COVID-19 in long-term care facilities in Brazil: serological survey in a post-outbreak setting

Eliana Nogueira Castro de Barros[1], **Adriana P. do Valle**[2], **Patricia Emilia Braga**[1], **Juliana Y. K. Viscondi**[1], **Antonio R. B. da Fonseca**[2], **Tazio Vanni**[1], **Anderson da Silva**[1], **Maria Regina Cardoso**[3], **Paulo José F. Villas Boas**[2], **Alexander Roberto Precioso**[1,4]

[1]Instituto Butantan, Centro de Farmacovigilância, Segurança Clínica e Gestão de Risco, São Paulo, São Paulo, Brazil

[2]Universidade Estadual Paulista, Faculdade de Medicina de Botucatu, Departamento de Clínica Médica, Botucatu, São Paulo, Brazil

[3]Universidade de São Paulo, Faculdade de Saúde Pública, São Paulo, São Paulo, Brazil

[4]Universidade de São Paulo, Faculdade de Medicina, Departamento de Pediatria, São Paulo, São Paulo, Brazil

Correspondence to: Eliana Nogueira Castro de Barros
Instituto Butantan, Centro de Farmacovigilância, Segurança Clínica e Gestão de Risco, Av. Vital Brasil, 1500, Butantã, CEP 05503-900, São Paulo, SP, Brazil
Tel: +55 11 3723-2121

E-mail: eliana.barros@butantan.gov.br

ABSTRACT

This cross-sectional seroepidemiological survey presents the seroprevalence of SARS-CoV-2 in a population living in 15 Long-Term Care Facilities (LTCFs), after two intra-institutional outbreaks of COVID-19 in the city of Botucatu, Sao Paulo State, Brazil. Residents were invited to participate in the serological survey performed in June and July 2020. Sociodemographic and clinical characterization of the participants as well as the LTCF profile were recorded. Blood samples were collected, processed and serum samples were tested using the rapid One Step COVID-19 immunochromatography test to detect IgM and IgG anti-SARS-CoV-2. Among 209 residents, the median of age was 81 years old, 135 (64.6%) were female and 171 (81.8%) self-referred as being white. An overall seroprevalence of 11.5% (95% CI: 7.5% – 16.6%) was found. The highest seroprevalences of 100% and 76.9% were observed in LTCFs that had experienced COVID-19 outbreaks. Most residents with positive immunochromatography tests (70.8%) referred previous contact with a confirmed COVID-19 case. Although there was a relatively low seroprevalence of COVID-19 in the total number of elderly people, this population is highly vulnerable and LTCFs are environments at higher risk for COVID-19 dissemination. A well-established test for COVID-19 policies, the adequate characterization of the level of interaction between residents and the healthcare provider team and the level of complexity of care are crucial to monitor and control the transmission of SARS-CoV-2 in these institutions.

KEYWORDS: COVID-19. SARS-CoV-2. Seroprevalence. Long-term care facility. Elderly.

Since December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its associated clinical syndrome (COVID-19) was responsible for more than 26 million cases and 900,000 deaths worldwide[1] and has challenged the global scientific community. In Brazil, the Ministry of Health confirmed on February 26th, 2020 the first case of coronavirus in the country, and the announcement of the first death by COVID-19 on March 17th of the same year. Up to October 3rd, 4,906,833 confirmed cases and 145,987 deaths due to COVID-19 were reported in the country, with 1,003,428 confirmed cases of COVID-19 and 36,136 deaths in Sao Paulo State[2], the first epicenter of COVID-19 in Brazil.

Since the first case of COVID-19 in the world, there has been an evolution in the understanding of how the virus spreads and what must be done to contain the viral transmission at high-risk settings. Long-term care facilities (LTCFs) are considered at higher risk for virus outbreaks with poorer outcomes of residents, which can be particularly devastating in low- and middle-income countries[3,4]. In March 2020,

the Brazilian Society of Geriatrics and Gerontology and the World Health Organization recommended the suspension of external visits to residents in LTCFs[5]. Therefore, the assessment of SARS CoV-2 seroprevalence is important in the definition of heath care policies in LTCFs.

Here, we present the results of a serological testing for SARS-CoV-2 in a population living in 15 LTCFs, following two intra-institutional outbreaks of COVID-19 in the city of Botucatu, Sao Paulo State, Brazil, with a population of 139,856 inhabitants and an elderly population of 22,756 inhabitants (16.3%)[6].

Starting on May 29th and May 30th, 2020, two LTCFs located in the city of Botucatu experienced COVID-19 outbreaks. The first cases, in both institutions, were confirmed in women residents by RT-PCR. From June 3rd to 25th, the local health authority collected nasopharyngeal and oropharyngeal secretions to perform the RT-PCR test for COVID-19 in all elderly residents and employees (called "Universal RT-PCR test") from the 20 LTCFs located in the city. In this study, 20 institutions were invited and 15 (75%) agreed to participate. Only the residents were invited to participate in the serological survey. The institutions were assessed for the complexity of the care provided based on the degree of dependence of the residents. The degree of dependence and the most frequent fragility observed among residents were used to define the level of care complexity of each LTCF. The functional capacity of the elderly was assessed using the Katz index, which includes actions related to self-care (bathing, personal hygiene, dressing, the ability to eat without help, the ability to move without help for transference and continence). The total score corresponds to the sum of the 'yes' answers in relation to the items related to independence. Residents were considered independent if they reached a score between 5 and 6 points, partially dependent when the result was 3 or 4 points and highly dependent with scores of zero, 1 or 2 points[7]. Frailty was assessed by the Frail Scale, in which residents were classified as robust (0 points), prefrail (1 to 2 points), and frail (3 points)[8] and for Frail Nursing Home (Frail-NH), [robust (0 to 1 point), prefrail (2 to 5 points), and frail (6 or more points)][9]. The presence of previous symptoms in the 14 days prior to this survey were obtained from a report by the resident or the LTCF team.

The rapid serological One Step COVID-19 tests (Guangzhou Wondfo Biotech Co., Ltd., China) was approved by the Brazilian Regulatory Agency – ANVISA and were supplied by Instituto Butantan, Sao Paulo, Brazil. The test consists of a lateral flow immunochromatographic assay that is able to detect both, IgM and IgG immunoglobulins together, with no discrimination of the immunoglobulin isotype[10].

Blood samples were collected, processed and the serological tests were performed on serum samples. Moreover, information was collected on the demographic and clinical status of the participants, as well as the characteristics of the institutions.

The rapid test kit showed sensitivity of 86.4% (95% CI: 82.4%-89.6%) and specificity of 99.6% (95% CI: 97.6%-99.9%)[10] according to the manufacturer. Additionally, there was a better performance of these kits using plasma or serum samples instead of capillary whole blood[11], so in this survey all tests were performed on serum samples.

The study was reviewed and approved by both Ethics Committees of the Clinical Hospital of University of Sao Paulo Medical School (CAPPesq CAAE: 32210620.9.2004.5421 – 4070345 – June 4th, 2020) and Botucatu Medical School (CAAE: 32210620.9.2003.5411 - 4.075.142 – June 8th, 2020).

COVID-19 seroprevalence rates were calculated based on the results of the rapid serological test for each participating resident from the LTCFs. The prevalence was reported as frequencies of positive tests corresponding to a proportion of the total sample considering a 95% confidence interval.

The demographic characteristics of the participants and the LTCFs were described as frequencies (counts and percentage), or their median, by age and by the rate of residents per team. Fisher's exact or chi-square tests were used to compare the rapid serological results. The Mann-Whitney test was carried out to compare the age of the population age. Statistical analyses were performed using Stata, version 13 (StataCorp, College Station, Texas, USA). The significance level was set at 5%. A total of 209 residents (73.3% of all residents in the 20 LTCFs in the city) were tested from June 22nd to July 8th, 2020. Their median age was 81 years old (min 50 – max 106), 135 (64.6%) were female and 171 (81.8%) self-referred as white. Regarding their clinical profiles, 129 (61.7%) residents had between 2 and 4 comorbidities and 120 (57.4%) were using 1 to 5 medicines daily; 194 (92.8%) had no previous COVID-19 symptoms in the 14 days prior to the test. Regarding the state of dependence and fragility, 91 (43.5%) residents were dependent for three or more daily activities (Katz index) and 89 (42.6%) were considered frail (Frail-NH index). Most residents (101; 48.3%) slept in multiple accommodation (Table 1).

An overall seroprevalence of 11.5% (95% CI: 7.5%-16.6%) was found in the population, ranging from 3.4% to 100% in seven LTCFs that presented at least one positive serological test (Table 2). The highest seroprevalences of 100% and 76.9% were observed in

Table 1 - Description of the study population and distribution of serological rapid test (SRT) results during the SARS-CoV-2 survey in LTCFs, Botucatu municipality, June-July, 2020.

Variables	Study population (N=209)		Positive SRT (N=24)		Negative SRT (N=185)		p-value
	N	%	N	%	N	%	
Age (years)							**0.471**
Median (min – max)	81 (50 - 106)		81 (50 - 106)		81 (56 - 103)		
Gender							**0.257**
Male	74	35.4	6	25.0	68	36.8	
Female	135	64.6	18	75.0	117	63.2	
Self-referred ethnicity							**0.041**
White	171	81.8	16	66.7	155	83.8	
Non-white	38	18.2	8	33.3	30	16.2	
Symptoms (during the previous 3 months)							**0.754**
No	162	77.5	18	75.0	144	77.8	
Yes	47	22.5	6	25.0	41	22.2	
Symptoms (14 days before testing)							**0.148**
No	194	92.8	24	100	170	91.9	
Yes	15	7.2	0	0.0	15	8.1	
Contact with suspected or confirmed COVID-19 cases							**< 0.001**
No	188	90.0	7	29.2	181	97.8	
Yes	21	10.0	17	70.8	4	2.2	
Number of underlying diseases							**0.149**
1	25	12.0	5	20.8	20	10.8	
2 to 4	129	61.7	16	66.7	113	61.1	
5 to 10	55	26.3	3	12.5	52	28.1	
Number of medicines in use							**0.592**
1 to 5	120	57.4	15	62.5	105	56.8	
6 to 12	89	42.6	9	37.5	80	43.2	
Katz Index							**0.838**
Independence	63	30.1	6	25.0	57	30.8	
Partial dependence	55	26.3	7	29.2	48	25.9	
Total dependence	91	43.5	11	45.8	80	43.2	
Frail-BR Index							**0.641**
Robust	48	23.0	4	16.7	44	23.8	
Pre-frail	73	34.9	8	33.3	65	35.1	
Frail	88	42.1	12	50.0	76	41.1	
Frail-NH Index							**0.467**
Robust	58	27.8	5	20.8	53	28.6	
Pre-frail	62	29.7	6	25.0	56	30.3	
Frail	89	42.6	13	54.2	76	41.1	
Complexity of the LTCF care level							**0.007***
Level I	78	37.3	3	12.5	75	40.5	
Level II	18	8.6	0	0.0	18	9.7	
Level III	113	54.1	21	87.5	92	49.7	
Accommodation type							**0.577**
Single	88	42.1	8	33.3	80	43.2	
Doble	20	9.6	2	8.3	18	9.7	
Multiple (+3 beds)	101	48.3	14	58.3	87	47.0	

*level I versus level II + level III; SRT = Serological Rapid Test; LTCF = Long-Term Care Facility

residents living in LTCFs that had already experienced COVID-19 outbreaks. During outbreaks, these two LTCFs registered six deaths from COVID-19, corresponding to an overall case fatality rate of 25% (33.3% at LTCF #8 and 16.7% at LTCF #14, Table 2).

The overall positivity rate of RT-PCR among health care teams was 4.2% (7/168); confirmed cases in team members were observed only in the two LTCFs that had experienced COVID-19 outbreaks, corresponding to a positivity rate of 40% (4/10, LTCF #8) and 60% (3/5 at LTCF #14) assessed by nasopharyngeal and oropharyngeal RT-PCR.

The frequency of non-white ethnicity was significantly higher in residents with positive serological test compared to the negative group (p=0.041). Most residents with positive serological tests (70.8%) referred previous contact with confirmed cases of COVID-19, whereas only 2.2% of residents with negative results did not report such exposure to the disease (p<0.001) (Table 1).

More than half of all residents (113 or 54.1%) lived in LTCFs classified as level III of care complexity. Most residents in LTCFs classified as level II/III had a positive serological test (87.5%) compared to seronegative cases (59.4%) (p=0.007) (Table 1).

The median rate of residents per health provider supervision was 1.3 (0.7 to 3.0); more than half of the LTCFs had 100% of the beds occupied, with bed occupancy rates ranging from 80.0% to 100%, and 12 (80.0%) of them with private financing. The dependency assessment showed 11 (73.3) LTCFs classified at level III of care complexity (Table 3).

The overall seroprevalence (11.5%) observed in the LTCF residents was relatively low, compared to some institutions in high-income countries[12], but it varied considerably when compared to the results obtained by RT-PCR in each LTCF, probably because many residents had already recovered from the symptoms of COVID-19 or were asymptomatic carriers at some stage and had detectable antibodies at the time of serological test.

Symptoms of COVID-19 in the elderly do not seem to be a good predictor of infection, since almost 93% of the residents examined did not show symptoms in the period of at least 14 days before the serological test, corroborating similar findings from other studies[13,14].

Table 2 - Universal RT-PCR and serological rapid test (SRT) results during the SARS-CoV2 survey in LTCFs, Botucatu municipality, June-July, 2020.

LTCF #	Universal RT-PCR								Serological Rapid Test			
	Residents				Positive PCR, Deaths		Health provider team		Residents			
	Tested	Positive PCR, Cases					Tested	Positive PCR	Tested	Positive SRT		
	n	n	%	95% CI	n	CFR (%)	n	n	n	n	%	95% CI
1	63	0	0.0	0.0 - 5.7			41	0	59	2	3.4	0.4 - 11.7
2	19	0	0.0	0.0 - 17.6*			13	0	18	0	0.0	0.0 - 18.5*
3	7	0	0.0	0.0 - 41.0*			6	0	7	0	0.0	0.0 - 41.0*
4	20	0	0.0	0.0 - 16.8*			30	0	20	0	0.0	0.0 - 16.8*
5	7	0	0.0	0.0 - 41.0*			7	0	7	0	0.0	0.0 - 41.0*
6	11	0	0.0	0.0 - 28.5*			5	0	11	1	9.1	0.2 - 41.3
7	7	0	0.0	0.0 - 41.0*			4	0	7	1	14.3	0.4 - 57.9
8	13	12	92.3	64.0 - 99.8	4	33.3	10	4	7	7	100	59.0 - 100*
9	14	0	0.0	0.0 - 23.2*			9	0	13	0	0.0	0.0 - 24.7*
10	6	0	0.0	0.0 - 45.9*			8	0	6	1	16.7	0.4 - 64.1
11	8	0	0.0	0.0 - 36.9*			5	0	8	0	0.0	0.0 - 36.9*
12	8	0	0.0	0.0 - 36.9*			6	0	8	0	0.0	0.0 - 36.9*
13	8	0	0.0	0.0 - 36.9*			6	0	9	0	0.0	0.0 - 33.6*
14	15	12	80.0	51.9 - 95.7	2	16.7	5	3	13	10	76.9	46.2 - 95.0
15	16	0	0.0	0.0 - 20.6*			13	0	16	2	12.5	1.6 - 38.3
Global	**222**	**24**	**10.8**	**7.1 - 15.7**	**6**	**25.0**	**168**	**7**	**209**	**24**	**11.5**	**7.5 - 16.6**

*one sided test, 97,5% CI; LTCF = Long term care facility; CFR = Case Fatality Rate; SRT = Serological Rapid Test; CI = Confidence Interval

Table 3 - LTCFs characteristics, Botucatu municipality, June-July, 2020.

LTCFs characteristics	Median (min – max)
Resident per health provider team rate[1]	1.3 (0.7 - 3.0)
Bed occupancy rate (%)[2]	100 (80.0 -100)
	N (%)
Funding type	
Private	12 (80.0)
Philanthropic	3 (20.0)
Complexity of care level[3]	
Level I	3 (20.0)
Level II	1 (6.7)
Level III	11 (73.3)

[1]Based on the number of residents and health provider team during the Universal RT-PCR testing; [2]Bed occupancy rate at the time of Universal RT-PCR testing; [3]Complexity of care level based on the highest proportion of residents of each level of dependency and fragility assessed by the Katz index.

Therefore, the immediate testing of all contacts in the first positive case should be performed regardless of the presence of symptoms[15]. However, the fact that the One Step COVID-19 test does not differentiate between IgM and IgG immunoglobulins may be a limitation for the interpretation of results during outbreaks in this population, so that other testing strategies or combined strategies should be planned.

The contact with the care giver team coming from outside the institution, facility, the presence of visitors and the living conditions of the elderly make the LTCFs highly vulnerable to the transmission of COVID-19[12]. Such vulnerability can be seen in the two LTCFs that had previous COVID-19 outbreaks and had seroprevalence rates above 70% and case fatality rates of 33.3% in their residents. In addition, only in those same two LTCFs, cases of COVID-19 in health care teams were confirmed, showing a RT-PCR positivity rate of 40% (4/10, LTCF #8) and 60% (3/5 at LTCF #14). High positivity rates of COVID-19 in care giver teams of LTCFs that experienced COVID-19 outbreaks have also been observed in investigations carried out in the United States. In these studies, an average of 7.4% positivity was reported in health care teams of 15 LTCFs tested soon after an initial case of COVID-19 was identified, contrasting with the average of 1.0% positivity in care giver teams of 13 LTCFs with no COVID-19 identified[16]. In our study, the LTCFs affected by outbreaks had a higher positivity rate among their team members than observed in the literature, suggesting that specific characteristics such as living conditions (frailty and degree of dependence) of the

residents in these LTCFs would require special care on the part of the health team and close contact for daily activities; however other specific risk factors for the transmission of SARS-CoV-2 should be investigated in these settings. The prevalence of COVID-19 in the community is another important factor that may impact the number COVID-19 cases and deaths in nursing homes[18] and should be considered in the context of investigations carried out in LTCFs during outbreaks.

Most residents with a positive test for COVID-19 tend to have a higher degree of dependence, comorbidities or different levels of cognitive decline or dementia, making it difficult to comply with contingency measures[17]. In this study, among residents with a positive test, 87.5% lived in complex care institutions level III, almost half of the population (45.8%) was totally dependent on the team care for daily activities, 54.2% were considered frail and 58.3% lived in accommodation with multiple beds, which favors the spread of the disease. Even so, the low seroprevalence in this population can be explained by the restriction of visits and group activities, as well as by the implementation of hygiene protocols in the LTCFs[5].

Normally, in health institutions of high complexity frailty and extreme dependent residents imply a greater number of healthcare givers, increasing the risks of transmission of SARS-CoV-2. This study showed a median rate of 1.3 residents per health team. However, there is no consensus on the impact of the proportion of resident per health team on the dissemination of COVID-19 in LTCFs settings[18,19].

Most LTCFs investigated in this study are financed by the private sector 80%). In fact, Sao Paulo State is the richest State in the federation[20]. However, the country presents many other challenges in relation to the elderly and COVID-19.

Equal acquisition and distribution of adequate personal protective equipment in quantity and quality for residents and workers, specialized training for health teams, scheduled periodic repetition of tests if someone develops symptoms or presents a positive test for the virus[17], laboratory capacity and for the last, but not least, the assessment of the mental and emotional state of the workforce in nursing homes. Faced with a possible second wave of COVID-19, LTCFs require special attention. The literature suggests that these units should be the last ones to reopen and isolation measures including restriction of visits should continue[17]. The government should discuss special lines of credit and new financing sources directed to these institutions to ensure the adequate isolation, routine examination and adequate care of residents, reducing transmission and avoiding lethal endpoints.

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CONFLICT OF INTERESTS

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