Review Article

COVID-19 in elderly patients

Serap Duru

ORCID:
Serap Duru: https://orcid.org/0000-0001-5030-5695

Abstract:

Causing several diseases since the 1st year of 21st century, coronaviruses have started to threaten human health by causing a pandemic of coronavirus disease-2019 (COVID-19) in a form of novel virus called severe acute respiratory syndrome-coronavirus-2. This outbreak with an increased mortality rate, especially in patients aged 65 and above, was declared a Public Health Emergency of International Concern by the World Health Organization. Elderly patients are at increased risk of a weaker immune system and comorbidities. This study was aimed to present updated information on the course and effects of the COVID-19 pandemic in elderly population.

Keywords:

COVID 19, elderly, SARS-CoV-2

Introduction

Human population across the world is evolving into a society with a longer life span. Factors such as health-care developments, patient access to and extent of using treatment options, and educational levels, and reduced fertility rate, particularly in developed countries, result in an increase in the population over the age of 65 years. In light of available information, the estimated elderly population by 2025 will be over 1.2 billion in the world and about 850 million of this population will have low and middle income, while the old-age population is expected to account for 22% of world population, and the young and old populations will be equal by 2050.[1] According to the Turkish Statistical Institute, our population of about 82.4 million include 7.2 million of old-age people. In 2018, the old-age-to-total population rate increased to 8.7% and the life expectancy at birth increased to an average of 78 years (75.3 years for men and 80.7 years for women). For our country, the old-age population is estimated to increase to 10.2% in 2023 and 16.3% in 2040.[2]

Coronaviruses (CoV) are a family of zoonotic viruses causing a wide spectrum of diseases ranging from cold to severe clinical pictures such as Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS). Although it has been established that SARS-CoV is transmitted from civet cats and MERS-CoV from dromedary camels, there are coronavirus species found in animals but not causing any disease in humans yet. First identified in 1965, human CoV cause influenza-like disease, acute exacerbation of chronic bronchitis, and pneumonia in elderly patients.[3-7]

A new coronavirus was identified in the etiology of pneumonia cases that started in Wuhan city, Hubei province, China, in December 2019 and had an unclear route of transmission despite the belief that it jumped to humans from wild animals. In the forthcoming days, the disease caused by the virus called SARS-CoV-2 was named as coronavirus disease-2019 (COVID-19).[8-10]

SARS-CoV-2 causes severe pneumonia and has a 79% genetic similarity to SARS-CoV that

Department of Chest Disease , Health Sciences University, Ankara Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey

Address for correspondence:
Dr. Serap Duru, Clinic of Pulmonary Medicine, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey.
E-mail: seraph.duru@gmail.com

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caused SARS outbreak between 2002 and 2003 and ~ 96% genetic similarity to the CoV present in bats. Apparently developed as a result of a new mutation, the primary feature of SARS-CoV-2 is to easily bind to the angiotensin-converting enzyme-2 receptor in the membranes of the pulmonary type 2 alveolar cells particularly and myocardium, renal proximal tubule, esophagus, ileum epithelial cells, and bladder urothelial cells.[11]

According to Worldometers, COVID-19 due to SARS-CoV-2 has been detected in nearly 2 million people with a mortality of 150,000 around the world as of April 12, 2020. These numbers are increasing every passing day. The global mortality rate is currently 2%–4%, with a higher rate in certain countries.[12]

Pandemic of COVID-19 and the Course in Elderly Patients

The global increase in old-age population, especially today with the SARS-CoV-2 outbreak, requires a better conception of potential issues in this age group. A multicenter study investigating a total of 1772 community-acquired pneumonia (CAP) cases in Japan identified an incidence of 16.9% for CAP, which was three times more in the age group of 65–69 years than the age group of 15–64 years and ten times more in people aged over 85 years. Aspiration pneumonia comes first in CAP etiology in elderly patients, which is followed by *Streptococcus pneumoniae*, *Haemophilus influenzae*, and respiratory viruses (including influenza). Effective pneumococcal and influenza vaccinations reduce the pneumonia risk in elderly patients.[13] Among people infected with SARS-CoV-2, approximately 80% have mild disease, 15% have severe disease, and 5% require intensive care. Adult respiratory distress syndrome developed in 10% of COVID-19 pneumonia patients who mainly consist of old-age individuals and require hospitalization.[14] Among hospitalized patients, 31%–70% were aged over 85 years and 30%–59% were aged between 65 and 84 years, while 6%–29% were over 85 years and 4%–11% were in the 65–84 years' age group among intensive care patients. In terms of mortality, 10%–27% were aged over 85 years and 4%–11% were aged between 65 and 84 years.[15,16] Another study followed up 1099 patients with SARS-CoV-2 pneumonia and found that 15.1% of the patients were aged 60 years and above, 27.0% of whom were severe.[17] A study of 4021 cases, in turn, established that 1052 (26.2%) were aged over 60 years and the mortality rate was 5.3%.[18] In conclusion, advanced age is a poor prognostic factor for SARS-CoV-2 as it is a poor prognostic factor for SARS and MERS outbreaks, other coronavirus infections from previous years. Figures 1 and 2 show the age distribution and mortality rates by gender for the COVID-19 infection based on available knowledge.[12,19]

Figure 3 shows the age and gender distributions of COVID-19 cases according to the data by the Republic of Turkey Ministry of Health. The disease is detected predominantly in the 20–50 years' age group, especially in men, and 75% of intensive care patients are aged over 60 years despite the reduced incidence over the age of 65 years. 68.8% of died patients and 63.3% of intensive care patients have hypertension. In Turkey, the mortality rate concentrates on the 65–85 years' age group and people with comorbidities, with male predominance, and the rate is 1.58% [Figure 4].[20,21]

The risk factors facilitating the development of pneumonia in old-age individuals include first of all comorbidities and adverse effects of the applied
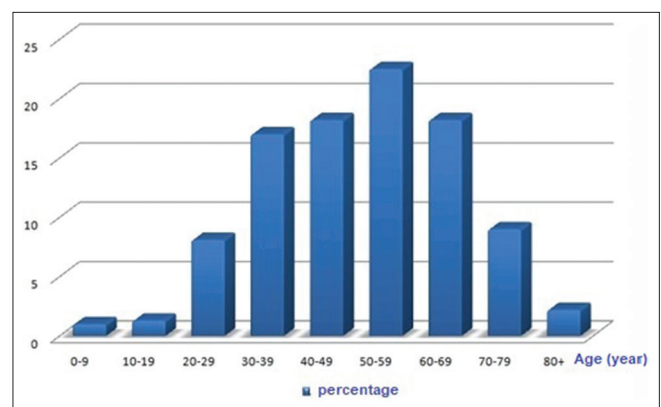

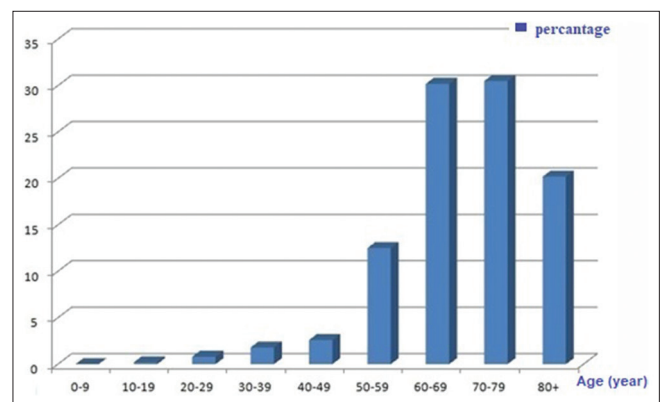**Figure 1:** Global incidence of COVID-19 by age groups

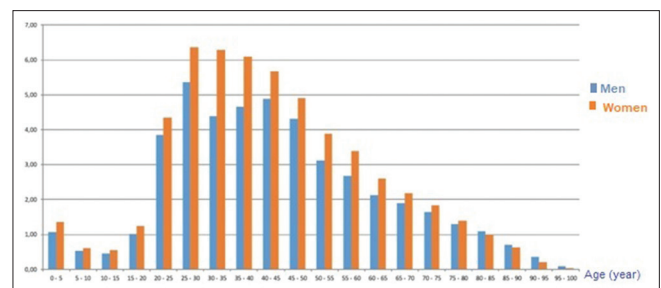**Figure 2:** Global mortality rates of COVID-19 by age groups

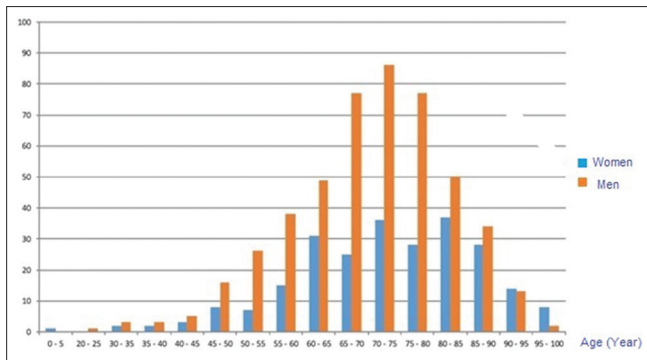**Figure 3:** Distribution of COVID-19 cases in Turkey by age and gender

Figure 4: Mortality rate distribution of COVID-19 in Turkey by age and gender
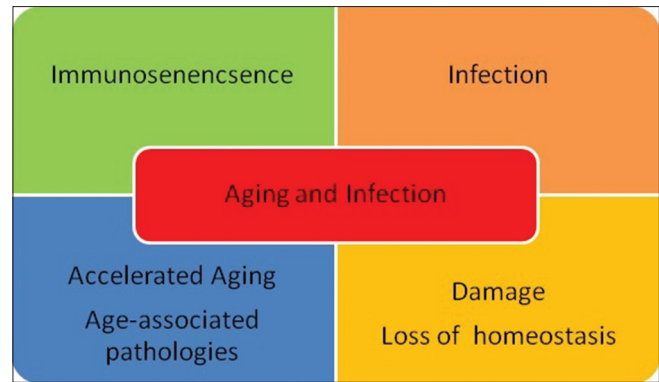

Figure 5: Vicious cycle of aging and infection

treatment on the lungs and changes in psychological parameters such as elastic recoil pressure of the lungs with old age, respiratory muscle strength and cough reflex, and associated weakened defense strength. Besides, virulence and amount of the infectious microorganism are also important. The more throat flora colonization by microorganisms and microaspiration of such microorganisms in elderly patients serves also as a facilitative factor. Pneumonia mortality is especially high over the age of 65 years. Aging is a complex condition that can lead to function loss in organs, cancer, diabetes, neurodegenerative diseases, and cardiovascular disorders. Fragility that increases with age is also a risk factor for many age-related diseases. Many gerophilic pathogens are more common in old-age individuals and are likely to result in a severe course of the disease. COVID-19 is not just gerophilic and affects also the young and children. The young are often with fewer symptoms or asymptomatic, while old-age individuals have a severe disease setting or high mortality rates.[22,23]

The expected changes with aging include reduction in respiratory functions and respiratory muscle strength in lungs, senile emphysema, decrease in respiratory center's sensitivity to hypoxia, and exhaled nitric oxide levels. As age increases, innate and acquired immunity decreases; sensitivity to infection, malignancy and autoimmunity increases; unresponsiveness to vaccines develops and wound recovery delays. Other potential problems with advanced age include telomere shortening, DNA and stem cell damage, oxidative stress, and dysfunctions of several organ systems.

The immune system ages with aging, the vicious cycle of aging and infection upon reduced ability of resistance leads to increased damage of infection, loss of homeostasis and acceleration of aging, which, in turn, facilitates the development of certain diseases and accelerates immune aging even more [Figure 5].[24]

Vaccinations since childhood increase the number of memory T-lymphocytes, providing a protection against

viral infections in the upcoming years. The numbers and functions of cells in both innate and acquired immunities decrease, and the antibody titer provided by vaccinations reduces with aging. The circulating naive T-lymphocytes decrease in number, while the number of memory cells is maintained or increases.[25,26] On the other hand, increased cytokine discharge (inflammaging) and increased autoimmunity occur with age. The thymus gland turns into a fibrotic tissue, especially over the age of 50 years. The involution of the thymus gland with advanced age increases the incidence of several infections such as COVID-19. T-cells play a less active role in defense system. Available studies report that the COVID-19 infection will be less mortal, particularly in people with comorbidities with previous vaccination against influenza.[27] Figure 6 shows the immunological changes and the causes of decreased immunity against COVID-19 infection in old-age individuals.

Antibody production may delay and the viral load due to viral infection may continue in the elderly.[28] Nutritional disorders that are typically seen in this age group and malnutrition due to the disease are associated with high mortality, morbidity, and delayed recovery.[29] A study of elderly patients diagnosed with COVID-19 suggested a poorer disease prognosis in those with malnutrition based on geriatric nutritional risk index and to increase nutritional support.[30]

In the elderly, the risk of mortality increases with diabetes, hypertension, chronic pulmonary, renal, cardiovascular, and cerebrovascular diseases, malignancies, obesity (body mass index $\geq 40 \, \text{kg/m}^2$), and smoking. Based on 2019 data, 23% of Italian population consist of individuals aged over 65 years. The review of the first 3200 patients who lost their lives in Italy, one of the countries with the highest COVID-19 mortality rate in the world, reveals that the average age of the patients died was 78.5 (31–103, interquartile range: 73–85) years. There are underlying disease data for only 481. Among these 481 patients, there were 1 underlying disease in 6 (1.2%), 2 diseases in 113 (23.5%), 3 diseases in 128 (26.6%),
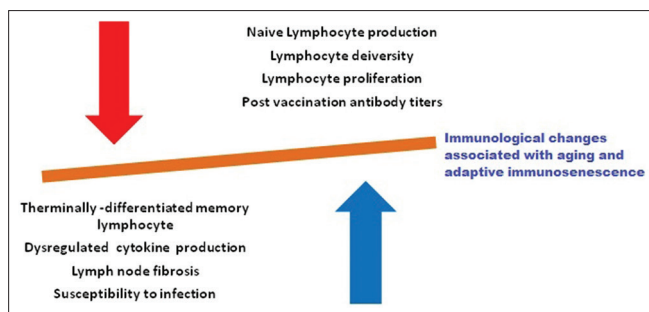
Figure 6: Immune system changes due to aging, adaptive immune aging

and 4 or more diseases in 234. The frequency of such underlying diseases is as follows: hypertension (355, 73.8%), diabetes (163, 33.9%), ischemic heart disease (145, 30.1%), atrial fibrillation (106, 22.0%), chronic renal failure (97, 20.2%), cancer (94, 19.5%), chronic obstructive pulmonary disease (66, 13.7%), dementia (57, 11.9%), stroke (54, 11.2%), and chronic hepatic disease (18, 3.7%). The incidence of comorbidities is very high, especially in intensive care patients (72.2%).[31] On the addition of comorbidities, the mortality rate for patients over the age of 70 years as of 17 March 2020 was 37.6% in Italy compared to 11.9% in China. The lower rates in China may be due to particularly large geographical area and inability to access people living in rural areas and the failure to report their mortality rates.[32] In Spain and the USA, which have high mortality rates based on available knowledge, the mortality rate is 70%–80% in people aged over 65 years. A study established mortality rates in England as 5.1% for patients aged between 60 and 79 years, and 9.3% for COVID-19 patients aged over 80 years, who had comorbidities.[33]

Chronic diseases are likely to diminish the effect of innate immune system and pro-inflammatory cytokines, resulting in adverse effects.[34,35] For instance, diabetes leads to insulin resistance and β-cell damage through the deposition of interleukin-1-βa and tumor necrosis factor-alpha in metabolic tissues such as pancreas.[36] Metabolic diseases also impair the function of macrophages and lymphocytes.[37] In terms of COVID-19 pandemic, the mortality rates are believed to increase due to the presence of chronic diseases and cytokine storm, particularly in elderly patients. A meta-analysis of 6 studies and 1527 patients reported the incidence of hypertension, cardiovascular disease, and diabetes in COVID-19 patients to be 17.1%, 16.4%, and 9.7%, respectively. The incidence of cardiovascular disease has been found higher in patients with intensive care need than those without such need.[38] A study with SARS-CoV-2-inoculated rhesus monkeys established an increase in gene expressions related to inflammation in old subjects compared to the young, while type I interferon-beta levels were found decreased.[39] Type I interferon has an

antiviral activity inducing the viral replication-limiting genes, and its reduced level causes cytokine storm and is a poor prognostic factor.

B-cells exhibit reduced proliferation and differentiation in lymph nodes with aging. As a result of aging, eating disorders may occur, also slower, less coordinated, less efficient immune responses immune responses in case of comorbidities can be seen, these make older adults more susceptible to developing infections.[40]

The leading symptom suggesting COVID-19 in elderly patients is fever. Fever may not be detected in people with a weak immune system and who are cachectic. In addition, there may be cough and shortness of breath, movement disorder, and loss of function. It may be challenging to assess symptoms and implement isolation strategies in elderly patients with dementia.

The treatment protocol for patients aged 65 years and above, who are under follow-up due to COVID-19, is the same for the young patients. However, there is a high rate of complications such as venous thromboembolism, catheter-related infections, pressure ulcers, and delirium incidence, especially among patients who are in the intensive care unit and administered mechanical ventilation.

The most important practices for minimizing mortality rates in the elderly include social isolation to avoid SARS-CoV-2 infection, a balanced diet, and comorbidity management with proper therapies.[41,42]

Conclusion

It is obvious that the pandemic of SARS-CoV-2 causes a more severe presentation than infections caused by other CoV and is associated with a mortality rate higher than the seasonal flu epidemic. The immune system response of elderly patients against this novel virus is a twilight zone. Although COVID-19 first affects upper respiratory tract and lungs, clinicians experience challenges in treatment process and complication management, and mortality rates increase because of fast multiorgan failure due to comorbidities such as hypertension, cardiovascular diseases, and diabetes in elderly patients. New treatment protocols and vaccination programs to be developed in the upcoming days will reduce both disease and economic burden caused by the disease in the societies.

Conflicts of interest
There are no conflicts of interest.

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