

Research Paper: The Relationship Between COVID-19-induced Death and Chronic Diseases



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ABSTRACT

Background: Morbidity and mortality due to Coronavirus Disease 2019 (COVID-19) are mainly related to age and comorbidity diseases (hypertension, diabetes, cardiovascular disease, malignancies, etc.). These conditions are associated with poorer clinical outcomes and sometimes lead to long-term hospitalization. The current study aimed to investigate the relationship between COVID-19-induced mortality and various chronic diseases in patients admitted to Ali Ibn Abitaleb Hospital in Rafsanjan City, Iran, in 2020.

Methods: In this retrospective, descriptive, and cross-sectional study, patients with COVID-19 referring to Ali Ibn Abitaleb Hospital in Rafsanjan City, Iran, from March 2020 to September 2020 were assessed. The required data were collected using patients' records and telephone calls by a researcher-made checklist and analyzed by Independent Samples t-test, Chi-squared test, Fisher's Exact test, Kaplan-Meier plots, and multivariate regression analysis in SPSS v. 20.

Results: This study assessed 238 hospitalized patients with COVID-19. The risk of death was significantly higher in patients aged over 75 years; they were 5.5 times more prone to expire, compared to the youngest age group ($P < 0.001$). Chronic diseases, such as hypertension, heart disease, lung disease, and various cancers were more prevalent in patients who expired, compared to those who survived ($P \leq 0.05$). Of the patients who died, 73.8% were transferred to the Intensive U (ICU), while only 7.5% of surviving patients were transferred to the ICU ($P < 0.001$). Longer hospitalization was associated with an increased risk of death among patients with underlying diseases and hypertension ($P < 0.05$).

Conclusion: This study identified the role of chronic diseases and other important indicators in the survival of patients with COVID-19 who were admitted to a hospital in Rafsanjan. It is recommended that nurses and healthcare staff consider these findings in the care of patients with COVID-19.

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Highlights

- The mean age of patients with COVID-19 who expired and survived was 72.21 and 56.61 years, respectively.
- The prevalence of chronic diseases was higher in patients who died, compared to those who survived.
- Chronic diseases, such as hypertension, heart disease, lung disease, and various cancers were more prevalent in patients who died than the survivors.
- No significant relationship was found between gender and COVID-19-related mortality.
- The most common signs and symptoms of COVID-19 were shortness of breath, fever, body aches, headache, cough, decreased sense of smell and taste, vomiting, diarrhea, and loss of consciousness, in sequence.
- The survival of patients aged over 75 years decreased by 40%, compared to patients under 49 years of age in 10 days.

Plain Language Summary

The morbidity and mortality of COVID-19 are related to many factors. This study assessed the relationship between COVID-19- mortality and various chronic diseases, such as hypertension, cardiovascular disease, cancer, and diabetes in patients admitted to Ali Ibn Abitaleb Hospital in Rafsanjan City, Iran, in 2020. The study findings suggested that the elderly and those with chronic conditions were more frequently hospitalized, admitted to the ICU, and were expired due to COVID-19. Furthermore, longer hospital stays were associated with higher mortality.

1. Introduction

On March 11, 2019, the World Health Organization announced the outbreak of a new coronavirus, called Coronavirus Disease 2019 (COVID-19) as a pandemic (Lai et al. 2020). COVID-19 is usually associated with respiratory disease and its most common clinical features are fever, fatigue, and dry cough. Some patients may experience pain, nasal congestion, runny nose, sore throat, or diarrhea. In more severe cases, the infection can cause pneumonia, acute respiratory syndrome, and sometimes death (Geleta et al. 2020). However, 80% of patients with COVID-19 may only present mild to moderate symptoms. The mortality rate is variable according to test methods, access to the healthcare system, and other unknown factors. Reports generally suggested a 2%-7% mortality; it may be up to 20% in the elderly (Verity et al. 2020).

Morbidity and mortality due to COVID-19 are related to age and comorbidity diseases (hypertension, diabetes, cardiovascular disease, malignancies, etc.). Besides, these diseases lead to poorer clinical outcomes and sometimes longer hospitalizations (Rothan & Byrared-dy 2020). A meta-analysis of patients with COVID-19 and chronic conditions indicated that those with hyper-

tension, diabetes, respiratory disease, cardiovascular disease, and other chronic diseases are more prone to COVID-19 infection (Yang et al. 2020). Evidence revealed that chronic illness increase the risk of severe COVID-19 as well as the need for hospitalization, Intensive Care Unit (ICU) admission, and intubation (Al-malki et al. 2020). Some studies explored the association between COVID-19 and chronic diseases. Regarding the importance of this subject and given the limited research on this issue in Iran, it was essential to perform this study. Therefore, this study aimed at assessing the relationship between COVID-19-related mortality and chronic diseases in Rafsanjan City, Iran, in 2020.

2. Materials and Methods

This was a retrospective, descriptive, and cross-sectional study. The research population was all patients with COVID-19 referring to Ali Ibn Abitaleb Hospital in Rafsanjan City, Iran. A total of 238 patients with COVID-19 were admitted to Ali Ibn Abitaleb Hospital in Rafsanjan from March to September 2020. The information was obtained by reviewing the records and making telephone calls with the patients. Telephone contacts were made with patients to complete the information not recorded in the files. The obtained data included age, gender, the presence of chronic disease, the length

of hospital stay, signs and symptoms and their duration, death due to the disease, and hospitalization in the ICU, i.e., recorded in a researcher-made checklist. This checklist was approved by the related experts. The necessary data were collected in 45 days and analyzed by Independent Samples t-test, Chi-squared test, Fisher's Exact test, Kaplan-Meier plots, and multivariate regression analysis using SPSS v. 20.

3. Results

This study assessed the records of 238 hospitalized patients with COVID-19. The mean age of those who died, compared to those who survived was 72.21 vs 56.61 ($P < 0.001$). The incidence of chronic diseases, such as hypertension, heart disease, lung disease, and various cancers was higher in patients who expired, compared to those who survived ($P \leq 0.05$). Diabetes was more prevalent in patients who died than those who survived; however, this difference was borderline concerning significance ($P = 0.07$). Among the patients who died, 73.8% were transferred to the ICU, while only 7.5% of those who survived were transferred to the ICU ($P < 0.001$). No significant relationship was found between gender and mortality due to COVID-19 (Table 1). The most common signs and symptoms of COVID-19 were shortness

of breath (73.5%), fever (59.7%), body aches (58.4%), headache (34%), cough (32.4%), decreased sense of smell and taste (24.4%), vomiting (22.3%), diarrhea (20.3%), and loss of consciousness (12.2%), in sequence (Table 2). Kaplan-Meier plot for the prognostic factors of COVID-19, i.e., statistically significant or borderline is presented in Figure 1. This graph illustrates that the odds of death among individuals with underlying diseases and hypertension increases over time ($P < 0.05$).

The odds of survival among patients with heart and lung diseases and cancer decreased over time; however, this reduction was statistically borderline ($P = 0.08$). The graph demonstrates that the patients who were transferred to the ICU presented a 50% lower odds of survival after about 10 days, compared to the other patients ($P < 0.001$). This graph also suggests that after about 10 days of hospitalization, the odds of the survival of patients, aged over 75 years, compared to those under 49 years of age, decreased by approximately 40% ($P < 0.001$). Multivariate Cox regression analysis was applied to examine the risk ratio (Table 3). Multivariate models containing statistically significant variables were statistically significant ($\chi^2 = 25.92$, $df = 9$, $P < 0.01$). In the presence of other variables, only the effect of age was significant. The risk of death was significantly higher in individuals aged over

Table 1. Distribution of the expired and surviving patients by important indicators

Type of Chronic Disease	No.(%)			P
	Total	Expired	Survived	
Age (y)	55.74(19.55)	72.21(18.78)	52.61(18.10)	<0.001*
Male	120(50.4)	20(52.6)	100(50)	0.77
Chronic Disease	142(59.66)	33(86.8)	109(54.5)	<0.001
Hypertension	68(28.6)	18(47.4)	50(25.0)	<0.05
Diabetes	65(27.3)	15(39.5)	50(25.0)	0.07
Heart Disease	43(18.1)	12(31.6)	31(15.5)	0.02
Thyroid Disease	12(5.0)	1(2.6)	11(4.5)	0.46
Cancers	9(3.8)	4(10.5)	5(2.5)	0.04***
Lung Disease	44(18.5)	13(34.2)	31(15.5)	<0.01
Alzheimer disease	8(3.4)	2(5.3)	6(3)	0.62***
Normal	79(33.2)	18(47.4)	61(30.5)	0.04
ICU	43(18.1)	28(73.8)	15(7.5)	<0.001
Total	238(100)	38(15.97)	200(84.03)	-

*Paired Samples t-test; ***Fisher's Exact test.

Table 2. Distribution of deceased and surviving patients according to the signs and symptoms

Signs and Symptoms	No. (%)			P
	Total	Expired	Survived	
Dyspnea	175(73.5)	28(73.8)	147(73.8)	0.98*
Cough	77(32.4)	7(18.4)	70(35)	0.04
Diarrhea	48(20.2)	2(5.3)	46(23)	0.01**
Vomiting	53(22.3)	7(18.4)	46 (23)	0.53
Vertigo	19(8)	0(0)	19(9.5)	0.05**
Fever	142(59.7)	13(34.2)	129(64.5)	<0.001
Anosmia	58(24.4)	0(0)	58(29)	<0.001**
Lack of taste	58(24.4)	0(0)	58(29)	<0.001**
Body ache	139(58.4)	7(18.4)	132(66)	<0.001
Headache	81(34)	2(5.3)	79(39.5)	<0.001**
Decreased level of consciousness	29(12.2)	17(44.7)	12(6)	<0.001
Total	238(100)	38(15.97)	200(84.03)	-

*Chi-squared test; **Fisher’s Exact test.

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Table 3. The hazard ratio for fatal outcomes

General Characteristics	Hazard Ratio (95%CI)	P	
Age (y)	≤49	Ref	
	50-74	1.88(0.55, 6.42)	0.3
	≥75	5.50(1.60, 18.31)	<0.01
Gender	Female	Ref	
	Male	1.17(0.58, 2.38)	0.66
Chronic disease	1.92(0.57, 6.43)	0.29	
Hypertension	1.55(0.70, 3.43)	0.28	
Diabetes	1.15(0.54, 2.49)	0.71	
Heart disease	0.87(0.40, 1.88)	0.71	
Thyroid disease	1.72(0.21, 13.86)	0.61	
Cancers	1.83(0.58, 5.79)	0.30	
Lung disease	0.96(0.43, 2.12)	0.91	
Alzheimer’s disease	0.72(0.15, 3.51)	0.69	
Normal	1.51(0.75, 3.05)	0.25	

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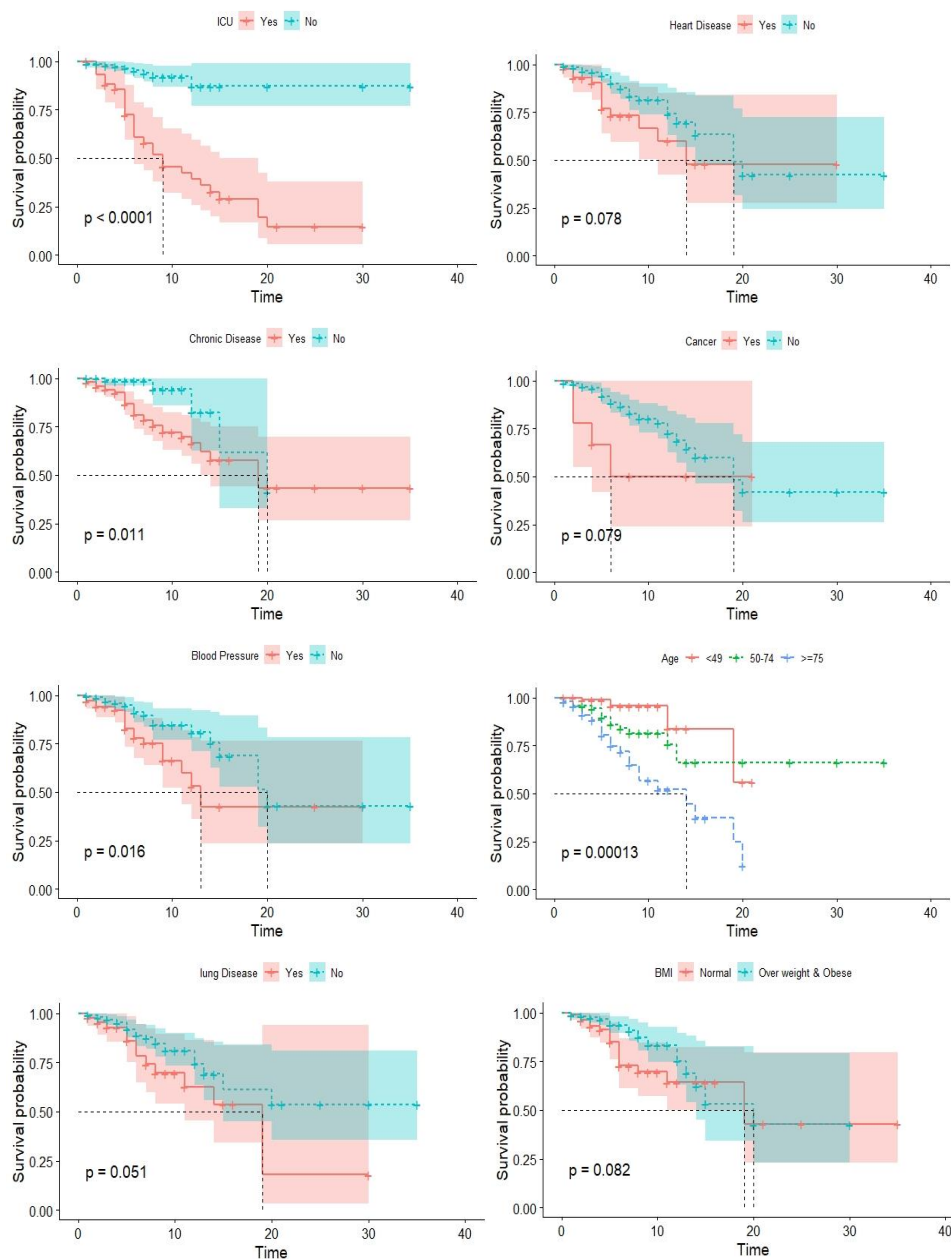


Figure 1. Kaplan-Meier survival plots for different prognostic factors

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75 years ($P < 0.01$). They were 5.5 times more prone to die than the youngest age group. Although having factors, such as hypertension, diabetes, cancers, thyroid disease, and male gender increased the risk of death, these values were not statistically significant.

4. Discussion

This retrospective descriptive, cross-sectional, and single-center study assessed the clinical characteristics and chronic underlying diseases of 238 hospitalized patients with COVID-19 and their relationship with the

patients' mortality. According to the obtained results, the mean age of patients who died from COVID-19, compared to those who survived was 72.21 and 56.61 years, respectively ($P < 0.001$). Other studies revealed that aging in patients with COVID-19 was associated with higher mortality (Zhou et al. 2020). A study in Japan indicated that the mortality rate among COVID-19 patients, aged 70-79 years and over 80 years was equal to 6.8% and 14.8%, respectively; however, COVID-19-induced mortality in all other age groups was measured as 2.6% (Shibata et al. 2020). Another study revealed that patients aged over 65 years have constituted

45% of hospitalizations, 53% of the ICU admissions, and 80% of all deaths due to COVID-19 (Wang et al. 2020b). Decreased immune function and low levels of immune response in the elderly might lead to higher mortality in these individuals (Wu et al. 2020).

The prevalence of chronic diseases, such as hypertension, heart disease, lung disease, and various cancers in our study was higher in patients who died, compared to those who survived ($P < 0.05$). Furthermore, the prevalence of diabetes was higher in the group of patients who died, compared to the survivors; however, this value was statistically borderline ($P = 0.07$). Other studies revealed that chronic diseases, such as cardiovascular disease (Yang et al. 2020; Soares et al. 2020), cancer (Soares et al. 2020; He et al. 2020), hypertension, and lung disease (Zhou et al. 2020) have led to more mortality in patients with COVID-19. A study published in March 2020 found that 19.5% of those with COVID-19 who died in Italy had active cancer (Onder et al. 2020). A UK study of 800 patients with COVID-19 and cancer found that half of the patients had mild COVID-19 and the mortality was significantly related to the patients' age and their comorbid conditions, such as hypertension and cardiovascular disease (Lee et al. 2020). In a meta-analysis of 6 studies with 1527 patients, hypertension and cardiovascular diseases were present in 17.1% and 16.4% of the population, respectively (Li et al. 2020). Zhou et al. stated that 45% of those with hypertension who died of COVID-19 have accounted about 28% of all COVID-19 deaths (Zhou et al. 2020).

A study in Italy found that patients with diabetes were up to 50% more prone to die from COVID-19 than the others (Remuzzi & Remuzzi 2020). Other studies signified hypertension and diabetes as the most common chronic diseases associated with COVID-19 and have a high mortality rate (Salam 2016). High blood glucose adversely affects clinical outcomes and reduces the effects of antiviral drugs (Sardu et al. 2020; Marfella et al. 2020). In the current study, among the patients who died, 73.8% were transferred to the ICU, while only 7.5% of those who survived were transferred to the ICU ($P < 0.001$); patients who were transferred to the ICU had a 50% lower chance of survival after about 10 days, compared to those who were not transferred to that ward ($P < 0.001$).

A study by Hasse et al. in Denmark found that the mortality rate in the ICU was 37%. This rate increased with a longer stay in the ICU; however, half of the patients who were hospitalized in the ICU for 4 weeks or more survived and were discharged from the hospital (Haase et al. 2021). Some other studies indicated higher mortality

than survival in COVID-19 patients admitted to the ICU (Docherty et al. 2020). In a study on patients with COVID-19 who were admitted to the ICU in China, the mortality rate equaled 39% (Wang et al. 2020c). Grasselli et al., in a study in Lombardy, Italy revealed that 87.3% of the subjects with COVID-19 were transferred to the ICU and 48.7% of them died (Grasselli et al. 2020).

A study on 138 hospitalized COVID-19 patients in Wuhan, China reported that the average age of those who were transferred to the ICU was 65 years, compared with 51 years in those who received no intensive care. It was also found that 72.2% of the patients admitted to the ICU had comorbidities, while 37.3% of those who were not admitted to the ICU had comorbidities (Wang et al. 2020a). In our study, there was no significant relationship between gender and mortality due to COVID-19. A study by Bhopal et al. in London, England, found that the gender ratio of male to female mortality was generally 1.4, which varied by age. This ratio was equal to 0.81 for the age of 0-9 years, 1.9 for the age of 40-49 years, 2.3 for the age of 50-59 years, 2.6 for the age of 60-69 years, and 1.65 for the age range of over 80 years (Bhopal & Bhopal 2020). In this study, the most common signs and symptoms of COVID-19 were as follows: shortness of breath, fever, body aches, headache, cough, decreased sense of smell and taste, vomiting, diarrhea, loss of consciousness, and vertigo, respectively. A study in Taiwan reported mild fever, shortness of breath, and mild hypoxemia as common symptoms of the disease (Cheng et al. 2020).

A study in Turkey investigated two groups of patients suspected to having COVID-19. The most common symptoms in the group with COVID-19 were cough (56.6%), weakness (56.6%), taste disturbance (35.7%), myalgia (34.3%), and fever (33.6%); in individuals without COVID-19 symptoms, the symptoms included cough (63%), weakness (45.5%), dyspnea (29.9%), and headache (24.7%). In this study, taste and smell disorders as well as diarrhea were significantly higher in the positive COVID-19 group (Çalica Utku et al. 2020). In a study in France, 7 symptoms were present in more than half of the patients, as follows: fatigue (93%), cough (80%), fever (77%), headache (73%), myalgia (59%), arthralgia (54%), and anosmia (53%) (Klopfenstein et al. 2020).

This was a single-center study and several patients did not cooperate in the data collection process. Additionally, the study population differed in terms of economic and health status as well as access to medical services; therefore, the obtained data may not reflect the whole population.

5. Conclusion

The current study results suggested that COVID-19 was significantly associated with older ages, chronic diseases, longer hospitalization, ICU admission, and mortality. Mortality increased as the length of stay was extended in the ICU. Individuals with chronic illnesses, such as hypertension, diabetes, heart disease, and cancer are also more prone to die over time.

Ethical Considerations

Compliance with ethical guidelines

The study protocol was approved by the Ethics Committee of Rafsanjani University of Medical Sciences (Code: IR.RUMS.REC.1398.164). Consent was obtained for using the files of the patients.

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Authors' contributions

Conceptualization and supervision: Hasan Alinejad, and Zeinab Hajaliakbari; Data collection: Zeinab Hajaliakbari and Ahmadreza Sayadi; Data analysis: Milad Ahmadi; Writing – original draft, and writing – review & editing: Zeinab Hajaliakbari; Final approval: All authors.

Conflict of interest

The authors declared no conflicts of interest.

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