Research, Freiburg, Germany) for sample inactivation and transportation to the laboratory. SARS-CoV-2 RNA was extracted from the majority of samples using the Quick-DNA/RNA Viral Mag Bead kit (Zymo Research), which was fully automated on a Tecan Dream Prep NAP Workstation (Tecan Trading AG, Switzerland). SARS-CoV-2 RT-PCR was performed in an Applied Biosystems 7900HT robot with 384-well block equipment according to the CDC-006-00019 protocol https://www.fda.gov/media/134922/download). Some samples were extracted by using the NucliSense easyMAG platform and reagents (bioMérieux, The Netherlands) or the MagMAX platform (Viral/Pathogen Nucleic Acid Isolation kit, Thermo Fisher, United States). In these samples, RNA amplification was performed by using different commercial in vitro diagnostic tests (TaqPath COVID-19 CE-IVD RT-PCR Kit, Thermo Fisher; Genefinder Plus RealAmp Kit, Genefinder laboratories and Allplex 2019-nCoV Assay is multiplex RT-PCR assay, Seegene Laboratories).

Rapid IgG/IgM COVID-19 tests (Sure Screen) were performed according to the manufacturer's instructions in finger-prick capillary blood specimens. Serum samples derived from full blood obtained by venepuncture were tested by an enzyme-linked immunoassay (ELISA) (Abbott). Abbott SARS-CoV-2 IgG assay on the Abbott Architect instrument according to the manufacturer's instructions. This assay is a chemiluminescent immunoassay for qualitative detection of IgG in human serum or plasma against the SARS-CoV-2 nucleoprotein.

Study data were collected and managed using REDCap electronic data capture tools hosted at HSJD.[11,12] Participant data were pseudonymized, i.e., patient history numbers were replaced by a number to reduce the link between the personal data and the individual it identifies.

The chi-square test was used for comparisons of categorical data, and the Student's *t*-test or the Mann–Whitney U test was used for quantitative variables depending on whether the distribution could be considered normal or not. To compare the epidemiological and microbiology results at the different diagnostic times, the Wilcoxon signed-rank test was used to compare paired numerical data. McNemar's test was used for paired nominal data. Statistical significance was set at $p < 0.05$ and confidence intervals at 95%. SPSS1 22.0 statistical package (IBM Corp. Software, Armonk, New York, United States) and R 3.6 (R Foundation for Statistical Computing, Vienna, Austria) were used.

Results

During the study period, 90 children were recruited. Of the total number of children included, 57 were recruited from a summer school study and 33 were recruited from the ED. Forty-seven percent were male, with a median age of 9.52 years (interquartile range: 3.97–12.36).

Regarding risk factor differences between symptomatic and asymptomatic children, Caucasian children were symptomatic more frequently (79.4% in Caucasian vs. 63.2% in Latin American vs. 43.9% in other ethnicities, $p = 0.044$). Additionally, symptomatic children had more adult cohabitants ($p = 0.009$), whereas asymptomatic children had more children living with them at home ($p = 0.03$). There were more smokers in symptomatic children households ($p = 0.008$). No other differences were found in the risk factors analyzed between symptomatic and asymptomatic children (►**Table 1**).

Table 1 Patient characteristics, lifestyle, and household details

Variable	All participants ($n = 90$)	Symptomatic ($n = 61$)	Asymptomatic ($n = 29$)	p-Value
Patient characteristics				
Gender (n)				0.197[a]
Male	47/90 (52%)	29/61 (48%)	18/29 (62%)	
Age in years median	9.52 (3.97–12.36)	9.65 (3.91–12.79)	8.17 (4.15–12.07)	0.268[b]
Ethnicity (n)	86	57	29	0.044[a]
Caucasian	34 (40%)	27 (47.37%)	7 (24.14%)	
Latin-American	38 (44%)	24 (42.11%)	14 (48.28%)	
Other	14 (16%)	6 (10.53%)	8 (27.59%)	
Risk factors (n)	16		29	
Obesity	1 (1%)	1/59 (1.69%)	0	0.480[a]
Allergy	9 (10%)	6/58 (10.34%)	3 (10.34%)	1[a]
Other	6 (6.67%)	5/59 (8.47%)	1 (3.45%)	0.379[a]
Infections in previous 3 mo	10	59	0	
Respiratory	5/88 (5.68%)	5/59 (8.47%)	0	0.106[a]
Gastrointestinal	5/88 (5.68%)	5/59 (8.47%)	0	0.106[a]
Lifestyle				
Type of food diet	80	51	29	0.182[a]
Omnivorous	79/80 (98.75%)	51/51 (100%)	28/29 (96.55%)	
Vegetarian	1/80 (1.25%)	0	1/29 (3.45%)	
Sport practice	63	42	21	0.708[a]
Yes	22/63 (34.92%)	14/42 (33.33%)	8/21 (38.10%)	
Handwashing	83	57	26	0.474[a]
>5 times/day	22/83 (26.51%)	15/57 (26.32%)	7/26 (26.92%)	
3–5 times/day	53/83 (63.86%)	35/57 (61.40%)	18/26 (69.23%)	
<3 times/day	8/83 (9.64%)	7/57	1/26 (3.85%)	
Household details				
Household inhabitants (n)				
Children	2 (1–3)	2 (1–2)	3 (1.75–3)	0.030[b]
Adults	2 (2–4)	3 (2–4)	2 (2–3)	0.009[b]
House surface (m^2)	80 (60–90)	80 (60–90)	85 (63.75–91.25)	0.993[b]
Number of bathrooms (n)	1 (1–2)	1 (1–2)	1 (1–2)	0.943[b]
Sharing room	85	56	29	0.393[a]
Yes	69/85 (81.18%)	44/56 (78.57%)	25/29 (86.21%)	
Domestic animals	84	55	29	0.258[a]
Yes	14/84 (16.67%)	11/55 (20%)	3/29 (10.34%)	
Parents work activity	80	51	29	0.978[a]
Yes	69/80 (86%)	44/51 (86.27%)	25/29 (86.21%)	
Smokers at home	82	53	29	0.008[a]
Yes	23/82 (28.05%)	20/53 (37.74%)	3/29 (10.34%)	
Previous confirmed COVID cases in household	89	60	29	0.003[a]
Yes	54/89 (60.67%)	30/60 (50%)	24/29 (82.76%)	
Probable origin of the household outbreak	66	41	25	0.088[a]

Table 1 (*Continued*)

Variable	All participants ($n = 90$)	Symptomatic ($n = 61$)	Asymptomatic ($n = 29$)	*p*-Value
Adult	41/66 (62.12%)	21/41 (51.22%)	20/25 (80%)	
Child	20/66 (30.30%)	15/41 (36.59%)	5/25 (20%)	
Both at the same time	2/66 (3.03%)	2/41 (4.88%)	0	
Unknown	3/66 (4.55%)	3/41 (7.32%)	0	

Notes: Values are expressed as frequency (percentage) for qualitative variables and as median (interquartile range) for quantitative variables.
n = number of patients.
[a]Chi-squared test.
[b]Mann–Whitney U test.

Among all children recruited, 29 (32%) had no evidence of symptomatic disease and were deemed asymptomatic cases. A total of 61 children had symptoms (68%), with fever (59%), gastrointestinal symptoms (39%), and headache (19%) being the most frequent symptoms. None of the studied children had severe disease, and the only one admitted was due to gastrointestinal symptoms that required intravenous analgesic treatment.

Information on transmission was obtained in 70 of the children studied. Data were missing for 20 cases for which it could not be determined if they transmitted the infection or not because the contacts were not studied or, although they were studied, it was not possible to know how the transmission occurred. In 12 cases (17%), transmission of the infection to other children or adults was observed within the summer school and/or in the family. Epidemiological and clinical differences between children who transmitted and those who did not were studied. No statistically significant differences were found in the analyzed characteristics (►**Tables 2**, **3**).

There was a decrease in NP PCR positivity throughout the weeks. All the participants were tested weekly until they had a negative PCR. In the first week of diagnosis, a total of 53 NP PCRs were performed. The rest of the children (up to 90 recruited children) do not have a PCR performed at week 1 for two reasons. Some of them had already had a PCR performed a few days before at the time of recruitment (and it was not repeated until the second week of diagnosis). Others, at the time of recruitment, were already in the second or third week of diagnosis. Of these 53 PCRs performed, 45 were positive, meaning that at least 50% (45/90) of all participants had a positive PCR at that time. Comparatively, in the fifth week, 22 PCRs were performed, of which 10 were positive. Taking into account that most of the remaining participants did not undergo PCR, because they already had a negative PCR before the fifth week, it could be assumed that at the end of the follow-up, approximately 11% (10/90) of NP PCR remained positive.

PCR in saliva followed the same trend as described for NP PCR. The total number of recruited NP and saliva samples per week and the results are reported in ►**Table 4**.

Comparing symptomatic and asymptomatic patients, no differences were found in terms of PCR positivity, either in NP swabs or saliva.

The serological response was studied in 73/90 children (►**Table 4**). Regarding serological response, 80.82% (59/73) of children with a SARS-COV-2 diagnosis seroconverted. In terms of time distribution, in the second week, 17.8% (13/73) of the children already had a positive serology, 26% (19/73) in the third, and 38.3% (28/73) in the fourth. At the end of the follow-up (fifth week), at least 65% (59/90) of the total participants had positive serology for SARS-CoV-2. The sample was venous in 53 children (72.6%) and capillary in 20 (27.4%). Serology was not repeated in 17/90 children (19%) because they were lost to follow-up; therefore, it is not possible to know whether seroconversion occurred.

At the moment of seroconversion, 22/59 (37.3%) of NP PCR performed remained positive, 23/59 (39%) were negative, and in 13/59 (22%) the result was inconclusive.

Discussion

Currently, it is well known that the severity of SARS-CoV-2 infection is lower in children and that a not insignificant

Table 2 Differences in symptoms depend on whether they transmit or not

Symptoms	Transmit ($n = 12$)	Did not transmit ($n = 58$)	*p*-Value[a]
Asymptomatic	2 (16.7%)	21 (36.2%)	0.19
Symptomatic	10 (83.3%)	37 (63.8%)	
Fever	9 (75%)	29 (50%)	0.11
Gastrointestinal symptoms	4 (33.33%)	15 (25.86%)	0.59
Headache	3 (25%)	10 (17.24%)	0.52
Cough	3 (25%)	8 (13.79%)	0.33
Other symptoms (odynophagia, fatigue, muscle pain)	2 (16.67%)	14 (24.14%)	0.57

[a]Chi-squared test values are expressed as frequency (percentage).

Table 3 Epidemiological differences between children who transmit the infection (at summer school and/or in the household) and those who do not

Variable	All participants ($n = 70$)	Transmit ($n = 12$)	Did not transmit ($n = 58$)	*p*-Value
Patient characteristics				
Gender (*n*)				0.840[a]
Male	39 (55.7%)	7 (58.3%)	32 (55.2%)	
Age (y)	9.52 (4.43–12.26)	9.58 (4.81–10.93)	9.51 (4.43–12.26)	0.925[b]
Ethnicity (*n*)	68	12	56	0.089[a]
Caucasian	28 (41.2%)	8 (66.7%)	20 (35.7%)	
Latin-American	30 (44.1%)	4 (33.3%)	26 (46.4%)	
Other	10 (14.7%)	0	10 (17.9%)	
Risk factors (*n*)	14			
Obesity	1 (1.4%)	0	1 (17.2%)	0.646[a]
Allergy	7 (1%)	0	7 (12.1%)	0.200[a]
Other	6 (8.6%)	2 (16.7%)	4 (6.9%)	0.271[a]
Infections in previous 3 mo	8 (11.4%)			
Respiratory	3 (4.3%)	0	3 (5.2%)	0.420[a]
Gastrointestinal	5 (7.1%)	3 (25%)	2 (3.5%)	0.008[a]
Lifestyle				
Sport practice	50	7	43	0.658[a]
Yes	18/50 (36%)	2 (28.6%)	16 (37.2%)	
Handwashing	65	11	54	0.949[a]
>5 times/day	16/65 (24.6%)	3/11 (27.3%)	13/54 (24.1%)	
3–5 times/day	44/65 (67.7%)	7/11 (63.6%)	37/54 (68.5%)	
<3 times/day	5/65 (7.7%)	1/11 (9.1%)	4/54 (7.4%)	
Household details				
Household inhabitants (*n*)				
Children	2 (1–3)	2 (2–3)	2 (1–3)	0.504[b]
Adults	2 (2–4)	2 (2–3.5)	2 (2–4)	0.573[b]
House surface (m^2)	80 (58.75–96.25)	90 (52.5–160)	80 (60–92)	0.273[b]
Number of bathrooms (*n*)	1 (1–2)	1 (1–2.5)	1 (1–2)	0.256[b]
Sharing room	67	12	55	0.479[a]
Yes	55/67 (82.1%)	9/12 (75%)	46/55 (83.6%)	
Domestic animals	66	12	54	0.204[a]
Yes	9/66 (13.6%)	3/12 (25%)	6/54 (11.1%)	
Parents work activity	62	8	54	0.770[a]
Yes	55/62 (88.7%)	7/8 (87.5%)	48/54 (88.9%)	
Smokers at home	64	10	54	0.593[a]
Yes	15/64 (23.4%)	3/10 (30%)	12/54 (22.2%)	
Previous confirmed COVID cases in household	69	12	57	0.373[a]
Yes	44/69 (63.8%)	9/12 (75%)	35/57 (61.4%)	
Probable origin of the household outbreak	52	9	43	0.118[a]

Table 3 (*Continued*)

Variable	All participants ($n = 70$)	Transmit ($n = 12$)	Did not transmit ($n = 58$)	*p*-Value
Adult	30/52 (57.7%)	4/9 (4.4%)	26/43 (60.4%)	
Child	17 (32.7%)	3/9 (3.3%)	14/43 (32.6%)	
Both at the same time	2 (3.8%)	0	2/43 (4.7%)	
Unknown	3 (5.8%)	2 (2.2%)	1/43 (2.3%)	

Notes: Only children for whom transmission information is available are included in this table. Values are expressed as frequency (percentage) for qualitative variables and as median (interquartile range) for quantitative variables. n = number of patients.
[a]Chi-squared test.
[b]Mann–Whitney U test.

Table 4 Overall polymerase chain reaction screening results and serology conversion, per week

Type of PCR screening test	Week 1	Week 2	Week 3	Week 4	Week 5
Nasopharyngeal	53	63	61	19	22
Positive	45 (84.9%)	35 (55.55%)	32 (52.46%)	12 (63.16%)	10 (45.45%)
Negative	7 (13.2%)	20 (31.75%)	23 (37.7%)	5 (26.32%)	9 (40.9%)
Indeterminate	1 (1.9%)	8 (12.7%)	6 (9.84%)	2 (10.52%)	3 (13.64%)
Saliva	51	57	40	17	14
Positive	36 (70.59%)	26 (45.61%)	13 (32.5%)	5 (29.4%)	1 (7.14%)
Negative	12 (23.53%)	24 (42.1%)	24 (60%)	8 (47.06%)	11 (78.57%)
Indeterminate	3 (5.88%)	7 (12.28%)	3 (7.5%)	4 (23.53%)	2 (14.29%)
IgG ELISA	41	28	7	5	32
Positive	0 (0%)	12 (42.86%)	4 (57.14%)	5 (100%)	22 (68.75%)
Negative	41 (100%)	16 (57.14%)	3 (42.86%)	0 (0%)	10 (31.25%)
Total IgG+	0	13	6	9	31
IgG ELISA	0	12	4	5	22
IgG capillary[a]	0	1	2	4	9
IgM	23	13	3	3	30
Positive	0 (0%)	5 (38.5%)	1 (33.3%)	3 (100%)	11 (36.7%)
Negative	23 (100%)	8 (61.5%)	2 (66.7%)	0 (0%)	19 (63.3%)

Abbreviations: ELISA, enzyme-linked immunoassay; PCR, polymerase chain reaction.
[a]IgG detected by capillary sample in children without ELISA sample taken.

proportion of children are asymptomatic.[3,5,13,14] Multiple studies have focused on the incidence of asymptomatic infections. For instance, Lu et al, in a study performed in a pediatric population in Wuhan, detected 15.8% of asymptomatic infected children.[4] Other studies detected up to 56.5% of asymptomatic infected children.[15] Indeed, this is consistent with our observation, where 32% of the recruited patients had asymptomatic disease and only one of them required hospitalization.

It has already been described that patients with asymptomatic COVID-19 can also transmit the disease. Asymptomatic infections have been observed to have the same infectivity as symptomatic infections.[16] Johansson et al estimated that at least 50% of new SARS-CoV-2 infections have been transmitted by people without symptoms.[17] In line with these data, in our observation, we found no differences in transmission between symptomatic and asymptomatic patients.

Furthermore, we also found no differences in the transmission of infection according to the type of symptom presented. For this reason, it was important at the time of the study to test contacts regardless of their symptomatology. Higher transmission rates have been observed in older children (>10 years)[18] and among minority ethnic groups.[19] However, in our study, no risk factors or epidemiological characteristics associated with the transmission of the infection were found. Consequently, in principle, it is not possible to differentiate between children who transmit the infection and those who do not.

Prolonged PCR positivity in a proportion of recovered COVID-19 patients was observed in several studies, although it seems not to be a relation between PCR positivity and infectiousness.[20,21] Carmo et al[22] observed that patients

with milder disease presented positive PCR for longer than those with more severe symptoms and that patients with milder disease (and therefore lower viral load) had lower antibody titers (a fact that may explain the need for more time viral RNA clearance). In keeping with this, in our study, all the patients presented with mild disease, which could be related to the fact that after the fifth week after the onset of symptoms, 9% of the children still had a positive PCR. We did not find differences in the persistence of PCR positivity in NP swabs between symptomatic and asymptomatic patients, which is consistent with the literature.[23] In addition, the fact that the PCR can remain positive for several weeks without this implying contagiousness means that it may not be an adequate method for deciding when to de-isolate patients. Other methods are currently being used in clinical practice that may be a better indicator of potential infectivity, such as cycle threshold (Ct) values and antigen tests (not available at the time of the study).

Regarding serology response, the literature describes a high percentage of seroconversion after SARS-CoV-2 infection in children that is comparable to that of the general population.[24,25] For instance, the study performed by Zhao et al detected 79.8% positive IgG by day 15 after onset.[26] According to the literature, in our case, in the second week after the onset of symptoms, 17.8% of children studied had IgG against SARS-CoV-2 increasing to 80.82% at the end of the follow-up. It seems evident that as the weeks go by after infection, most people develop antibodies (more than 80%). The reason why some people do not develop antibodies is still unknown, although this does not mean that they do not present protection against infection.

The present study has several limitations, such as the number of missing observations in the samples and information collected, due to an irregular follow-up of certain patients. Even if risk factors may play a role in the evolution of the disease, the low incidence of comorbidities in the children studied makes it difficult to find differences in terms of the symptoms presented. Although a significant proportion of the children studied were asymptomatic, it is possible that in reality, the actual percentage is even higher, since in our study there is a detection bias since a part of the sample were children who attended the ED because they had symptoms. We found a limited number of children who transmitted the infection, making it difficult to find consistent results in this group. Finally, regarding the serological response, seroconversion was observed in the fifth week in the majority of children. The fact that no more serological response was observed in the previous weeks could be because most of the serological samples were taken in the fifth week (because of the study methodology).

Conclusion

Epidemiological characteristics could explain differences in the course of the disease. Conversely, it does not appear to be possible to differentiate those children who transmit the infection from those who do not by clinical presentation or by epidemiological characteristics. In this sense, it is important to emphasize that a significant proportion of children remain asymptomatic after SARS-CoV-2 infection, and despite this, they can transmit it. Finally, it is also important to highlight that the fact that PCR is persistently positive does not depend on whether the child has symptoms or not, or whether the child remains infectious or not.

Ethical Approval

The study was approved by the Institutional Review Board and the HSJD Ethics Committee (PIC-153-20) and followed the recommendations of the Helsinki Declaration.

Consent to Participate

All participants or their legal guardians provided written informed consent.

Consent for Publication

Patients signed informed consent regarding publishing their data.

Availability of Data and Material

The datasets generated and/or analyzed during the current study are not publicly available due to individual privacy could be compromised but are available from the corresponding author on reasonable request.

Authors' Contributions

All authors have made substantial contributions to all the following: (1) the conception and design of the study, acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, and (3) final approval of the submitted version.

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Conflict of Interest

None declared.

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