VACCINE BREAKTHROUGH INFECTIONS WITH SARS-COV-2 IN A RETIREMENT HOME

José Cherem[1], M.S., Ph.D., Joseane Camilla de Castro[2], Ph.D, Victor Satler Pylro[3], Ph.D., Ingrid Marciano Alvarenga[2], M.S, Karla Silva Teixeira[2] Ph.D., Denise Alvarenga Rocha[2], Ph.D., Margareth Maria Pretti Dalcolmo[4], PhD., Joziana Muniz de Paiva Barçante[1]*, Ph.D.

[1] Department of Medicine, Federal University of Lavras, Brazil. Câmpus Universitário, Caixa Postal 3037, CEP 37200-900, Lavras/MG – Brazil.

[2] Department of Veterinary Sciences, Federal University of Lavras, Brazil. Câmpus Universitário, Caixa Postal 3037, CEP 37200-900, Lavras/MG – Brazil.

[3] Department of Biology, Federal University of Lavras, Brazil. Câmpus Universitário, Caixa Postal 3037, CEP 37200-900, Lavras/MG – Brazil.

[4] Fundação Oswaldo Cruz, Escola Nacional de Saúde Pública, Centro de Referência Professor Hélio Fraga. Estrada de Curicica 2000, Jacarepaguá 22710552, Rio de Janeiro/RJ – Brazil.

* corresponding author: Dr. Joziana Muniz de Paiva Barçante Infectious and Parasitic Diseases Lab., Department of Medicine, Federal University of Lavras. Telephone: +55 35 991955858. E-mail address: joziana@ufla.br. Câmpus Universitário, Caixa Postal 3037, CEP 37200-900, Lavras/MG – Brazil.

Abstract

The coronavirus disease 2019 pandemic triggered a series of concerns and changes worldwide, and even after the development and application of coronavirus vaccines, some cases of infection continued to occur. Here, we report an outbreak of SARS-CoV-2 in a Brazilian retirement home in fully vaccinated elderly residents and workers. This observational cohort study evaluated residents and workers within a retirement home who became infected with the coronavirus after COVID-19 vaccination between January and February 2021. Of the 85 residents, 31 were infected with the virus, later classified as the B.1.1 variant. Most of the individuals showed mild symptoms, and four died. We applied a contact tracing and surface testing strategy, allowing us to slow down and control the spread of SARS-CoV-2 in the retirement home. Our report reinforces the role played by the vaccine in protecting individuals against severe COVID-19 and the importance of maintaining all recommended nonpharmacological interventions to reduce virus transmission.

Introduction

The progression of COVID-19 to a severe state relates to several risk factors, such as old age, male sex, the presence of any comorbidity, and pregnancy.[1] Older age was associated with increased COVID-19 morbidity, admission to the intensive care unit (ICU), progression to acute respiratory distress syndrome (ARDS), fever, and higher mortality rates.[2]

The COVID-19 pandemic also brought social, economic, and scientific impacts,[3] justifying the unprecedented efforts to combat this disease. Several vaccine candidates emerged, and some of these received emergency approval for use in humans.[4] The CoronaVac vaccine, produced by Sinovac Life Sciences (Beijing, China) in partnership with the Butantan Institute (São Paulo, Brazil), is a vaccine containing inactivated SARS-CoV-2 and was the first vaccine to become available in Brazil.[5]

Despite the proven efficacy of the CoronaVac vaccine against symptomatic SARS-CoV-2 infection,[6] some studies have shown COVID-19 cases in individuals postvaccination.[5,7] The aimed of the present study was report cases of breakthrough SARS-CoV-2 infections in residents of a retirement home after receiving two doses of immunization with the CoronaVac vaccine. It

demonstrates that elderly vaccinated and resident in long-term care institutions can be infected by SARS-CoV-2. However, with the proposed model, it is possible to track viral circulation and thus control the outbreak, avoiding the occurrence of severe cases and reducing the number of deaths. In addition, with the proposed monitoring, it is possible to maintain the team of professionals, without reducing care for the elderly.

Methods

The retirement home is in the municipality of Lavras in the state of Minas Gerais, southeastern Brazil. It has 20 rooms, accommodating two residents per room, with two nurses (one male and one female), four social rooms, one kitchen, and one 20-seat refectory. During our study, this home hosted 47 seniors and had 38 working employees. On 01/20/2021 and 02/04/2021, all workers and residents were vaccinated with the CoronaVac vaccine, with the first and second doses, respectively.[8]

On April 30, the head nurse recognized flu-like symptoms in a 55-year-old male volunteer. The man and his wife had positive results on an RT-qPCR diagnostic test for SARS-CoV-2 infection. With this first confirmation, we started monitoring employees, seniors, and surfaces of the retirement home more rigorously. Beginning with this first confirmation, employees, volunteers and residents were monitored for SARS-CoV-2 infection with periodic RTqPCR tests on samples collected using nasal swabs and/or oral swabs.

Environmental samples were collected in common areas and of greater circulation to search for viral RNA. Patients positive for SARS-CoV-2 were isolated and had their contacts retested between 3 to 5 days. This procedure was repeated until all tested patients had negative results. Sanitary measures were immediately implemented, like the adequate use of equipment of individual protection by all employees.

We sequenced the SARS-CoV-2 genome of one of the positive samples using the Ion AmpliSeq™ SARS-CoV-2 Research Panel (Thermo Fisher Scientific). Genomic data were collected and processed using the Ion PGM™ Torrent Server. Briefly, de novo assembly was performed using

Trinity assembler v. 1.3.0.2. Pangolin 3.0 was run to assign the genome to the most likely lineage according to the Pango dynamic lineage nomenclature scheme.

Results and Discussion

The present work was conducted with a cohort of 85 individuals, 38 of whom were employees and 47 of whom were seniors. With the exception of two administrative employees, all others followed the complete (international) vaccination protocol with the SinoVac/CoronaVac vaccine, with the first dose on 01/20/2021, and the second dose on February 4th of the same year, and were considered immunized 14 days after the second dose.[8]

Index case identification

On April 30, the head nurse recognized flu-like symptoms in a 55-year-old volunteer, whose diagnostic confirmation was performed by RTqPCR, confirming its classification as an index case.

Outbreak monitoring and outcomes

On 05/05/2021, six of the eight residents who underwent antigen tests were positive for SARS-CoV-2 infection, resulting in an attack ratio (AR) of 75%.

First follow-up

Once the outbreak was identified, testing of the entire population of LSIE was begun using the RTqPCR technique for SARS-CoV-2, which is considered the gold standard. On the 7th of May 2021, testing proceeded to the collection of material from 17 employees and 46 residents. To standardize the data, the eight residents who were tested by the antigen method were submitted to retesting by RTqPCR. Mass and multisegment testing was the crux of the research model presented in this study. The individuals in the main population affected by the COVID-19 outbreak belonged to one or more risk groups (age and/or comorbidities), and the caregivers were mostly health professionals with jobs in other establishments. In this sense, the rapid identification of an outbreak was essential to contain it at its source and interrupt the chain of transmission, both internally and outside of the establishment, and consequently reduce COVID-19-related morbidity and mortality.

Of the 63 tested individuals, 33 were positive for SARS-CoV-2, resulting in an RA of 52.38%. Of the positive patients, 31 (94%) were residents, one was a volunteer and one was a nurse. Among the residents, eight had no comorbidities, 18 had comorbidities, seven had two comorbidities and one had three comorbidities. The most frequent comorbidity in this follow-up was hypertension, which was observed in 24 individuals.

Of the 13 symptomatic patients, three had only one symptom, three had two symptoms and seven had three or more manifestations. Fever was the most frequent symptom, which was present in 46.15% of the symptomatic patients. In the present study, 60.6% of the positive patients did not show any symptoms of COVID-19.

Second follow-up

The second follow-up consisted of testing employees/volunteers and residents with a negative diagnosis or those who had not been tested in the first segment. Therefore, on 05/11/2021, 25 individuals were tested, of whom 12 were positive for SARS-CoV-2, resulting in an RA of 48%. Of these individuals, eight were men, and four were women, with an average age of 65 years. Thus, as in the first follow-up, most infected people (11/12) were asymptomatic (91.7%) and one was symptomatic (9.3%). Eight of the positive cases were residents (66.6%), three were employees and one was a volunteer.

Third follow-up

The third follow-up consisted of testing employees/volunteers and residents with a negative diagnosis in the second segment. Thus, on 05/14/2021, 10 individuals were tested, one of whom was male and nine of whom were female with an average age of 60 years. Only one individual presented positive results, a 92-year-old female resident who was hypertensive and asymptomatic for COVID-19, resulting in an RA of 10%.

Fourth follow-up

The fourth follow-up consisted of testing employees/volunteers and residents with a negative diagnosis in the third segment. Thus, on 05/19/2021, six employees and four volunteers were tested. All subjects had negative results (Table 1).

Fifth follow-up

In the return carried out seven months after the end of the outbreak, it was possible to verify that all residents received the booster dose with an interval of seven months and eighteen days after the second dose with Coronavac, as recommended in the protocols of the Ministry of Health. The application of the booster was initially indicated for people who took the second dose more than six months ago, regardless of the immunizing agent used in the first immunization cycle.

Residents were vaccinated with the Pfizer/BioNTech immunizer on 09/22/2021, that is, seven months and 18 days after the second dose. The only exception refers to an elderly woman who received the booster dose on 10/27/2021.

Control measures

When identifying the first positive cases, all employees were divided into two sectors to prevent the spread of the virus. One group worked with infected people and the other worked with individuals who tested negative. The workers received additional training in the use of personal protective equipment, such as a respiratory mask with a filter, gloves, an isolation apron and 70% alcohol. Additionally, they were instructed to keep windows and doors open and disinfect all surfaces in the house.

There was a suspension of social activities. All employees who had positive test results were instructed to stay at home in isolation, and those with negative results were instructed to intensify distancing measures and avoid public transit until the outbreak was considered over. Residents who had positive test results and contact with the index case or a person with a positive test were accommodated on the second floor. In this environment, the negative contacts were separated from infected contacts. Elderly individuals who had negative results were accommodated in first-floor suites.

Regarding the occurrence of asymptomatic individuals, the results of the present study reiterate the importance of testing asymptomatic people in contact screening. Except by the first one, in all the other investigation follow-ups, the occurrence of positive individuals without any symptoms was higher than 60%. Thus, it can be stated that testing only symptomatic individuals may fail to detect more than half of the infected people who effectively contribute to the transmission of SARS-CoV-2. Recent studies have shown that mass testing, contact tracking and isolation are effective mechanisms to prevent the spread of the coronavirus and control disease.[9,10] A total of 116 diagnostic tests from the detection of the first case until the last day of outbreak follow-up were performed by RTqPCR. It should be noted that the resources were public, and the examinations were performed by staff from a federal public university. Of these tests, 66 exams were conducted for residents, and 50 were conducted for LSIE staff/volunteers.

Of the 85 people (38 employees and 47 residents) who made up the study cohort, 53 were positive for SARS-CoV-2 infection, of whom seven (13.2%) were employees and 46 (86.8%) were residents, with only two individuals not being vaccinated (employees) (Table 2). Of the infected residents, three were hospitalized and died. One patient died in LSIE for causes unrelated to COVID-19, resulting in a mortality rate of 7.5%. Compared to the unvaccinated period, as reported in the United States, where 40% of deaths from COVID-19 occurred in nursing homes,[11] the mortality rate reported in this work corroborates the increased protection provided by the vaccine.

Surface Tests for SARS-CoV-2

Surface samples of materials present in common areas collected during the outbreak were positive for RNA screening of SARS-CoV-2, with 3/3 on May 7th and 11/7 on May 14th. Similar studies have failed to demonstrate viral viability in environmental samples collected under the same conditions as those described in this study.[12] However, surface contamination may suggest the presence of infected individuals, reinforcing the need for protective measures.[12] The environmental trail of viral RNA may point to the need to adopt prophylactic measures, such as surface disinfection and directing of
efforts for mass testing, as well as intensifying individual protection measures, such as the use of masks and hand hygiene. Since the test results of the surface samples were positive for coronavirus

contamination, the employees received additional training for the proper cleaning and safe disinfection of surfaces. On May 19, all six environmental samples collected were negative for the presence of SARS-CoV-2 RNA.

Identification of viral variants

We performed sequencing of the SARS-CoV-2 genome isolated from a positive sample using the Ion AmpliSeq™ SARS-CoV-2 Research Panel (Thermo Fisher Scientific). The data genomics were collected and processed using the Ion PGM™ Torrent Server. Briefly, the assembly was again performed using Trinity assembler v. 1.3.0.2. O Pangolin 3.0 was run to assign the genome to the most likely lineage, according to the Pango dynamic lineage naming scheme. The viral sample was classified as belonging to the B.1.1 variant, which is characterized by the P314L mutation in the ORF1b gene, the D614G mutation in the S gene and the G204R and R203K mutations in the N gene. The genome was deposited and is available from GenBank (NCBI database - https://www.ncbi.nlm.nih.gov/) with the access number OK396828.

The present study demonstrated that vaccinated and fully immunized individuals can become infected (elderly or not). Similarly, in France, an outbreak in an ILPI, in which there was an infection of elderly people vaccinated with an immunizing agent from the manufacturer Pfizer, involved the B.1.1.7 variant. In that study, a smaller number of infected residents (23%), of whom eight developed the severe form of COVID-19, two were hospitalized and one was an unvaccinated individual who died.[13] An intriguing fact of that study refers to the hospitalization of only two of the eight residents with serious disease.

In the present study, of the seven infected and vaccinated employees/volunteers, none of them developed the severe form of the disease. Of the 46 infected elderly individuals, only three developed the severe form of COVID-19 and were hospitalized, and all three died. One-fourth of the individuals, despite being infected, died of natural causes within the institution. Studies on effective vaccine protection in the real world for all vaccines are an object of study. In a recent study by Cohn et al.,[14] a reduction from 91.9% to 53.9% in vaccination protection was described among veterans in the United States between March and August 2021. There was a difference in the decline in protection in relation to immunizing agents, with Janssen being the highest, followed

by Pfizer and later Moderna. Yoshikawa[15] warned that doctors who take care of adult patients must have knowledge of the dynamics of the relationship between aging, immune system senescence and infection due to the high prevalence of infectious diseases in the elderly population, in addition to greater morbidity and lethality.

In a cohort of 522 patients with COVID-19, there was a strong association between lymphopenia and age, in addition to the association between lymphopenia and disease severity, where patients older than 60 years of age had the lowest total number of T cells in the blood.[16] It is known that the adaptive immune system has a fundamental role in coping with infectious processes; specifically, T cells are responsible, among other things, for recognizing infected cells triggering a process of local apoptosis with the intention of decreasing viral replication and infectivity, alerting the immune system to the involved site, and stimulating B cells to produce antibodies or reactivating memory cells themselves. Lymphopenia has been associated with a high risk of severe outcomes from COVID-19.

Additional studies will be needed to understand the impact of the SinoVac/CoronaVac vaccine on limiting the transmission of SARS-CoV-2. The results of the present study demonstrated SARS-CoV-2 transmission among vaccinated people but corroborated the protective power provided by the vaccine against the severe conditions of COVID-19.[4] In this way, the need to continue practicing public health and social measures to prevent the infection and transmission of SARS-CoV-2 should be emphasized.

We reported 100% agreement between the RTqPCR test results from NPS and saliva samples. Saliva samples offer advantages over nasopharyngeal swabs because they avert the need for trained professionals and patient discomfort during sample collection.[17,18] Once test results on surface samples were positive for contamination with coronavirus, employees received additional training for the proper cleaning and safe disinfection of surfaces. Positive test results show contamination with SARS-CoV-2 RNA but do not prove viral viability.[19] Surface contamination may suggest positive infected people present in the surrounding environment.[19] The environmental track for viral RNA may indicate the need for adopting prophylactic measures, such as surface disinfection, and directing efforts for mass testing.

Despite some patients presenting COVID-19 symptoms, testing only symptomatic people may fail to detect approximately half of the infected people who contribute to the transmission of SARS-CoV-2.[19] Mass testing in the retirement home, including those of close contacts, allowed for the identification of asymptomatic positive patients. Recent studies demonstrated that mass testing, contact tracing, and isolation were effective mechanisms to avoid the spread of the coronavirus and early infection control. [12]

Of the infected residents, three were hospitalized and died, and one died in the nursing home, resulting in a 7.5% mortality rate. Compared with the unvaccinated period, as reported in the United States, where 40% of COVID-19 deaths occurred at nursing homes,[7] the mortality rate reported in this paper corroborates the protection increase provided by the vaccine.

Additional studies will be needed to understand the impact of the Sinovac-CoronaVac vaccine on limiting SARS-CoV-2 transmission.[8] Our results show SARS-CoV-2 transmission between vaccinated people but corroborate the protective power provided by the vaccine against severe conditions of COVID-19.

The COVID-19 pandemic requires monitoring and tracking of outbreaks to prevent the spread of the virus and retirement homes should receive priority attention. The present study allowed us to conclude that: (1) contact tracing and the search for asymptomatic individuals must, mandatorily, be carried out during the monitoring of an outbreak, to avoid uncontrolled transmission, if only the symptomatic were tested; (2) infection can occur even in fully vaccinated individuals, regardless of age; (3) although they are susceptible to infection, the elderly, even when they are debilitated and in fragile health, when vaccinated tend to have a low frequency of progression to severe disease; (4) in the cohort studied, younger and vaccinated individuals were less infected; (5) the search for viral RNA in environmental samples is a useful tool, and can even be used alone to assess the indirect presence of infected people, that is, contaminated environments can have infected people, (6) viral sequencing allowed the identification of a variant that still circulates with the potential to cause outbreaks, demonstrating that genomic surveillance is a very important tool for a better understanding of the epidemiology of COVID-19 and finally (7) in the studied cohort,

booster doses proved to be effective in protecting against COVID-19. 19, when used in conjunction with health education measures, even in a population at risk and in an unfavorable transmission scenario.

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Authors and contributors

José Cherem: Monitoring employees, seniors, and surfaces of the retirement home and writing of the manuscript.

Joseane Camilla de Castro and Victor Satler Pylro: Writing of the manuscript

Ingrid Marciano Alvarenga, Karla Silva Teixeira and Denise Alvarenga Rocha: Monitoring employees, seniors, and surfaces of the retirement home

Margareth Maria Pretti Dalcolmo and Joziana Muniz de Paiva Barçante: Writing of the manuscript.

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Table 1. Results of RT–PCR tests in vaccine breakthrough infections with SARS-CoV-2 in one Brazilian retirement home

Test day	People tested	Positive results	Symptomatic	Asymptomatic	Resident	Employee
04/30	1 (Antigen test)	1	1	0	0	1
05/05	8 (Antigen test)	6	6	0	6	0
05/07	63 (RT–PCR)	33	13	20	31	2
05/11	25 (RT–PCR)	12	2	10	8	4
05/14	10 (RT–PCR)	1	0	1	1	0
05/19	9 (RT–PCR)	0	0	0	0	0
Total	116	53	22	31	46	7

Table 2. Descriptions of positive patients using RT—PCR tests for SARS-CoV-2 infections

Patient type	Age	Cycle Threshold (Ct)*	Sex	Symptoms	Comorbidity
Resident	81	27.24 NPS 23.09 Saliva test	F	Productive cough	Hypertension
Resident	69	33.75 Saliva test	F	Asymptomatic	Hypertension
Resident	65	23.02 NPS 30.03 Saliva test	F	Asymptomatic	Hypertension, diabetes, and stroke

Resident	73	22.46 NPS 29.32 Saliva test	F	Asymptomatic	-
Resident	72	20.17 NPS 27.03 Saliva test	F	Flu-like symptoms	Diabetes
Resident	96	19.38 NPS 28.9 Saliva test	F	Asymptomatic	Hypertension
Resident	88	16.33 NPS 24.11 Saliva test	F	Asymptomatic	-
Resident	80	21.21 NPS	M	Unspecified	-
Resident	78	17.12 NPS	F	Asymptomatic	Hypertension
Resident	85	19.34 NPS 30.42 Saliva test	F	Asymptomatic	-
Resident	85	16.17 NPS	F	Asymptomatic	Diabetes and hypertension
Resident	58	22.56 NPS	F	Asymptomatic	Hypertension
Resident	94	17.59 NPS	F	Fatigue	Hypertension
Resident	80	22.11 NPS 31.73 Saliva test	M	Fatigue, fever, and diarrhea	Hypertension
Volunteer	32	16.35 NPS	M	Fever, fatigue, and rhinorrhea	-
Resident	57	18.25 NPS	F	Asymptomatic	Hypertension
Resident	83	27.5 NPS	F	Asymptomatic	Hypertension

Resident	80	13.24 NPS	F	Asymptomatic	Hypertension
Resident	85	17.9 NPS 30.89 Saliva test	F	Asymptomatic	Hypertension
Resident	84	16.38 NPS	F	Asymptomatic	Hypertension
Resident	85	21.76 NPS	F	Fever and muscle pain	Diabetes and hypertension
Resident	83	34.06 NPS	M	Asymptomatic	Diabetes and hypertension
Resident	76	21.25 NPS	F	Dry cough, rhinorrhea, and a sinus infection	-
Resident	69	23.34 NPS	M	Asymptomatic	Cancer and hypertension
Resident	72	25.27 NPS	M	Fever, muscle pain, and rhinorrhea	Hypertension
Resident	77	19.27 NPS	M	Asymptomatic	-
Resident	88	28.42 NPS	M	Dry cough, rhinorrhea, and fatigue	Parkinson's disease
Resident	76	24.94 NPS	F	Dry cough, rhinorrhea, fatigue, and inappetence	Stroke and hypertension
Resident	64	18.53 NPS	F	Dry cough and fever	Hypertension and obesity
Nurse	43	27.29 NPS	M	Asymptomatic	Hypertension
Resident	85	34.09 NPS	M	Asymptomatic	-
Resident	83	29.9 Saliva test	F	Asymptomatic	Hypertension

Resident	90	29.12 Saliva test	M	Dry cough, fever, and fatigue	Stroke and Hypertension
Resident	77	14.4 NPS	F	Asymptomatic	Hypertension and diabetes
Employee	41	34.32 Saliva test	F	Asymptomatic	Hypertension
Volunteer	34	36.32 Saliva test	M	Asymptomatic	-
Resident	77	35.44 Saliva test	F	Asymptomatic	Hypertension
Resident	74	28.21 Saliva test	F	Flu-like symptoms	-
Resident	69	27.42 Saliva test	M	Asymptomatic	-
Employee	29	35.46 Saliva test	F	Asymptomatic	-
Resident	79	33.02 Saliva test	M	Asymptomatic	-
Employee	41	29.18 Saliva test	F	Fever, productive cough, and headache	-
Resident	79	34.68 Saliva test	F	Asymptomatic	Hypertension
Resident	67	35.22 Saliva test	M	Asymptomatic	-

Resident	85	35.01 Saliva test	F	Asymptomatic	-

* Testing was performed at LabCovid- Federal University of Lavras using either the Allplex™ 2019-nCoV Assay (using multiplex real-time PCR, cycle threshold <40 defining a positive result)

** NPS: Nasopharyngeal swabs