Coronavirus Pandemic

Clinical laboratory and dispersion pattern of COVID-19 in a family cluster in the social-distancing period

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Abstract

Introduction: Since the first reports of coronavirus disease 2019 (COVID-19) in December 2019, the disease has spread worldwide. Different social isolation strategies have been adopted to reduce community transmission, but few studies have evaluated the pattern of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) infection in a family cluster during periods of isolation. We report an outbreak in 24 members of a family cluster during a period of social distancing.

Methodology: We carried out an observational descriptive study of a family cluster infected with SARS-CoV-2 in Pernambuco, Northeast Brazil. Laboratory confirmation included RT-PCR of nasopharyngeal samples or IgM or IgG serology.

Results: The attack rates were 75% (19/24) based on laboratory-confirmed cases and 87.5% (21/24) including probable cases. The time of spread was 17 days from the first case. All patients had mild symptoms, requiring no hospitalization, and none of them died. The frequency of symptomatic, laboratory-confirmed patients was higher among adults (94%) than among children (50%); the paediatric age group also had a higher frequency of exposed individuals who remained negative for infection. Ground-glass opacities on chest computed tomography were present in all patients with reported dyspnoea.

Conclusion: This study highlights a high risk of intrahousehold transmission from an index case, suggesting the need for (I) specific guidelines during periods of social distancing, (II) minimization of external exposures and, above all, (III) adoption of strict quarantine measures for suspected cases and family members to prevent outbreaks from spreading.

Key words: COVID-19; cluster; dispersion; social distancing.

Introduction

The first reports of what is now known as COVID-19 (coronavirus disease 2019) emerged in December 2019 in China, and infection with SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), the COVID-19 aetiological agent, subsequently spread worldwide [1]. The first case in Latin America was reported in Brazil on 25 February, and in the first week of July, Brazil had 1,600,000 cases and 64,000 deaths [2,3].

Different strategies of social isolation have been adopted in different countries to reduce community transmission; these strategies include school closures, the prohibition of non-essential worker activities, and more extreme measures, such as lockdowns [4,5].

Reports of household transmission began to emerge in the beginning of the epidemic in China and, later, in other countries prior to the recommendation of social distancing measures; however, few studies have evaluated the pattern of SARS-CoV-2 infection within family clusters after the public was advised to stay home [6,7].

We report the clinical characteristics and dispersion pattern of an outbreak in 24 members of a family cluster that occurred during a period of social isolation in the state of Pernambuco, Northeast Brazil.

Methodology

We carried out an observational descriptive study of a family cluster infected with SARS-CoV-2 in

Pernambuco, Northeast Brazil. The patients were classified as positive for COVID-19 if SARS-CoV-2 was detected by a real-time polymerase chain reaction (RT-PCR) test using a nasopharyngeal or oropharyngeal sample or confirmed by IgM or IgG serology with chemiluminescence 4 weeks after contact with the index case.

The primary case (index case) was defined as the first member of the cluster who had symptoms and who had a known risk of exposure outside the household during the family's stay in the same condominium; secondary cases were defined as contacts with the index case. We defined asymptomatic patients as those who had household contact and positive serology but no symptoms. Probable cases corresponded to confirmed case contacts who developed symptoms compatible with COVID despite negative serology and/or negative RT-PCR results. The serial interval of an infectious disease is defined as the duration of time between the onset of symptoms in the index individual and the onset of symptoms in an infected contact [8,9].

Results

On 12 March, the state of Pernambuco reported the first autochthonous case of the disease, and on 18 March, social distancing measures were announced. On the first of April, 24 individuals from the same extended family went to a private condominium on the coast of Pernambuco to fulfil the social distancing

recommendations. The condominium consisted of three houses and a common leisure area, with a swimming pool and open living area. Only two of the houses were occupied. Each house had 5 rooms, all with their own bathrooms, and there was another bedroom attached to both houses for the caregiver and baby-sitters (Figure 1).

The cluster consisted of 5 family units; 3 of them (families 1, 2 and 3) stayed in house A and the other two in house B. Each family stayed in one of the rooms, except for family 4, which was distributed in three different rooms of house B. The 3 baby-sitters, the cook and a caregiver shared the same bedroom, attached to houses A and B.

The group consisted of 9 (37.5%) males and 15 (62.5%) females, with a mean age of 28.9 years (2 months-81 years); there were 16 adults and 8 children (Table 1, 2).

The first symptomatic case occurred on 20 April in patient 1, who was staying in house A (P1-A); this patient, the baby-sitter, complained of fever, cough, nasal congestion, asthenia and headache. From an epidemiological point of view, it is suspected that exposure to an infected individual occurred when P1-A visited a bank four days before the onset of symptoms and remained in line for approximately 2 hours. She reported wearing a mask, but the bank was a crowded location, and social distancing between people was not practiced.

Figure 1. Timeline of symptom onset and laboratory results in a family cluster of COVID-19.
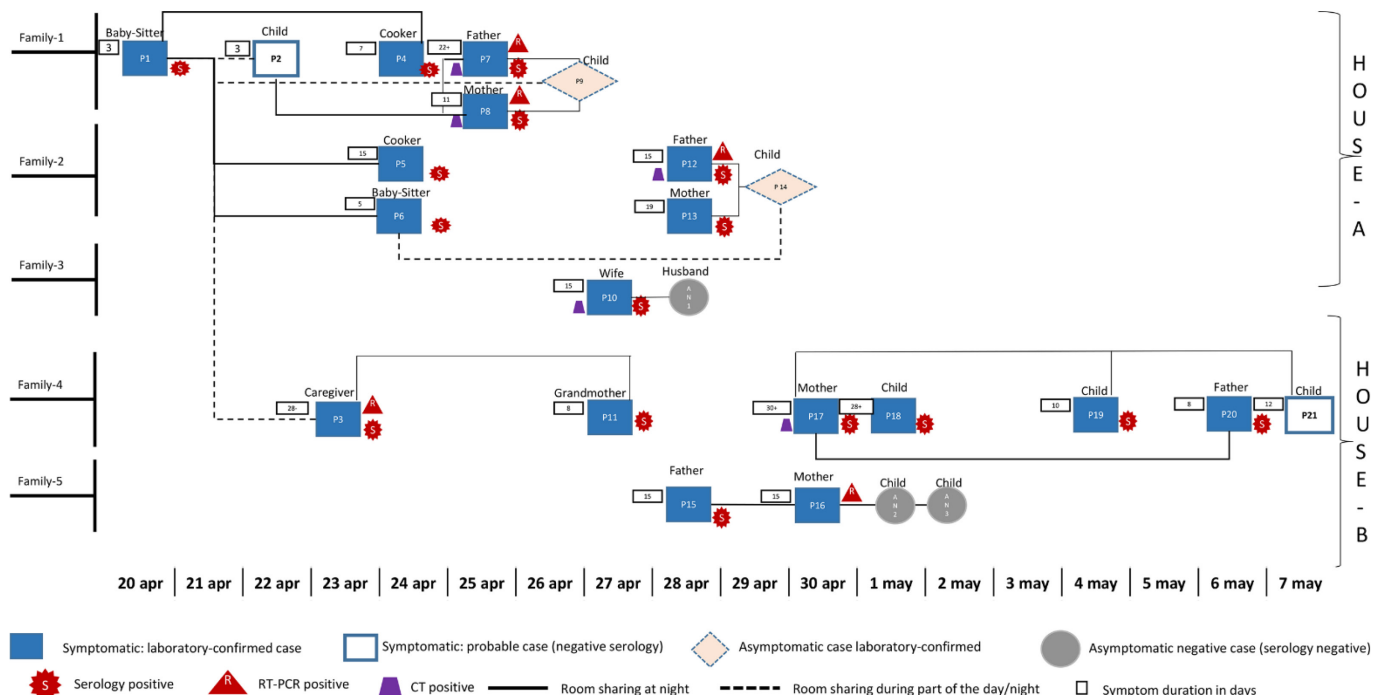
After the index case (P1-A) came another 10 laboratory-confirmed cases, with eight symptomatic adults and two asymptomatic children aged 2 years and 1 year with positive serology in house A. A two-month-old child (P2-A) from family 1 developed respiratory symptoms but had negative serology; this child was considered a probable case. The only person in house A who was asymptomatic and had negative serology was a 32-year-old adult (AN1-A), the husband of P10-A.

The serial interval ranged from 2 to 4 days between the index case and the five subsequent cases, with two days for P2-A and 3-4 days for the other four cases (P3-B, P4-A, P5-A, P6-B), who had close and prolonged contact in the same room. For the other cases, it is not

Table 1. Demographic data and clinical characteristics of the family cluster.

	P1-A	P2-A	P3-B	P4-A	P5-A	P6-A	P7-A	P8-A	P9-A	P10-A	P11-B	P12-A
Age, years	41	4 months	56	52	43	26	33	32	2 years and 8 months	29	87	34
Gender	F	F	F	F	F	F	M	F	M	F	F	M
Comorbidities	SAH	None	SAH, rinitis	None	SAH	None	Asthma	None	None	None	SAH, coronary disease (in use of pacemaker), Alzheimer	Severe Asthma + Hepatic steatosis + smoker for 6 years + obese
Drugs in regular use	Losartan	None	Losartan + Carvedilol	None	Losartan + Atenolol	None	None	None	None	None	Losartan, Simvastatin, Acetylsalicylic acid, Quetiapine	Aerolin + Clenyl
Symptom onset date	04/20/20	04/22/20	04/23/20	04/24/20	04/24/20	04/24/20	04/25/20	04/25/20	Asymptomatic	04/27/20	04/27/20	04/28/20
Date of positive RT-PCR COVID-19	Unperformed	Unperformed	05/05/20	Unperformed	Unperformed	Unperformed	05/04/20	05/04/20	Unperformed	Unperformed	Unperformed	05/04/20
Serology	Positive	Negative	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive
Instituted therapy	Symptomatic	Symptomatic	Symptomatic	Symptomatic	Nitazoxanide + Azithromycin (3)	Nitazoxanide + Azithromycin (3)	Hydroxychloroquine + Azithromycin (5)	Symptomatic	None	Symptomatic	Symptomatic	Nitazoxanide + Azithromycin (3)
Symptoms (duration in)												
Fever	Yes (2)	Yes (3)	No	No	Yes (1)	Yes (1)	No	Yes (2)	No	Yes (2)	Yes (3)	No
Maximum temperature 0C	38,5	38,2	-	-	38,7	39,6	-	38	-	38,4	38	-
Chills	No	*	No	No	Yes (2)	Yes (2)	No	Yes (1)	No	No	*	No
Non-productive cough	Yes (3)	Yes (2)	No	No	No	Yes (2)	No	Yes (7)	No	Yes (15)	No	Yes (8)
Sputum production	No	No	No	No	No	No	No	No	No	No	Yes (3)	No
Rhinorrhea	No	Yes (2)	No	No	Yes (7)	No	Yes (21)	Yes (2)	No	No	No	Yes (1)
Nasal congestion	Yes (2)	Yes (2)	Yes (4)	Yes (7)	Não	Yes (1)	No	Yes (2)	No	Yes (10)	Yes (3)	Yes (3)
Otalgia	No	*	No	No	Não	No	No	No	No	No	*	Yes (2)
Sore throat	No	*	No	No	No	Yes (5)	No	No	No	Yes (2)	*	Yes (10)
Anorexia	No	Yes (2)	Yes (5)	Yes (3)	Yes (3)	Yes (4)	No	No	No	No	Yes (8)	Yes (7)
Asthenia	Yes (2)	No	Yes (3)	No	Yes (7)	Yes (1)	No	No	No	Yes (8)	Yes (6)	Yes (1)
Myalgia	No	*	Yes (3)	No	No	No	Yes (5)	Yes (2)	No	Yes (5)	*	Yes (2)
Arthralgia	No	*	No	No	No	No	No	No	No	No	*	Yes (2)
Anosmia	No	*	Yes (35+)	Yes (7)	Yes (15)	No	Yes (22)	Yes (9)	No	Yes (10)	*	No
Dysgeusia	No	*	Yes (35+)	Yes (7)	Yes (15)	Yes (3)	Yes (9)	Yes (11)	No	Yes (10)	*	No
Headache	Yes (3)	*	Yes (2)	No	Yes (1)	Yes (3)	No	Yes (11)	No	Yes (7)	*	Yes (15)
Diarrhoea	No	Yes (2)	Yes (3)	No	Yes (4)	No	No	No	No	Yes (2)	Yes (2)	Yes (3)
Nausea	No	*	No	No	Yes (4)	Yes (4)	No	No	No	No	*	No
Vomiting	No	No	No	No	No	No	No	No	No	No	Yes (2 episodes)	No
Abdominal pain	No	*	No	No	Yes (4)	No	No	No	No	No	*	Yes (3)
Dyspnea	No	No	No	No	No	Yes (1)	Yes (6)	No	No	Yes (8)	No	Yes (4)
Rash	No	No	No	No	No	No	No	No	No	Yes (4)	No	No
Eye redness	No	No	No	No	No	Yes (4)	No	No	No	No	No	Yes (1)
Others	Hoarseness (2)	*	No	No	No	Tachycardia (1)	No	No	No	Retroorbital pain (2)	*	No
Computed Tomography	Unperformed	Unperformed	Unperformed	Unperformed	Unperformed	Unperformed	Abnormal	Abnormal	Unperformed	Abnormal	Unperformed	Abnormal

F = female; M = male; SAH = systemic arterial hypertension. *A 4-month-old child and an elderly person with dementia were excluded from symptom evaluation.

possible to state whether infection occurred from the index case or secondary contacts.

In house B, the first case, P3-B, showed symptom onset after 3 days of high-risk contact (sharing a bedroom) with the index case P1-A. Another 7 cases in house B had laboratory confirmation, and a seven-year-old child (P21-B), who was symptomatic but have negative serology, was considered a probable case. Two other children aged seven (AN2-B) and ten years (AN3-B) were asymptomatic and had negative serology.

The total attack rate in this family cluster was 75% (19/24) based on laboratory-confirmed cases or 87.5% (21/24) if we included probable cases. With regard to laboratory-confirmed infections by age group, the attack rate in the adult group was 94% (15/16), and the rate in the paediatric age group was 50% (4/8). If we included the two probable cases, the attack rate rose to 75% (6/8) among children. The spread time from the first to the 21st case, as determined from the onset of symptoms, was 17 days (Figure 1).

Table 2. Demographic data and clinical characteristics of the family cluster (continuation).

	P13-A	P14-A	P15-B	P16-B	P17-B	P18-B	P19-B	P20-B	P21-B	AN1-A	AN2-B	AN3-B
Age (years)	27	1 year and 8 months	46	35	47	14	12	48	7	32	10	7
Gender	F	M	M	F	F	M	F	M	M	M	F	F
Comorbidities	Pregnant + Gestational diabetes	None	Depression	Thrombophilia (MTHSR mutation) + myofascial syndrome + hashimoto thyroiditis	Asthma, SAH	None	None	Osteoarthritis	None	None	None	None
Drugs in regular use	None	None	Vortioxetine + Trazodone	None	Valsartan	None	None	None	None	None	None	None
Symptom onset date	04/28/20	Asymptomatic	04/28/20	04/30/20	04/30/20	05/01/20	05/04/20	05/06/20	05/07/20	Asymptomatic	Asymptomatic	Asymptomatic
RT-PCR COVID-19	05/04/20	Unperformed	Unperformed	05/06/20	Unperformed	Unperformed	Unperformed	Unperformed	Unperformed	Unperformed	Unperformed	Unperformed
Serology	Positive	Positive	Positive	Negative	Positive	Positive	Positive	Positive	Negative	Negative	Negative	Negative
Instituted therapy	Symptomatic	None	Symptomatic	Symptomatic	Azytromicine	Symptomatic	Symptomatic	Symptomatic	Azytromicine	None	None	None
Symptoms (duration in)												
Fever	Yes (1)	No	Yes (1)	No	No	Yes (3)	No	No	Yes (3)	No	No	No
Maximum temperature	37,8	-	38,5	-	-	38,5	-	-	38	-	-	-
Chills	Yes (3)	No	No	Yes (6)	No	No	No	No	No	No	No	No
Non-productive cough	Yes (19)	No	Yes (1)	Yes (6)	Yes (21)	Yes (3)	No	No	No	No	No	No
Sputum production	No	No	Yes (10)	No	No	Yes (8)	No	No	Yes (3)	No	No	No
Rhinorrhea	No	No	Yes (15)	Yes (1)	Yes (21)	Yes (8)	Yes (10)	No	Yes (6)	No	No	No
Nasal congestion	Yes (9)	No	No	Yes (15)	Yes (21)	Yes (12)	Yes (2)	No	Yes (6)	No	No	No
Otalgia	Yes (10)	No	No	Yes (15)	No	No	No	No	No	No	No	No
Sore throat	Yes (15)	No	Yes (3)	Yes (4)	No	No	Yes (2)	No	No	No	No	No
Anorexia	Yes (7)	No	No	No	No	No	No	No	No	No	No	No
Asthenia	Yes (7)	No	Yes (7)	Yes (7)	No	No	Yes (3)	No	No	No	No	No
Myalgia	Yes (7)	No	Yes (3)	Yes (2)	Yes (9)	No	No	No	No	No	No	No
Arthralgia	Yes (7)	No	Yes (3)	No	No	No	No	No	No	No	No	No
Anosmia	Yes (19)	No	Yes (5)	Yes (10)	#Yes (30+)	#Yes (28+)	No	Yes (8)	No	No	No	No
Dysgeusia	Yes (15)	No	No	Yes (10)	#Yes (30+)	No	No	Yes (8)	No	No	No	No
Headache	Yes (15)	No	Yes (20)	Yes (4)	No	Yes (5)	Yes (10)	No	No	No	No	No
Diarrhoea	No	No	Yes (14)	No	Yes (1)	No	Yes (5)	No	Yes (5)	No	No	No
Nausea	No	No	Yes (3)	No	No	No	No	No	No	No	No	No
Vomiting	No	No	No	No	No	No	No	No	No	No	No	No
Abdominal pain	No	No	No	No	No	No	Yes (4)	No	No	No	No	No
Dyspnea	Yes (2)	No	No	No	Yes (21)	No	No	No	No	No	No	No
Rash	No	No	No	No	No	No	No	No	No	No	No	No
Eye redness	No	No	No	No	No	No	No	No	No	No	No	No
Others	Gingival bleeding (1 episode); Tachycardia (1)	No	No	Paresthesia in the extremities (6) + Retroorbital pain (3)	Retroorbital pain (2)	No	Retroorbital pain (10)	No	Epistaxis (2 episodes)	No	No	No
Computed Tomography	Unperformed	Unperformed	Unperformed	Unperformed	Abnormal	Unperformed	Unperformed	Unperformed	Unperformed	Normal	Unperformed	Unperformed

F = female; M = male; SAH = Systemic arterial hypertension; #Symptoms present until the day of the interview.

Symptoms

The frequency of symptomatic patients was 94% (15/16) among adults and 50% (4/8) among children. Two cases in the paediatric age group were asymptomatic but had laboratory-confirmed COVID-19 (Table 1, 2).

The most frequent symptom among adults was nasal congestion (80%), followed by asthenia, anosmia and dysgeusia in 79%; respiratory symptoms such as non-productive cough occurred in 60%; and rhinorrhoea (53%), with only 2 (13%) patients reporting productive cough. Fever was reported in half of the cases (Table 1, 2). Among children, respiratory symptoms predominated, such as nasal congestion (100%) and rhinorrhoea (75%); productive cough occurred in half of the cases. Fever and diarrhoea were present in 75% of patients (Table 1, 2).

Laboratory diagnosis

All family members underwent IgM and IgG serology at least 4 weeks after the onset of symptoms, with 75% (18/24) positivity. Among adults, 87.5% were positive (14/16); among children, 50% were positive (4/8). In the paediatric age group, there were two symptomatic patients (P2-A, P21-B) who had COVID-19-compatible signs and a high risk of exposure but negative serology, and two asymptomatic cases had positive serology (P9-A and P14-A) (Figure 1). RT-PCR was performed in seven patients (P3-B, P7-A, P8-A, P12-A, P13-A, P16-B, AN1-A), with six being

positive (86%; 6/7) and only one asymptomatic adult (AN1-A) being negative on RT-PCR and serology. One patient (P16-B) with positive RT-PCR had negative serology (Figure 1).
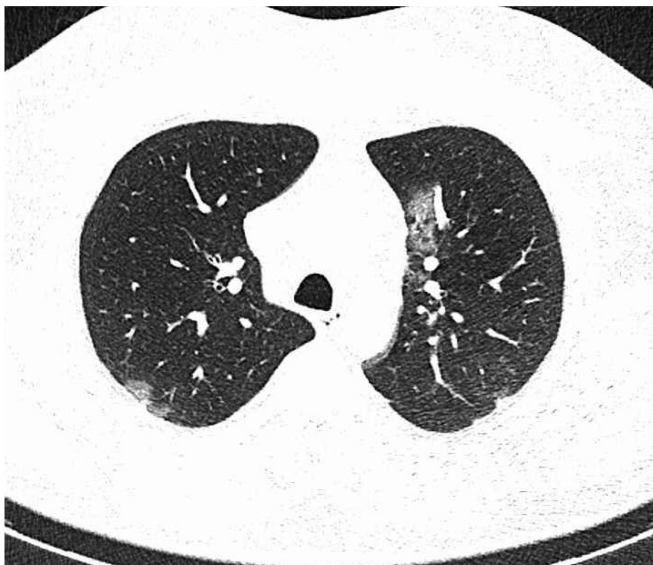
Computed tomography findings

Computed tomography (CT) examinations were performed in 5 of the 6 patients with complaints of dyspnoea (P7-A, P8-A, P10-A, P12-A, P-17-B); all 5 examinations showed bilateral ground-glass opacities, with areas of consolidations between the lesions, affecting less than 25% of the lung parenchyma (Figures 2 and 3). One asymptomatic patient (NA-1) underwent a CT scan that yielded no abnormal findings, and the patient's RT-PCR and serology results were negative.

Discussion

In this household cluster, a high attack rate was observed, with more than 75% of family members affected in a period of 17 days and a short incubation period of 2-4 days among symptomatic individuals. All patients had mild symptoms, requiring no hospitalization; no deaths occurred.

Analysis of family clusters varies considerably in the literature with regard to the number, age group,

Figure 3. 3D chest image showing the extent of lung involvement.

Figure 2. Chest tomography of one of the patients, P12.

Bilateral sparse ground-glass opacities, predominating in the peripheral regions, associated with thickening of interlobular septa (mosaic paving). There are also small foci of intermingled consolidations.

Bilateral sparse ground-glass opacities, predominating in the peripheral regions, associated with thickening of interlobular septa (mosaic paving). There are also small foci of intermingled consolidations.

attack rates and isolation strategies based on the index case [6,7,10-13].

For a family cluster in Taiwan, five symptomatic adults and one 11-year-old child with a high attack rate of 60% were reported, but the time between the first symptomatic case and the subsequent case was 12 days, longer than in our study, and the illness lasted up to 60 days, including one fatal outcome; however, the Taiwanese report had an older patient population [11].

In our cluster, the clinical manifestations of the cases were mild, with no hospitalization, and the predominant symptoms in adults were anosmia (69%) and dysgeusia (56%), with a lower frequency of respiratory symptoms and fever.

Our results differ from those of other studies that reported clusters of severe disease in families. In a study that evaluated family clusters from patients admitted to a hospital in Wuhan, the authors identified 35 primary cases, 59 secondary cases and 36 uninfected family members, with approximately 56% of cases classified as severe and critical and with lethality of 10%, but these findings may be related to the fact that the index cases were identified starting with hospitalized patients [6,11].

In our study, the population was predominantly young adults without comorbidities, which may explain the relatively mild clinical manifestations. Only two patients, aged 83 and 56 years, both with systemic arterial hypertension and a history of arrhythmia, were considered at risk, but even these patients developed only mild illness.

A different pattern was observed in the paediatric age group, with a higher frequency of rhinorrhoea, nasal congestion and fever than in the adults and a lower symptomatic rate (50% vs 94%), with two asymptomatic cases being laboratory-confirmed COVID-19 and two others being asymptomatic with negative serology despite high exposure to confirmed cases.

Children in family clusters have been reported to have milder symptoms and a higher frequency of asymptomatic than adults [7,12,14-16]. In a study involving 25 children infected with SARS-CoV-2 from a family cluster outbreak, Bai et al. reported 32% (8/25) of asymptomatic cases; among symptomatic cases, 16% (4/25) were classified as mild and 50% (13/25) as ordinary, and no serious or critical cases were reported [15]. Sun et al reported a family cluster in which the parents had a positive RT-PCR for COVID-19, with the mother presenting a severe form, and the child was negative for the disease despite close contact with the parents [16].

Different mechanisms have been suggested to explain the mild and asymptomatic forms of COVID-19 in the paediatric age group. ACE2 receptors, which are necessary for internalization of the virus in the host cell, are less active in children than in adults, hindering entry of the virus. Increased susceptibility to other respiratory viral diseases in childhood can, by a competitive mechanism, limit infection with SARS-CoV-2. In addition, cross-reactive antibodies for these other infections, including other coronaviruses, might play a partly protective role against SARS-CoV-2 [17-20].

Despite clinical and epidemiological variations between family cluster studies, it is observed that dispersion of the virus among members of households involves a large proportion of the family members in a short period of time, which may lead to serious consequences in some risk groups that are in isolation at home. The World Health Organization has reinforced the importance of breaking the chains of community transmission by detecting cases early and testing and isolating infected individuals and contacts; however, a specific approach or isolation strategy in the household environment has not been clearly proposed [13,14,20].

Conclusions

In the cluster that we describe, although the families inhabited a large middle-class condominium, there was no isolation at the time of detection of the index case, and rooms were shared among members of the cluster, which may explain the high attack rates. In Brazil and many other countries, the limited availability of hospital beds or the inability to use adapted hotels to house confirmed or suspected cases impairs strategies for isolation from the primary case. Precarious housing conditions with members of the same family inhabiting small physical spaces facilitate the risk of transmission. In addition, the absence of a clear strategy to guide the population towards necessary precautions at home in the presence of a suspected case increases the risk of household transmission in periods of isolation. Inevitably, index cases tend to arise when family members need to leave isolation to perform essential tasks and to go to supermarkets, pharmacies and banks to receive benefits made available by the government, as in Brazil.

This cluster highlights the relevance of family cluster studies and reinforces the necessity of measures to isolate members of a household during pandemic periods, avoiding external exposure as much as possible. Overall, this study highlights the high risk of intrahousehold transmission from an index case,

suggesting the need for specific isolation guidelines. Moreover, strict isolation measures for suspected cases and between family members must be implemented, including not sharing rooms or utensils, properly ventilating living areas, and reinforcing the use of masks and social distancing, to mitigate the spread of the virus and reduce the numbers of cases and complications.

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