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COVID-19 Disease and Viral Characteristics in a Long-Term Care Facility

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ABSTRACT

Due to the combination of age, comorbidities, and close living quarters, residents at long-term care facilities (LTCFs) are at particularly high risk of severe symptoms and death due to COVID-19. This cross-sectional study examines the relationship between demographic characteristics, symptom severity, and length of viral shedding in 49 residents testing positive for SARS-CoV-2 at a LTCF in West Virginia (WV). Over half of the residents were asymptomatic, while nearly a quarter experienced severe symptoms. Women were more likely to be asymptomatic, and age was not associated with symptom severity. While no specific medical condition was associated with symptom severity, having more chronic illnesses was associated. The length of time from initially positive to PCR negative ranged from 2 to 63 days, with an average of 29 days. Given the variability in PCR testing reliability, 30 days of isolation and two consecutive negative PCR tests are recommended before reintegrating residents.

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INTRODUCTION

SARS-CoV-2 is a novel coronavirus that causes the illness COVID-19. The virus is readily transmitted through respiratory droplets and has long viability on surfaces.[1] Like other coronaviruses, COVID-19 has a wide spectrum of clinical presentations, including symptoms ranging from a common cold to severe respiratory distress. Recent studies show a viral incubation period of 2 to 12 days, with five days being most common.[2-3] The viral load is highest during the first few symptomatic days.[4-5] Most studies have shown that respiratory symptoms tend to follow a similar pattern in individuals, with fever, dry cough, and fatigue appearing around 3 to 7 days after exposure. More severe respiratory symptoms, including pneumonia and respiratory distress, have been found to vary in when and whom they affect.[6] Symptoms of diarrhea, headache, and rash have also had varied appearances in study populations. Overall, the viral characteristics and severity are variable across patient populations.

Studies throughout the world have shown that the risk factors most predictive of the most severe symptoms and death include being male, being over 60 years old, and having multiple medical comorbidities.[7] The comorbidities that tend to coincide with higher disease severity include hypertension, diabetes mellitus, cardiovascular disease, chronic pulmonary disease, and malignancy.[7] A recent study across 208 hospitals in England has shown similar results: patients requiring admission to a critical care facility had higher rates of cardiac disease, chronic pulmonary disease, diabetes mellitus, and chronic kidney disease.8 Age was also predictive of patients requiring ICU admission, with those 70 and older most likely needing intensive care unit (ICU)-level care.[8]

The combined risk factors of age and multiple comorbidities have led to long-term care facilities (LTCFs) being heavily impacted by the virus, given the age, health, and close living quarters of the residents. Due to the severity of this disease, it has been difficult to track the symptomology of LTCF residents as they

are often taken out of the facility to higher levels of care. During the first LTCF outbreak of COVID-19 in the United States (U.S.) in King County, Washington, a research team studying the epidemiology of the outbreak had difficulty tracking the exact timing of symptoms due to the need for higher levels of care and subsequent transfer out of the facility.[9] There was also a significant gap in symptoms and testing for this facility, leading to an average time from symptom onset to diagnosis of 8 days. By the time the outbreak was identified, it had spread to greater than 80% of the facility's population.

Focused research on closed populations, such as those at LTCFs, will facilitate a greater understanding of the viral dynamics of SARS-CoV-2, including the course and severity of COVID-19. Such knowledge may contribute to developing better pandemic plans for LTCFs in the short term and to reducing the burden on health systems in the long term. The purpose of this paper is to share both the symptom course and the viral shedding characteristics most predictive of disease severity in geriatric residents in an LTCF. This LTCF was the site of the sentinel COVID-19 case in West Virginia (WV).

METHODS

Participants and Setting

Ninety-six residents from a 98-bed LTCF in WV were tracked from the time of notification of the first positive resident with SARS-CoV-2 until the facility became COVID-19 recovered (defined as 2 consecutive weeks of negative status via real-time reverse transcriptase-polymerase chain reaction [rRT-PCR or "PCR" for short] analysis). All 49 patients that were positive are included in this study. This study was approved and monitored by our Institutional Review Board (protocol # 2006023468), and written documentation of informed consent was obtained from each participant or their medical power of attorney.

Measures

COVID-19 Symptoms Experienced

All residents testing positive for SARS-CoV-2 were tracked, and symptoms noted by staff physicians or nursing staff were documented in the resident's paper charts or their electronic medical record. Three residents were transferred out of the facility to a higher level of care. Given the close relationships with the local medical system and the LTCF, we were still able to track the patients through their treatment course.

SARS-CoV-2 rRT-PCR Testing

All residents underwent diagnostic PCR testing of nasopharyngeal swab collections at 1 to 2 days post-initial, facility-positive test. Residents who tested positive then underwent weekly testing until negative for 2 weeks. As per standard protocol, nasopharyngeal swab specimens were collected from the upper respiratory tracts of residents. Swabs were placed into a collection tube with appropriate viral preservation media. Nucleic acid extraction and qualitative duplex PCR targeting proprietary signatures of viral RdRp and N genes were performed using the Abbott RealTime SARS-CoV-2 assay on the M-2000 automated platform (Abbott Laboratories, Chicago, IL) per the manufacturer's instruction. Days from the initial positive to first negative PCR were calculated.

Covariates

Demographic factors (age, race/ethnicity, and sex), medical conditions, medications, and reported symptoms were retrospectively extracted from paper and/or electronic health record reviews. Residents' symptoms were grouped into asymptomatic, mild to moderate, or severe based on respiratory status. Severe symptoms were described as those that required oxygen supplementation beyond nasal cannula (non-rebreather, high-flow nasal cannula, BiPAP, or intubation).

ANALYSIS

Stata Statistical Software: Release 16 (College Station, TX: StataCorp LP) was used for all statistical analyses. Means and proportions were calculated for each demographic characteristic and symptom

category. Associations between categorical covariates and length of time of PCR positivity were tested using a 2-sample t-test. Correlations between continuous covariates and length of time of PCR positivity were tested using Pearson correlation. Significance was set at a p-value of < 0.05.

RESULTS

Demographic and health characteristics of residents who tested positive for SARS-CoV-2 are described in Table 1. Residents averaged 84 years of age, and 77.5% were female. Residents had an average of 7 chronic medical conditions, with dementia (69.4%) and heart disease (53.1%) being most common. Medications most common in this population were antiplatelets (55.1%) and proton pump inhibitors (32.6%). About 1 in 10 were on an immune modulator (including aromatase inhibitors, methotrexate, prednisone, and biologics).

	Overall
Total	49
Sex, n (%)	
Male	11 (22.5)
Female	38 (77.5)
Age, mean (std dev)	84 (9.1)
Race, n (%)	
White	49 (100)
Medical Conditions, n (%)	
Dementia	34 (69.4)
Cancer	5 (10.2)
Autoimmune Disease^	18 (36.7)
Type 2 Diabetes	19 (38.8)
Chronic lung disease+	9 (18.4)
Heart Disease†	26 (53.1)
Chronic kidney disease	6 (12.2)
Thrombotic history	9 (18.4)
Number of chronic medical conditions, mean (std dev)	7 (2.1)
Medications, n (%)	
Blood thinners	11 (22.5)
Antiplatelet	27 (55.1)
Non-steroidal anti-inflammatory (NSAID)	1 (2.0)
Angiotensin-converting enzyme (ACE) Inhibitors	10 (20.4)
Angiotensin II receptor blockers (ARB)	8 (16.3)
Proton pump inhibitor (PPI)	16 (32.6)
Immune modulator‡	5 (10.2)
Insulin	8 (16.3)

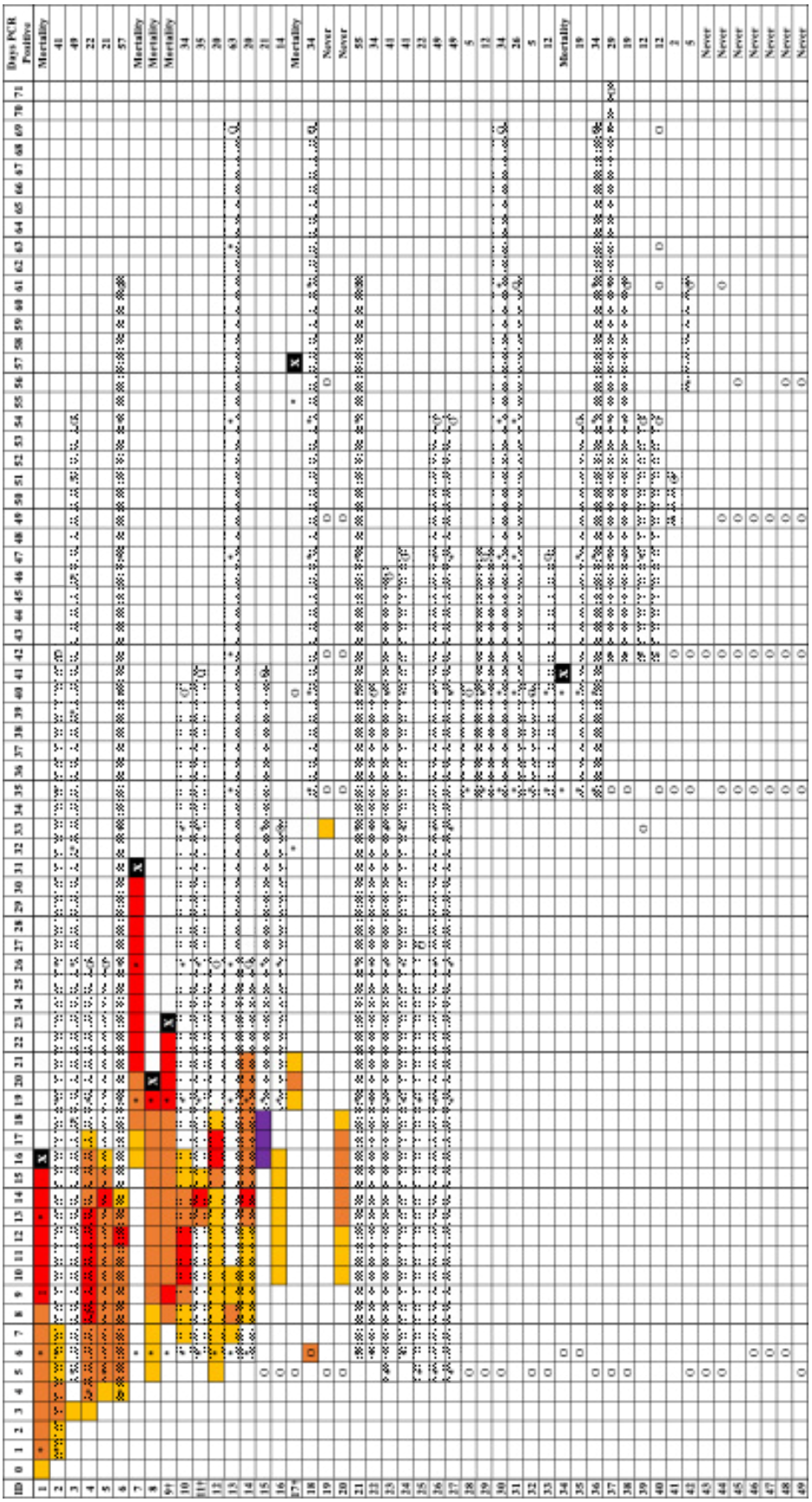
^ Includes myasthenia gravis, multiple sclerosis, rheumatoid arthritis, and hypothyroidism
+ Includes asthma and chronic obstructive pulmonary disease (COPD)
† Includes congestive heart failure (CHF) and coronary artery disease (CAD)
‡ Includes aromatase inhibitors, methotrexate, prednisone, and biologics

TABLE 1. Demographic and health characteristics of SARS-CoV-2-positive residents at a long-term care facility (LTCF).

Symptoms experienced and length of time testing PCR positive for SARS-CoV-2 are described in Figure 1 and Table 2. Overall, 59.2% of residents who tested positive were asymptomatic, while 22.4% experienced severe symptoms. In residents with symptoms, the most common experienced were fever (70.0%) and respiratory distress (85.0%). Overall, mortality was 12.2%. The disease course was similar for all symptomatic patients. Fever and cough were the first symptoms experienced with shortness of breath presenting on days 3 to 5. This early shortness of breath occasionally resulted in a need for increased oxygen but was usually minimal. For those who experienced severe symptoms, acute respiratory decline occurred between days 7 and 10 and was most often rapid. Only one symptomatic patient (number 7 in Figure 1) did not follow this pattern and was asymptomatic until sudden respiratory distress. The time from the initial positive to PCR negative ranged from 2 to 63 days, with an average of 29 days. The length of time patients tested PCR positive varied widely. One resident (17) tested negative but on later testing was again positive before finally testing negative consistently.

Differences in the severity of symptoms experienced by selected demographic and health characteristics are described in Table 3. Women were more likely to be asymptomatic ($p = 0.030$). Age was not associated with symptom severity in this population. Although no specific medical condition was associated with increased symptom severity, having fewer chronic medical conditions was associated with an asymptomatic course. No medications were associated with more severe symptoms, although proton pump inhibitor and immune modulator use trended towards significance. A full table of demographic and health characteristics by symptom severity is available in Supplementary Table S1.

FIGURE 1. Symptom course and PCR testing results in SARS-CoV-2-positive residents at a LTCF



	Overall
Symptom severity, n (%)	
Asymptomatic	29 (59.2)
Mild to Moderate	9 (18.4)
Severe*	11 (22.4)
^Fever, n (%)	14 (70.0)
^Respiratory distress, n (%)	17 (85)
^Rash, n (%)	2 (10.0)
^Behavioral change, n (%)	7 (35.0)
Mortality, n (%)	6 (12.2)
Days to PCR positive, mean (std dev)	28 (16)
Days to PCR positive, range	2 to 63

* Severe symptoms defined by need for oxygen supplementation beyond a common nasal canula including non-rebreather, high-flow nasal canula, BiPAP, and/or intubation.
^ Denominator for percentages is those symptomatic (N=20).

TABLE 2. Symptom and viral shedding characteristics of SARS-CoV-2-positive residents at LTCF.

	Asymptomatic	Mild/Moderate Symptoms	Severe Symptoms	p value
Total	29 (59.2)	9 (18.4)	11 (22.4)	
Age, mean (std dev)	83.5 (9.9)	84.1 (8.9)	83.7 (7.4)	0.986
Sex, n (%)				
Male	4 (36.4)	5 (45.5)	2 (18.2)	**0.030***
Female	25 (65.8)	4 (10.5)	9 (23.7)	
Medical Conditions, n (%)				
Cancer				
Yes	1 (20.0)	1 (20.0)	3 (60.0)	0.084
No	28 (63.6)	8 (18.2)	8 (18.2)	
Number of chronic medical conditions, mean (std dev)	6.2 (1.7)	7.6 (2.0)	8.0 (2.4)	**0.036***
Medications, n (%)				
Proton pump inhibitor (PPI)				
Yes	6 (37.5)	5 (31.3)	5 (31.3)	0.080
No	23 (69.7)	4 (12.1)	6 (18.2)	
Immune modulator‡				
Yes	2 (40.0)	0 (0.0)	3 (60.0)	0.080
No	27 (61.4)	9 (20.5)	8 (18.2)	

* Indicates statistically significant result based on p value < 0.05
‡ Includes aromatase inhibitors, methotrexate, prednisone, or biologics
*** Complete table of all results in Supplementary Table S1

TABLE 3. Selected demographic and health characteristics of SARS-CoV-2-positive residents at LTCF by symptom severity.

	Asymptomatic	Mild/Moderate Symptoms	Severe Symptoms	p value
Total	29 (59.2)	9 (18.4)	11 (22.4)	
Age, mean (std dev)	83.5 (9.9)	84.1 (8.9)	83.7 (7.4)	0.986
Sex, n (%)				
Male	4 (36.4)	5 (45.5)	2 (18.2)	**0.030***
Female	25 (65.8)	4 (10.5)	9 (23.7)	
Medical Conditions, n (%)				
Dementia				
Yes	20 (58.8)	6 (17.7)	11 (23.5)	0.955
No	9 (60.0)	3 (20.0)	3 (20.0)	
Cancer				
Yes	1 (20.0)	1 (20.0)	3 (60.0)	0.084
No	28 (63.6)	8 (18.2)	8 (18.2)	
Autoimmune Disease^				
Yes	10 (55.6)	3 (16.7)	5 (27.8)	0.791
No	19 (61.3)	6 (19.4)	6 (19.4)	
Type 2 Diabetes				
Yes	9 (47.4)	5 (26.3)	5 (26.3)	0.367
No	20 (66.7)	4 (13.3)	6 (20.0)	
Chronic lung disease+				
Yes	3 (33.3)	2 (22.2)	4 (44.4)	0.156
No	26 (65.0)	7 (17.5)	7 (17.5)	
Heart Disease†				
Yes	14 (53.9)	5 (19.2)	7 (26.9)	0.676
No	15 (65.2)	4 (17.4)	4 (17.4)	
Chronic kidney disease				
Yes	3 (50.0)	1 (16.7)	2 (33.3)	0.791
No	26 (60.5)	8 (18.6)	9 (20.9)	
Thrombotic history				
Yes	7 (77.8)	1 (11.1)	1 (11.1)	0.451
No	22 (55.0)	8 (20.0)	10 (25.0)	
Number of chronic medical conditions, mean (std dev)	6.2 (1.7)	7.6 (2.0)	8.0 (2.4)	**0.036***
Medications, n (%)				
Blood thinners				
Yes	5 (45.5)	3 (27.3)	3 (27.3)	0.546
No	24 (63.2)	6 (15.8)	8 (21.1)	
Antiplatelet				
Yes	16 (59.3)	5 (18.5)	6 (22.2)	0.999
No	13 (59.1)	4 (18.2)	5 (22.7)	
Non-steroidal anti-inflammatory (NSAID)				
Yes	1 (100)	0 (0.0)	0 (0.0)	0.703
No	28 (58.3)	9 (18.7)	11 (22.9)	
Angiotensin-converting enzyme (ACE) Inhibitors				
Yes	8 (80.0)	0 (0.0)	2 (20.0)	0.196
No	21 (53.8)	9 (23.1)	9 (23.1)	
Angiotensin II receptor blockers (ARB)				
Yes	5 (62.5)	2 (25.0)	1 (12.5)	0.716
No	24 (58.5)	7 (17.1)	10 (24.4)	
Proton pump inhibitor (PPI)				
Yes	6 (37.5)	5 (31.3)	5 (31.3)	0.088
No	23 (69.7)	4 (12.1)	6 (18.2)	
Immune modulator‡				
Yes	2 (40.0)	0 (0.0)	3 (60.0)	0.088
No	27 (61.4)	9 (20.5)	8 (18.2)	
Insulin				
Yes	4 (50.0)	3 (37.5)	1 (12.5)	0.292
No	25 (61.0)	6 (14.6)	10 (24.4)	

* Indicates statistically significant result based on p value < 0.05
^ Includes myasthenia gravis, multiple sclerosis, rheumatoid arthritis, or hypothyroidism
+ Includes asthma and chronic obstructive pulmonary disease (COPD)
† Includes congestive heart failure (CHF) and coronary artery disease (CAD)
‡ Includes aromatase inhibitors, methotrexate, prednisone, or biologics

SUPPLEMENTARY TABLE S1. Demographic and health characteristics of COVID positive residents at LTCF by symptom severity.

Associations between demographic and disease characteristics and length of time of PCR positivity are described in Table 4. The development of a rash was associated with a longer time of PCR positivity (p of 0.03). No other factors were associated with length of PCR positivity including symptom severity, age, or sex.

DISCUSSION

Geriatric patients are well known for atypical symptom presentation, rapid decline, and higher mortality with respect to illness.[10] Early recognition of concerning symptoms or risk factors provides the best hope for lowering mortality risks in these patients. Being able to track symptoms of COVID-19 and predict respiratory decline is imperative to battling this illness in LTCFs. In our facility, we assessed the vitals of residents testing PCR positive every four hours to ensure no symptoms were missed. Upon diagnosis of the index COVID-19 case, the entire LTCF was tested to quickly identify further residents with the disease. Forty-one percent of residents at the LTCF tested PCR positive for the SARS-CoV-2 virus.

Much to our surprise, a large proportion, 59.2%, never developed symptoms despite their high-risk status due to age and preexisting medical conditions. It quickly became apparent this disease can quietly and quickly spread amongst a large group of individuals living in close quarters, like an LTCF. Unlike other common infectious diseases, such as influenza, the high rate of asymptomatic patients with COVID-19 made broad testing a necessity for proper isolation. This cohort had 11 patients who were classified as having severe symptoms or requiring more than a nasal cannula for oxygen supplementation. With those 11 patients, severe respiratory decline generally followed a pattern of occurring seven days (SD of 4 days) after initial symptom onset. These patients usually had an oxygen requirement early in symptom onset but did not require significant oxygen supplementation until further in their course. A study in Wuhan showed similar patterns of respiratory decline at the 1-week mark, but their focus was on patients in the community that presented to hospital settings with complaints of shortness of breath.[3]

Studies have shown that certain medical conditions, including heart disease, diabetes, and pulmonary disease, were associated with higher severity of illness.[7] In our LTCF population, no specific medical condition was associated with disease severity. However, fewer medical conditions were associated with an asymptomatic course. In this facility, age was noted to be equal across all groups of symptom severity. Other studies, however, have found differences in disease severity when comparing a geriatric population to a non-geriatric population.[8] The average age of this cohort was 84 years old, which raises the question of whether age or the overall health of the geriatric patient is more predictive of disease severity. Studies of influenza and pneumonia severity in a geriatric population have shown that age-related changes, the severity of chronic illnesses, and nutritional status are all correlated to disease severity.[10] With respect to COVID-19 severity, the overall health of the geriatric patient will likely be more predictive of their respiratory decline and need for escalation of care. This information could allow improved evaluation and risk stratification in LTCF populations.

Identifying all affected residents is just as important as establishing when a resident can reintegrate into the general population of the LTCF. We tested all positive residents weekly to identify this transition point. This conservative testing strategy was employed to prevent another outbreak in the facility. The amount of time of PCR positivity varied significantly amongst the residents, but the average duration of positivity was 29 days, with one resident remaining positive for greater than 2 months. The only symptom associated with longer PCR positivity was a rash. Because we could not be sure whether PCR was picking up fragments of virus or active virus, we elected the most conservative approach and assumed that all PCR results were picking up the active virus.

Major strengths of this study include an isolated cohort that was able to be tracked from symptom onset until they became PCR negative. This allowed for comprehensive data collection and close monitoring of the disease course. Limitations of this study include the small sample size, all-white population, and all patients residing in the same facility. Assessment on the impact of race and

TABLE 4. Association of demographic and health characteristics of SARS-CoV-2-positive residents at LTCF with days to PCR negative.

	Days to PCR negative mean, (std dev)	p value
Age		0.240
Sex		
Male	40.7 (5.8)	**0.030***
Female	25.1 (3.0)	
Medical Conditions		
Dementia		
Yes	26.2 (3.2)	0.272
No	33.5 (5.8)	
Cancer		
Yes	33.2 (6.7)	0.439
No	27.0 (3.1)	
Autoimmune Disease^		
Yes	22.9 (4.2)	0.118
No	31.8 (3.6)	
Type 2 Diabetes		
Yes	27.3 (3.4)	0.835
No	28.5 (4.4)	
Chronic lung disease+		
Yes	27.6 (3.4)	0.956
No	28.0 (3.4)	
Heart Disease†		
Yes	24.1 (4.1)	0.156
No	32.1 (3.6)	
Chronic kidney disease		
Yes	17.0 (8.7)	0.232
No	28.9 (2.9)	
Thrombotic history		
Yes	31.3 (13.3)	0.668
No	27.4 (2.8)	
Number of chronic medical conditions, mean (std dev)		0.339
Medications		
Blood thinners		
Yes	36.2 (6.6)	0.175
No	26.1 (3.0)	
Antiplatelet		
Yes	28.2 (3.2)	0.895
No	27.4 (5.2)	
Angiotensin-converting enzyme (ACE) Inhibitors		
Yes	29.7 (6.1)	0.773
No	27.5 (3.2)	
Angiotensin II receptor blockers (ARB)		
Yes	18.7 (7.0)	0.096
No	30.3 (2.9)	
Proton pump inhibitor (PPI)		
Yes	34.4 (5.0)	0.135
No	25.2 (3.3)	
Immune modulator‡		
Yes	36.8 (7.3)	0.254
No	26.7 (3.0)	
Insulin		
Yes	24.8 (4.3)	0.622
No	28.5 (3.3)	
Symptom severity		
Asymptomatic	25.7 (3.9)	0.575
Mild to Moderate	33.3 (5.4)	
Severe¥	29.9 (5.2)	
Fever		
Yes	30.9 (4.3)	0.463
No	26.4 (3.6)	
Rash		
Yes	53.0 (4.0)	**0.023***
No	26.3 (2.7)	
Behavioral change		
Yes	25.8 (3.4)	0.763
No	28.2 (3.2)	

* Indicates statistically significant result based on p value < 0.05
^ Includes myasthenia gravis, multiple sclerosis, rheumatoid arthritis, or hypothyroidism
+ Includes asthma and chronic obstructive pulmonary disease (COPD)
† Includes congestive heart failure (CHF) and coronary artery disease (CAD)
‡ Includes aromatase inhibitors, methotrexate, prednisone, or biologics
¥ Severe symptoms defined by need for oxygen supplementation beyond a common nasal canula including non-rebreather, high-flow nasal canula, BiPAP, and/or intubation.

COVID-19 severity could not be made with this cohort. Many studies have found that this disease has disproportionately impacted some racial and ethnic minority groups. Further research in a more diverse LTCF cohort will be needed to study those groups. Further studies at other LTCFs will also be imperative to monitor patterns across multiple age groups and locations. This has been difficult due to many of the cohorts at other facilities being separated into different hospitals and other facilities during outbreaks.

COVID-19 has had a devastating impact on LTCFs across the country. This study was able to focus on an LTCF cohort and provide information on symptom timing and risk factors associated with decline. Understanding patterns in overall patient health and symptom presentation could help determine resource allocation and monitoring needs at LTCFs, as well as help, inform care discussions with patients and their families. A complete understanding of these patterns could also help communication with nearby hospitals prior to the significant respiratory decline, allowing for better preparation by the hospital and safer transfer of SARS-CoV-2-positive patients. As COVID-19 continues to have such a grave impact on LTCFs, understanding the timing of respiratory decline and factors that can predict disease severity will help LTCFs create pandemic plans.

CONCLUSION

Given the variability of PCR test reliability, we recommend a minimum of 2 consecutive weeks of negative PCR tests prior to reintegrating residents. LTCFs that have the capability should isolate residents for at least one month in the event of a facility SARS-CoV-2 viral outbreak, given the average duration of positivity was 29 days. Given the high rate of asymptomatic carriers, we recommend broad testing of LTCF populations with outbreaks. Aggressive disease identification measures are necessary to prevent widespread transmission of the virus in an LTCF.

AUTHOR AFFILIATIONS

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