The Effect of Chronic Diseases, Age and Gender on Morbidity and Mortality of COVID-19 Infection

Hümeyra Aslaner [1], *Hacı Ahmet Aslaner [2], Mebrure Beyza Gökçek [3], Ali Ramazan Benli [3], Orhan Yıldız [4]

1. Kayseri City Hospital, Family Medicine, Kayseri, Turkey
2. İncesu County State Hospital, Internal Medicine, Kayseri, Turkey
3. Health Directorate of Kayseri, Kayseri, Turkey
4. Department of Infectious Diseases and Clinical Microbiology, School of Medicine, Erciyes University, Kayseri, Turkey

*Corresponding Author: Email: draslaner@gmail.com

Abstract

Background: We aimed to reveal how chronic diseases, age and gender affected morbidity and mortality in patients with Coronavirus disease of 2019 (COVID-19).

Methods: Medical records of all reverse transcription polymerase chain reaction (RT-PCR) positive COVID-19 patients followed up in hospital and home isolation between 13th of Mar 2020 and 12th of May 2020 were retrospectively reviewed. The patients were from Kayseri Province, Turkey. Patients' demographic and clinical characteristics and the factors associated with morbidity and mortality were analyzed.

Results: Of all the patients, 773 (95.8%) were alive and 34 (4.24%) died. The fatality rate was 4.2%. There were differences between the age groups in terms of fatality rate ($P<0.001$). The fatality rate in patients above the age of 65 yr was significantly higher. The fatality rate in the male gender was 2.44 times higher ($P<0.05$). It was 1.104 times higher in advanced age ($P<0.001$) and 10.893 times higher in patients with at least one comorbid disease ($P<0.05$). Hypertension increased mortality by 3.635 times ($P<0.05$) and chronic pulmonary diseases by 2.926 times ($P<0.05$).

Conclusion: Advanced age, male gender and accompanying chronic diseases have adverse effects on the course and severity of the disease and hospitalization. They also increased the rate and risk of mortality.

Keywords: COVID-19; Chronic disease; Morbidity; Mortality

Introduction

COVID-19 epidemic caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) that emerged in Wuhan, Hubei, China on the 31st of Dec2019 has taken place in the history as the first pandemic quickly spreading into six continents and hundreds of countries and caused by coronaviruses. Coronaviruses affect the upper and lower respiratory tracts of humans and animals and lead to the disease. COVID-19 has an incubation period of 14 days and patients are generally observed within 2-5 days after a contact(1, 2). In China, while this period in 1,099 COVID-19 patients was stated as mean 4 days it was stated in another study that the symptoms developed within 11.5 days in 97.5% of the infected patients and 2.2 days in 2.5% (3, 4).

When the clinical spectrum of the disease is evaluated conditions that require mechanical ventilation such as respiratory failure, sepsis, septic shock and multiorgan failure can be observed as well as asymptomatic form.

SARS-CoV-2 is basically transmitted by cough or sneeze generated droplets of the patients after a person touches the surface with these droplets as the agent contacts mucosa. While the transmission is mostly caused by the patients, asymptomatic cases also play a critical role in the transmission of the disease (5).

All age groups are sensitive to COVID-19. Of the cases in China, 87% were in the age range from 30 to 79 yr. The probability of a severe course in the disease and mortality was higher in individuals of advanced age. The fatality rate was found 2.3% in all the cases, 8% in the age group between 70-79 and 14.8% in the age group above 80 yr(6).

Mortality increases and morbidity becomes severe with accompanying chronic diseases in COVID-19. In a study on 51 patients, the mean age for the incidence of the disease was 49 yr. Twenty two percent of the patients had comorbidities such as diabetes, hypertension, chronic liver disease, chronic obstructive pulmonary disease and heart disease (7). Oversell, 201 of the patients had chronic diseases and that course of the infection was more severe in these patients (8).

We aimed to reveal how chronic diseases, age and gender affected morbidity and mortality in patients with COVID-19.

Materials and Methods

Study design and patient population

Patients found to be positive for COVID-19 in their first RT-PCR test in healthcare centers determined as "COVID-19 Pandemic Hospitals" in Kayseri Province by the Turkish Ministry of Health between 13th of Mar 2020 and 12th of May 2020 were included in this study. Throat or nasal swab samples were used for RT-PCR. Patients from all age groups were included. Records of the patients were retrospectively analyzed. Information about the comorbidities and process of the disease in patients was obtained from Public Health Management System (HSYS). As for comorbidities, histories of hypertension, diabetes mellitus, cardiovascular, respiratory disease, hyperlipidemia, chronic renal diseases, cerebrovascular disease and malignancy were screened. Coronary artery disease, congestive heart failure, and arrhythmias were classified as cardiovascular diseases; chronic obstructive pulmonary disease and asthma were classified as chronic pulmonary diseases.

All hospitalized patients had a national unique code, so there were no duplicates. Patients were divided into two groups as patients hospitalized and patients who were followed up at home. According to the hospitalization guideline published by the Ministry of Health, we considered "Confusion or tachycardia (>125/min) or respiratory distress or tachypnea (>22/min) or hypotension (<90/60 mmHg) or SPO2<93% or bilateral pneumonia findings on computed tomography (CT) or posterior anterior chest x-ray or blood lymphocyte count <800/µl or serum CRP>40 mg/l or ferritin>500 ng/ml or D-Dimer>100 ng/m". If patients had one of this findings or symptoms at the first admission, they were hospitalized. Patients who were not hospitalized were quarantined and followed up at home. The study variables were as follows: gender, age, outcome (including death or survival), type of comorbidity, and the result of RT-PCR tests.

The approval of the Erciyes University Medical Faculty Ethics Committee was obtained (Date: 08.07.2020; Decision No: 2020/362) and additionally, Turkish Ministry of Health approval was obtained on 19th of May 2020 for this study as required.

Statistical analysis

SPSS version 22.0 (IBM Corp., Armonk, NY, USA) was used for analyses. While descriptive statistics for continuous variables were expressed as mean, standard deviation, minimum and maximum values categorical variables were expressed as numbers and percentiles. Data were given as mean ± standard deviation. Kolmogorov Smirnov test was used to determine whether numerical data belonging to the variables were compatible with the normal distribution. Chi-square test was used to determine the relationship

between the groups and categorical variables. Statistical significance level was accepted as 5% in the calculations and *P* value equal to or lowers than this value was commented as the relationship between the parameters was statistically significant. The linear relationship between the variables was evaluated with Spearman correlation test. Independent factors affecting mortality in COVID-19 infection were evaluated by logistic regression analysis.

Results

A total of 807 patients whose RT-PCR test results were positive and who were diagnosed with COVID-19 between 13th of Mar 2020 and 12th of May 2020 were enrolled in this study. The clinical characteristics, fatality rate and case fatality rate (CFR) of patients are presented in Tables 1 and 2. The median age of patients was 39 [0-96] and the highest number of patients was in the age range between 20 and 60 yr. Percentage of male patients was 50.3%. The age group above 65 yr had the highest fatality rate among the age groups (*P*: 0.001). The fatality rate in men (n=21; 5.2%) was higher, but there was no statistically significant difference. Median value of the number of chronic diseases in all patients was 0 [0-6]. There were 36.8% patients with at least one chronic disease.

Table 1: The epidemiological factors on mortality of COVID-19 patients

Variable	Patient n, %	Fatality rate (n,%)	P value
Age (yr)			
0-18	122 (15.1)	1 (0.8)	
19-65	587 (72.7)	3 (0.5)	0.001
66 and older	98 (12.1)	30 (30.6)	
Gender			
Male	406 (50.3)	21 (5.2)	0.172
Female	401 (49.7)	13 (3.2)	
Smoking			
Yes	207 (25.7)	5 (2.4)	0.135
No	600 (74.3)	29 (4.8)	
Patient Current Status			
Hospitalized	514 (63.7)	34(6.6)	0.001
Home	293 (36.3)	0 (0.0)	

Fatality rate in patients with chronic disease was 11.1% (n=33) (*P*: 0.001). While fatality rate was 66.7%in patients with 6 chronic diseases as comorbidities it was 0.2% in patients without any comorbidities (*P*: 0.001). As it is shown in Table 2, cerebrovascular disease, cancer, cardiovascular diseases, hypertension and diabetes were the diagnoses with statistically significantly highest case fatality rates (66.7%, 27.3%, 21.7%, and 15.5% respectively). Fatality rate of patients who were hospitalized was higher than that of patients who were followed up at home (*P*: 0.001).Of all the patients, 514 (63.7%) patients were hospitalized. Out of these 514 patients, 91.6% received inpatient treatment, 9 (1.8%) patients were followed

up in intensive care unit and 6 (1.2%) were intubated and 34 (6.6%) patients died. Age ranges of hospitalized patients and patients who were followed up at home were similar as shown in Table 3 (*P*: 0.188). Out of 34 patients who died, 33 (97.1%) had at least one comorbidity (*P*:0.001). However, hospitalization status of patients with chronic disease was similar (*P*: 0.376). As in Table 3, patients diagnosed with hypertension were hospitalized more (*P*:0.025). Hospitalization status of the patients with other chronic diseases was similar. However, patients with CVH, chronic renal disease and coroner disease were hospitalized more.

Table 2: The case fatality rate of COVID-19 patients

Variable	Patient (n,%)	CFR (n,%)	P value
Comorbidity			
Yes	297 (36.8)	33 (11.1)	0.001
No	510 (63.2)	1 (0.2)	
Chronic disease type			
Hypertension	148 (18.3)	23 (15.5)	0.001
Diabetes Mellitus	80 (9.9)	10 (12.5)	0.001
Hyperlipidemia	85 (10,5)	17 (20)	0.001
Cardiovascular disease	69 (8.6)	15 (21.7)	0.001
Psychiatric	65 (8.1)	4 (6.2)	0.290
Chronic pulmonary disease	56 (6,9)	8 (14.3)	0.001
Rheumatological	17 (2.1)	2 (11.8)	0.158
Cancer	11 (1.4)	3 (27.3)	0.009
Chronic kidney disease	5 (0.6)	1 (20)	0.194
Cerebrovascular disease	3 (0.4)	2 (66.7)	0.005
Chronic disease count			
0	510 (63.2)	1 (0.20)	
1	161 (20)	11 (6.8)	
2	48 (5.9)	4 (8.3)	
3	48 (5.9)	6 (12.5)	0.001
4	27 (3.3)	4 (14.8)	
5	11 (1.4)	6 (54.5)	
6	3 (0.4)	2 (66.7)	

Table 3: The evaluation of patients according to follow-up status

Variabl	Hospitalized (n=514, %)	Home (n=293, %)	P value
Age, yr, median	40 (0-96)	38 (0-88)	0.188
Survival status			
Alive	480 (62.1)	293 (37.9)	0.000
Exitus	34 (100)	0 (0.0)	
Gender			
Male	265 (0.65)	141 (0.34)	0.348
Female	249 (0.62)	152 (0.37)	
Smoking			
Yes	153 (73.9)	54 (26.1)	
No	361 (60.2)	239 (39.8)	0.001
Chronic disease			
Yes	195 (65.70)	102 (34.30)	0.376
No	319 (62.50)	191 (37.50)	
Chronic disease type			
Hypertension	105 (70.9)	43 (29.1)	0.025
Cardiovascular disease	50 (72.5)	19 (27.5)	0.71
Diabetes Mellitus	49 (61.3)	31 (38.8)	0.358
Chronic pulmonary disease	40 (71.4)	16 (28.6)	0.134
Cancer	9 (81.4)	2 (18.6)	0.174
Cerebrovascular disease	3 (100)	0 (0.0)	0.212

The control RT-PCR positive of the patients followed in the hospital was more than those followed at home (41.8% vs. 27.3%) (*P*:0.001). When the factors affecting mortality were evaluated in Table 4 it was observed that age increased mortality by 1.104 times more (*P*:0.001), male gender affected mortality by 2.44 times more (*P*:0.037), presence of a comorbidity increased mortality by 10.893 times more (*P*:0.025), hypertension by 3.635 times more (*P*:0.013), chronic pulmonary diseases by 2.926 times more (*P*:0.031) and malignancy by 10.557 times more (*P*:0.009).

Table 4: The effects of age, gender and comorbidity on mortality of COVID-19 patients

Variable	*OR*	*S.E*	*Sig.*	*95% C.I.for EXP(B)*	
Age(yr)	1.104	0.017	0.000	1.061	1.138
Male gender	2.443	0.429	0.037	1.09	5.977
Comorbidity	10.893	1.064	0.025	0.819	66.931
Hypertension	3.635	0.521	0.013	1.309	10.09
Chronic pulmonary disease	2.926	0.497	0.031	1.105	7.747
Cancer	10.557	0.901	0.009	1.807	61.673

Discussion

This epidemiological study gives information about comorbid diseases affecting the disease and epidemic in Turkey. The effects of especially comorbid diseases on morbidity and mortality of patients with COVID-19 were investigated. Median age of the patients was 39.85 ± 18 yr and 50.3% were male. In Turkey,the median age of patients was 42 [19–92]yr and the percentage of male patients was 53.8%(9). In the another study, the number of male patients with COVID-19 was higher with a rate of 54.3% and most (n=30; 88.23%) of 34 patients were in the age group of ≥65 yr and had comorbidities such as diabetes, hypertension and chronic pulmonary diseases(10). The CFR in this study was 4.2% in all patient groups (the ones who were hospitalized or the ones who were followed up at home), 6.6% in hospitalized patients, 11.1% in patients with comorbidities and 0.2% in patients without any comorbidities. CFR was calculated as 1.85% in general population and 8.06% in hospitalized patients (11).The high CFR of the hospitalized patients was considered normal because of the clinical status of the patients who were followed at home was better. Logistic regression results revealed significant effects of age, male gender and underlying diseases on mortality risk in patients with COVID-19.

In parallel with another study (12), regression analysis in our study revealed that advanced age was associated more with high mortality risk (OR=1.10, 95% CI: 1.06-1.13). This high rate was considered to be affected by nutritional deficiency, weak immune system and higher number of additional diseases in advanced age (13).

In our study, male gender significantly increased mortality (OR=2.44, 95% CI: 1.09-5.97). This rate may be lower in women due to sex hormones and X chromosome known to play role in innate and acquired immunity system. Moreover, according tothe studies performed in China, ACE2 expression is more dominant in smokers and smoking is more common among men compared to women, which explains the higher rate in men (14, 15).

According to our results, 36.8% of our patients had chronic diseases such as diabetes, chronic respiratory tract diseases, cardiovascular diseases and mainly hypertension. Besides, comorbidity significantly increased mortality (OR=10.89, 95% CI: 0.81-66.93). Zhou Fei et al found in their study on 191 patients that mortality increased in patients with hypertension (OR=3.05, 95% CI: 1.57-5.92) and respiratory tract diseases

(OR=5.40, 95% CI: 0.96-30.40). In the results of our study, the risk of mortality was significantly higher in hypertension, chronic respiratory tract diseases and cancer (16).

Of the patients included in our study, 72.7% were in the age group of 19-65 yr. Lower rates of cases among the two age groups under 20 and above 65 were considered to be as a result of precautions taken (all educational institutions were closed one day after the first case was detected in Turkey on the 10th of March and lockdown was announced for the age group above 65 on the 21st of Mar and for the age group under 20 on the 10thof Apr) and decreasing the risk for contact with COVID-19 positive individuals to minimum. Social distancing was an important tool in decreasing infections and mortality during previous pandemics and its effect against COVID-19 in China is obvious (17–19).

The limitation of this study was retrospective and small number of patients.

Conclusion

Chronic disease and advanced age seriously increase mortality and morbidity in COVID-19 infection. For this reason, people in this group should be more careful in measures such as the use of personal protective equipment, hygiene and social distance compliance, as recommended by the WHO. In studies with larger patient groups, these effects will be more pronounced.

Ethical considerations

Ethical issues (including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgements

Conflict of interest

The authors declare that there is no conflict of interest.

References

1. Li Q, Guan X, Wu P, et al (2020). Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med*, 382 (13): 1199–1207.
2. Chan JF-W, Yuan S, Kok K-H, et al (2020). A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster.*The Lancet*, 395 (10223): P514–523.
3. Guan W, Ni Z, Hu Y, et al (2020). Clinical characteristics of 2019 novel coronavirus infection in China. *N Engl J Med*, 382: 1708-1720.
4. Lauer SA, Grantz KH, Bi Q, et al (2020). The incubation period of coronavirus disease 2019 (CoVID-19) from publicly reported confirmed cases: Estimation and application. *Ann Intern Med*, 172 (9): 577–582.
5. Wu D, Wu T, Liu Q, Yang Z (2020). The SARS-CoV-2 outbreak: What we know. *Int J Infect Dis*, 94: 44–48.
6. The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team (2020). The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) - China, 2020. *China CDC Weekly*, 2 (8): 113–122.
7. Song F, Shi N, Shan F, et al (2020). Emerging 2019 Novel Coronavirus (2019-nCoV) Pneumonia. *Radiology*, 295 (1): 210–217.
8. Qin C, Zhou L, Hu Z, et al (2020). Dysregulation of Immune Response in Patients With Coronavirus 2019 (COVID-19) in Wuhan, China. *Clin Infect Dis*, 71 (15): 762–768.
9. Göker H, Aladağ-Karakulak E, Demiroğlu H, et al (2020). The effects of blood group types on the risk of COVID-19 infection and its clinical outcome. *Turk J Med Sci*, 50 (4): 679–683.
10. Wang D, Hu B, Hu C, et al (2020). Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected

Pneumonia in Wuhan, China. *JAMA*, 323 (11): 1061–1069.

11. Zhao X, Zhang B, Li P, et al (2020). Incidence, clinical characteristics and prognostic factor of patients with COVID-19: a systematic review and meta-analysis. *MedRxiv*, doi:10.1101/2020.03.17.20037572.

12. Zhao S, Lin Q, Ran J, et al (2020). Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early phase of the outbreak. *Int J Infect Dis*, 92: 214–217.

13. Calder PC, Bosco N, Bourdet-Sicard R, et al (2017). Health relevance of the modification of low grade inflammation in ageing (inflammageing) and the role of nutrition. *Ageing Res Rev*, 40: 95–119.

14. Jaillon S, Berthenet K, Garlanda C (2019). Sexual Dimorphism in Innate Immunity. *Clin Rev Allergy Immunol*, 56 (3): 308–321.

15. Cai H (2020). Sex difference and smoking predisposition in patients with COVID-19. *Lancet Respir Med*, 8 (4): e20.

16. Zhou F, Yu T, Du R, et al (2020). Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*, 395 (10229): 1054–1062.

17. Yu D, Lin Q, Chiu AP, He D (2017). Effects of reactive social distancing on the 1918 influenza pandemic. *PLoS One*, 12 (7): e0180545.

18. Earn DJD (2012). Effects of School Closure on Incidence of Pandemic Influenza in Alberta, Canada. *Ann Intern Med*, 156 (3): 173-81.

19. Prem K, Liu Y, Russell TW, et al (2020). The effect of control strategies to reduce social mixing on outcomes of the COVID-19 epidemic in Wuhan, China: a modelling study. *Lancet Public Health*, 5 (5): e261–e270.