

2020

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Z Shahid

R Kalayanamitra  
*Northwell Health*

B McClafferty

D Kepko

D Ramgobin

*See next page for additional authors*

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### Recommended Citation

Shahid Z, Kalayanamitra R, McClafferty B, Kepko D, Ramgobin D, Patel R, Aggarwal C, Vunnam R, Sahu N, Jain R, . COVID-19 and Older Adults: What We Know. . 2020 Jan 01; 68(5):Article 6446 [ p.]. Available from: <https://academicworks.medicine.hofstra.edu/articles/6446>. Free full text article.

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**Authors**

Z Shahid, R Kalayanamitra, B McClafferty, D Kepko, D Ramgobin, R Patel, CS Aggarwal, R Vunnam, N Sahu, R Jain, and +3 additional authors

## COVID-19 and Older Adults: What We Know

Zainab Shahid, BS,<sup>\*†</sup> Ricci Kalayanamitra, BS,<sup>‡§</sup> Brendan McClafferty, BS,<sup>\*</sup>  
Douglas Kepko, BS,<sup>\*</sup> Devyani Ramgobin, BS,<sup>¶</sup> Ravi Patel, DO,<sup>||</sup>  
Chander Shekher Aggarwal, MBBS,<sup>\*\*</sup> Ramarao Vunnam, MD,<sup>||</sup> Nitasa Sahu, MD,<sup>||</sup>  
Dhirisha Bhatt, MD,<sup>||</sup> Kirk Jones, PharmD,<sup>††</sup> Reshma Golamari, MD,<sup>||</sup> and Rohit Jain, MD<sup>||</sup>

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel virus that causes COVID-19 infection, has recently emerged and caused a deadly pandemic. Studies have shown that this virus causes worse outcomes and a higher mortality rate in older adults and those with comorbidities such as hypertension, cardiovascular disease, diabetes, chronic respiratory disease, and chronic kidney disease (CKD). A significant percentage of older American adults have these diseases, putting them at a higher risk of infection. Additionally, many adults with hypertension, diabetes, and CKD are placed on angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers. Studies have shown that these medications upregulate the ACE-2 receptor, the very receptor that the SARS-CoV-2 virus uses to enter host cells. Although it has been hypothesized that this may cause a further increased risk of infection, more studies on the role of these medications in COVID-19 infections are necessary. In this review, we discuss the transmission, symptomatology, and mortality of COVID-19 as they relate to older adults, and possible treatments that are currently under investigation. *J Am Geriatr Soc* 68:926-929, 2020.

**Keywords:** coronavirus; COVID-19; mortality; older adults; SARS-CoV-2

From the <sup>\*</sup>Lake Erie College of Osteopathic Medicine, Erie, Pennsylvania; <sup>†</sup>Internal Medicine, Rowan University SOM, Stratford, New Jersey; <sup>‡</sup>Penn State College of Medicine, Hershey, Pennsylvania; <sup>§</sup>Emergency Medicine, Staten Island University Hospital, Zucker School of Medicine at Hofstra/Northwell, Staten Island, New York; <sup>¶</sup>Touro College of Osteopathic Medicine, Middletown, New York; <sup>||</sup>Department of Internal Medicine, Penn State Health Milton S. Hershey Medical Center, Hershey, Pennsylvania; <sup>\*\*</sup>University College of Medical Sciences Delhi, Delhi, India; and the <sup>††</sup>Department of Pharmacy, Western Maryland Health System, Cumberland, Maryland.

Address correspondence to Zainab Shahid, BS, Lake Erie College of Osteopathic Medicine, 1858 W. Grandview Blvd, Erie PA, 16509.  
E-mail: zshahid44251@med.lecom.edu

DOI: 10.1111/jgs.16472

Clusters of pneumonia cases occurring in the city of Wuhan in December 2019 led to the eventual identification of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).<sup>1,2</sup> Through an epidemiological investigation, the Chinese government narrowed down the origin of the virus to the Huanan seafood market in Wuhan. The viral sequence had a 96% similarity to a bat coronavirus, and, with no evidence of bat-to-human transmission, it was hypothesized that the virus spread to humans through an intermediate host.<sup>1,3</sup> Genomic sequence studies from Malaysia later suggested that the intermediate hosts were pangolins that were smuggled into China from Malaysia and sold at the Huanan seafood market.<sup>4</sup> The subsequent human-to-human spread set off what later turned into a pandemic.

The World Health Organization (WHO) declared SARS-CoV-2 as a pandemic on March 11, 2020. As of March 23, 2020, at 13:25 EST, there were 362,019 confirmed cases of SARS-CoV-2 reported from 168 different countries, with 15,488 deaths and an overall projected case fatality rate (CFR) of 4.3%.<sup>5</sup> The Centers for Disease Control and Prevention (CDC) reported that although individuals older than age 65 comprise 17% of the total population in the United States, they make up 31% of COVID-19 infections, 45% of hospitalizations, 53% of intensive care unit admissions, and 80% of deaths caused by this infection.<sup>6</sup> This suggests that older individuals are more likely to get COVID-19 and have worse outcomes compared with the general population.

### PATHOPHYSIOLOGY

SARS-CoV-2 spreads via direct, contact, and aerosol transmission of respiratory droplets and has a median incubation period of 5.1 days.<sup>7,8</sup> A recent study found that SARS-CoV-2 lasts in aerosols for up to 3 hours and remains detectable for up to 72 hours on plastic and stainless-steel surfaces, 24 hours on cardboard, and 4 hours on copper.<sup>9</sup> Another possible mode of transmission of SARS-CoV-2 may be through fecal-oral transmission. In a study done

on 10 pediatric patients with SARS-CoV-2 infections, 8 continuously tested positive for the virus on rectal swabbing, despite testing negative on nasopharyngeal swabs.<sup>10</sup> Given these findings, patients who test negative on a nasopharyngeal swab could potentially still have an active infection.

The current proposed mechanism for cell entry is via the angiotensin-converting enzyme-2 (ACE-2) receptor found in the lungs, endothelium, heart, kidneys, and gastrointestinal system.<sup>1</sup> Spike proteins on the exterior of SARS-CoV-2 anchor the virus to ACE-2 receptors on cells in the lower respiratory tract. This specific mechanism of action may propose a higher risk of infection for older adults. According to the CDC, 63.1% of adults older than age 60 have hypertension, 38% of people older than 65 years have chronic kidney disease (CKD), and 26.8% of adults older than age 65 have diabetes.<sup>11-13</sup> Many of these patients use ACE inhibitors and angiotensin-receptor blockers (ARBs) that upregulate the ACE-2 receptor.<sup>14</sup> Thus it is hypothesized that older individuals with such comorbidities may have an elevated risk of and experience a more severe course of infection with SARS-CoV-2.

## CLINICAL PRESENTATION

The most common presenting symptoms in the general population are fever (98%), cough (76%), dyspnea (55%), and myalgias or fatigue (up to 44%).<sup>15,16</sup> These symptoms are also common in older adults; one study on 21 critically ill patients with SARS-CoV-2 infection, with a mean age of 70 years, found that the most common presenting symptoms were shortness of breath (76%), fever (52%), and cough (48%). Up to 86% of older adults presented with comorbidities, and the most significant ones were CKD (48%), congestive heart failure (43%), chronic obstructive pulmonary disease (COPD) (33%), and diabetes (33%).<sup>17</sup>

Most older adults have some form of organ damage occurring due to SARS-CoV-2 including acute respiratory disease syndrome (71%), acute kidney injury (20%), cardiac injury (33%), and liver dysfunction (15%), and 67% required vasopressor support for treatment.<sup>17</sup> In all age groups, chest computed tomography imaging of patients with SARS-CoV-2 revealed ground glass opacities (GGOs) (87%), mixed GGOs and consolidation (65%), vascular enlargement (72%), and traction bronchiectasis (53%). Among these, lesions had peripheral distribution (87.1%), bilateral lung involvement (82.2%), lower lung predominance (54.5%), and multifocality (54.5%).<sup>18</sup> Comparatively, chest radiograph findings in older adults showed bilateral reticular-nodular opacities (58%), GGOs (48%), pleural effusions (about 33%), peribronchial thickening (about 25%), and focal consolidations (20%).<sup>17</sup>

## MORTALITY IN OLDER ADULTS

The mortality of the SARS-CoV-2 pandemic in older adults has been striking. According to the joint WHO-China fact-finding mission, the overall CFR of 17.3% in January decreased to .7% in February, whereas the CFR in adults older than age 80 had increased to 21.9%.<sup>19</sup> Another analysis of 72,314 cases indicated an overall CFR of 2.3%, but a CFR of 8% in patients aged 70 to 79 years and 14.5% in patients older than age 80.<sup>20</sup> A report on 355 patients with

SARS-CoV-2 found that patients who died had an average age of 79.5 years.<sup>21</sup> Another report on 4,226 cases in the United States indicated a CFR less than 1% in patients younger than age 54 but a CFR of 3% to 11% in patients aged 65 to 84 and 10% to 27% in patients older than age 85. More than 80% of deaths among adult patients occurred in those older than age 65.<sup>6</sup> Most of the fatal cases to date have involved older adults and patients with comorbidities.<sup>20,22</sup>

Many older adults in the United States have cardiovascular disease (17%), diabetes (26.8%), hypertension (63.1%), COPD (23.7%), and CKD (38%).<sup>13,23-26</sup> An analysis by the joint WHO-China fact-finding mission found that patients older than age 60 and those with comorbidities had the highest risk for severe disease and death. The CFR in patients without comorbidities was 1.4%, whereas the CFR was 13.2% for patients with cardiovascular disease, 9.2% for patients with diabetes, 8.4% for patients with hypertension, 8% for patients with chronic respiratory disease, and 7.6% for patients with cancer.<sup>19</sup> One study on 46 fatal cases of SARS-CoV-2, in which 84% of patients were older than age 60, found that diabetes is likely associated with increased mortality.<sup>15</sup> Another study on critically ill older patients with SARS-CoV-2 found that 86% of patients had comorbid conditions such as CKD, congestive heart failure, COPD, and diabetes.<sup>17</sup> This likelihood of having multiple comorbidities places older adults at an even greater risk of increased mortality from SARS-CoV-2.

## TREATMENT

SARS-CoV-2 can be described as a superspreading event that has a rapidly early growth that is then sustained.<sup>27</sup> The best precautions are maintaining regular hand hygiene (because viral stool shedding and viability on surfaces can last from 2 hours to 9 days), decreasing social contact, and, for healthcare workers, wearing personal protective equipment.<sup>27-29</sup> The reproductive number ( $R_0$ ) for the virus dropped from 3.86 to .32 in a 5-week period once these precautions were taken in China.<sup>27</sup> For patients with COVID-19 infection, treatment is focused on supportive care. Although there is currently no FDA-approved treatment, many medications are being studied for effectiveness against SARS-CoV-2.

Chloroquine, a drug approved by the Food and Drug Administration (FDA) for malarial and autoimmune diseases, has shown efficacy against SARS-CoV-2 in vitro. It works by increasing the endosomal pH required for viral-cell fusion and by interfering with the terminal glycosylation of ACE-2.<sup>30</sup> More than 20 clinical trials are currently ongoing in China to assess chloroquine as a possible treatment for COVID-19, and the State Council of China has stated that chloroquine has demonstrated marked efficacy in treating COVID-19-associated pneumonia in multicenter clinical trials conducted in China.<sup>31,32</sup> A nonrandomized clinical trial on 20 patients with confirmed COVID-19 infection showed that after a daily dose of 600 mg hydroxychloroquine, a less toxic derivative of chloroquine, 57.1% of patients were virus free in 6 days.<sup>33</sup>

Another drug with promising results is remdesivir, an intravenous drug that inhibits SARS-CoV-2 replication through premature termination of viral RNA. Remdesivir is a non-FDA-approved investigational drug that has been

effective against COVID-19 in vitro and has been used on an expanded access, or compassionate use, basis in the United States.<sup>34,35</sup> In one case, the patient received remdesivir on day 7 of hospitalization due to his worsening condition, and he subsequently had an improvement in symptoms, no longer required oxygen supplementation, and had no adverse effects due to treatment.<sup>36</sup> Currently six clinical trials for remdesivir are ongoing.<sup>37-42</sup> There is also currently an ongoing phase I clinical trial sponsored by the National Institute of Allergy and Infectious Diseases testing the safety and immunogenicity of a vaccine for SARS-CoV-2.<sup>43</sup> There is no benefit of the influenza vaccine for prevention of SARS-CoV-2 infection, and the CDC recommends all individuals older than age 6 months receive the influenza vaccine to prevent influenza and unnecessary evaluation for SARS-CoV-2.<sup>44</sup>

In conclusion, the SARS-CoV-2 pandemic has a much higher mortality rate in older adults, and older adults who have certain comorbidities and take ACE inhibitors or ARBs may have a greater risk of infection and worse outcomes. Although many medications and a vaccine are currently under investigation, no FDA-approved treatments or vaccines are available for this virus.

## ACKNOWLEDGMENTS

**Conflicts of Interest:** The authors have declared no conflicts of interest for this article.

**Author Contributions:** ZS, RK, BM, DK, DR, RP, and CSA assisted in article concept and design, acquisition of data, drafting of the manuscript, and final approval. ZS, RV, NS, DB, KJ, RG, and RJ assisted in article concept and design, analysis and interpretation of data, revision of the manuscript for important intellectual content, and final approval. ZS, RK, RG, and RJ further assisted in revisions of the final manuscript.

**Sponsor's Role:** We have no sponsors to disclose.

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