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Effect of Comorbidities on In-hospital COVID-19 Mortality across Age Groups: A Retrospective Cohort Study in Iran

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Abstract

Background: COVID-19 has emerged as one of the most significant healthcare challenges globally in recent years, affecting numerous individuals and resulting in fatalities, particularly among older adults and those with comorbidities. While the influence of comorbidities on mortality in COVID-19 patients has been explored in various studies, it has not been examined across different age groups. We evaluated the impact of comorbidities on COVID-19 mortality in three distinct age groups.

Methods: A total of 10,496 hospitalized patients with positive PCR results for COVID-19 in Sirjan city were included in the study. Underlying conditions, including diabetes, hypertension, cardiovascular disease, and chronic kidney disease, were documented alongside age, sex, and COVID-19 status. The chi-square test and logistic regression were employed to assess the impact of comorbidities on mortality across different age groups.

Results: A total of 2,038 (19.4%) patients had at least one comorbidity. The number of deaths from COVID-19 was 466 (4.4%), of which 197 had comorbidities. Hypertension and diabetes were the most prevalent underlying conditions among COVID-19 patients, occurring in 11.9% and 8.6% of cases, respectively. The presence of comorbidities was significantly associated with mortality in the overall population (OR=3.26, 95% CI: 2.69-3.94) as well as in individuals aged between 30 and 60 years (OR=2.63, 95% CI: 1.77-3.91) and those over 60 years (OR=1.58, 95% CI: 1.26-1.99). Furthermore, the number of comorbidities influenced the mortality rate among COVID-19 patients (OR=1.65 for two comorbidities and OR=1.97 for three or more comorbidities compared to patients with one comorbidity), although it did not vary across different age groups.

Conclusion: Comorbidities can influence the mortality rate associated with COVID-19 among individuals aged 30, particularly within the 30-60 year age group. While the presence of multiple comorbidities significantly elevates the risk of death in the overall population, this association was not found to be statistically significant when analyzed by age group.

Keywords: COVID-19 Mortality, Comorbidities, Underlying Disease, Risk of Mortality, Age Groups

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Introduction

During the five years since the outbreak of the coronavirus, many people worldwide have been exposed to COVID-19, resulting in a significant number of deaths. Approximately 780 million confirmed cases and 7.1 million deaths have been reported globally. The number of confirmed cases in the Eastern Mediterranean and Iran was 23.4 million and 7.6 million, respectively. The total deaths from COVID-19 in the Eastern Mediterranean region and Iran were 352,000 and 147,000, respectively (1).

Numerous studies on COVID-19 have been conducted across various fields. While some research has indicated that age and sex are two variables influencing COVID-19 morbidity and mortality (2-5), other studies have not found significant results regarding these variables (6-8).

In addition to these variables, comorbidities are significant factors in patients with COVID-19 (9-12). Hyperten-

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↑What is "already known" in this topic:
Some of comorbidities can affect the severity and death of COVID-19, with different effects reported in various studies. The death rate from Covid-19 is also related to age.

→What this article adds:
This study evaluated the association between comorbidities and death from COVID-19 in different age groups in Iran. The results showed that comorbidities can affect the number of deaths from COVID-19, especially in those aged 30 to 60 years. Also, while the number of comorbidities increased the risk of death in the overall population, this relationship was not seen in age groups.

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sion and diabetes are the most prevalent comorbidities among COVID-19 patients (13-17). Although underlying comorbidities such as diabetes (5, 12, 16), chronic kidney disease (CKD) (5, 16, 18), hypertension (5, 12, 16), cardiovascular disease (CVD) (5, 16, 18), and cancer influence the mortality of patients with COVID-19, the results obtained vary across studies.

Notably, the prevalence of underlying diseases and the level of immunity vary across different age groups in each region or country. The prevalence of certain comorbidities, such as diabetes, cardiovascular disease (CVD), and chronic kidney disease (CKD), is notably high in Iran (19-22). Furthermore, hypertension, diabetes, CVD, pulmonary disease, and cancer represent the most prevalent comorbidities among Iranian COVID-19 patients (23).

The associations between COVID-19 mortality and comorbidities may vary across different age groups. To the best of our knowledge, no study has explored the relationships between comorbidities and mortality from COVID-19 across various age categories. In this study, we investigated a range of comorbidities and their impact on mortality in diverse age groups of COVID-19 patients in Iran. Additionally, we will examine the effect of the number of comorbidities present in each patient.

Methods

The data concerning COVID-19 patients admitted to Imam Reza and Gharazi hospitals, two medical centers dedicated to managing COVID-19 infections in Sirjan city (Iran), from May 2020 to the beginning of 2022, were used for this retrospective Cohort Study. Only hospitalized patients with positive PCR tests for COVID-19 were included in the analysis (10,496 in total). We employed recorded and encoded data, ensuring that all patient identification information remained confidential.

Several patient-related variables, including age group, sex, ICU admission (yes/no), early symptoms at hospital admission (fever, cough, muscular pain, respiratory distress, loss of consciousness, loss of olfactory sense, loss of taste, stomachache, nausea, vomiting, diarrhea, anorexia, headache, vertigo, and chest pain, with yes/no responses), PO_2 status (≥93/<93), and final status (alive/deceased), were recorded by nursing staff and entered into the Medical Care Monitoring Center (MCMC) system by the head of the statistics and information unit at each hospital. Additionally, information regarding comorbidities (yes/no), such as liver disease, diabetes, cardiovascular disease (CVD), chronic kidney disease (CKD), hypertension, immunodeficiency, hematologic disease, asthma, pulmonary disease, and neurological disorders, was collected in the MCMC through self-reports from patients. All methods and procedures adhered to the relevant guidelines and regulations, and informed consent was obtained from all study participants.

Statistical analysis

We conducted several statistical analyses, including the chi-square test and logistic regression. Logistic regression analysis was employed to report the odds ratio (OR) of mortality in both the crude and adjusted models. Variables that were significant in the crude model were utilized for the adjusted analysis. All analyses were performed using SPSS version 26, with a significance level set at 0.05. Additionally, Excel 2019 was utilized to prepare the charts.

Results

Among the 10,496 patients included in the study, 5,592 (53.3%) were women, 539 (5.1%) were admitted to the ICU, 5,816 (55.4%) had PO_2 levels below 93, and 466 (4.4%) died. A total of 2,038 (19.4%) patients and 197 (42.3%) patients who died had at least one comorbidity.

The early symptoms of COVID-19 in patients are illustrated in Figure 1. Cough, muscular pain, and fever were the most prevalent symptoms.

Figure 2 (A) illustrates the associations between age groups, total deaths, and the presence of comorbidities. The associations between sex, total deaths, and comorbidi-

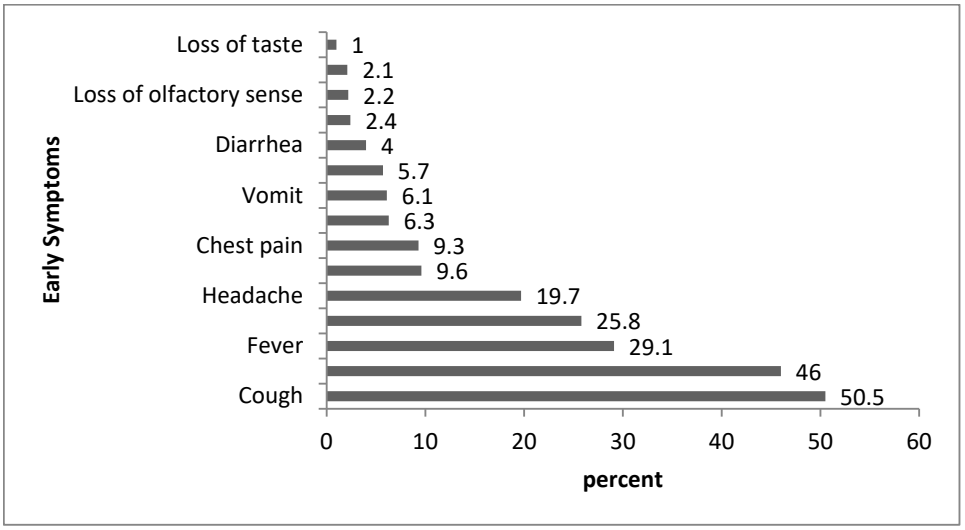

Figure 1. Percent of early symptoms of COVID-19

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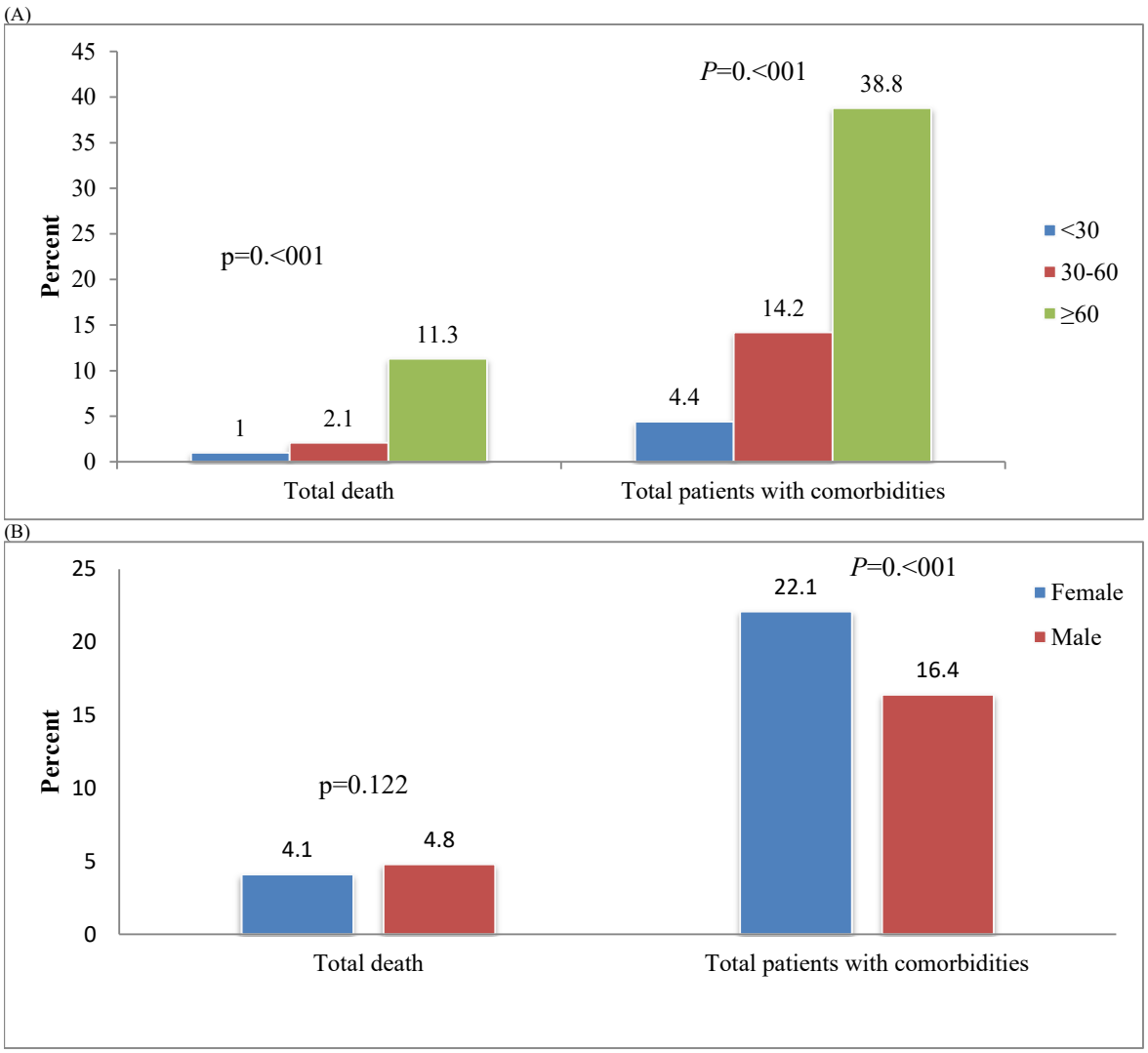

Figure 2.(A) Comparison of total deaths and total patients with comorbidities by age group. *(B)* Comparison of total deaths and total patients with comorbidities by sex

ties are depicted in Figure 2 (B). The relationships between final status and comorbidities across each age group, sex, PO_2 status, and ICU admission are presented in Table 1. Unlike patients aged 30 years and older, the deaths of individuals under the age of 30 were not associated with the presence of comorbidities (*P*=0.535). In both sexes, a significant relationship was observed between comorbidities and mortality. Furthermore, this relationship was significant within each subgroup of PO_2 and ICU admission.

Table 2 presents the distribution of each comorbidity across the different age groups. The prevalence rates of liver disease, diabetes, hematologic disease, cardiovascular disease (CVD), chronic kidney disease (CKD), pulmonary disease, and hypertension vary among the various age groups.

Table 3 illustrates the impact of each underlying disease on the number of deaths attributable to COVID-19 in both the crude and adjusted models. Comorbidities that were significant in the crude models were included in the adjusted model. All underlying diseases were significant in both the crude and adjusted models, with the exception of immunodeficiency, hematologic conditions, and asthma.

Table 4 illustrates the significant relationship between comorbidities and mortality in the overall population. Although the presence of comorbidities was statistically significant overall, the odds ratio (1.37) was not significant for individuals under the age of 30 (*P*=0.763). Additionally, the association between the number of comorbidities and mortality was significant solely in the total population.

Discussion

In this study, we investigated the relationships between underlying diseases and mortality due to COVID-19, considering different age groups. As illustrated in Figure

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Table 1. Association between comorbidities and final status based on some characteristics of patients

Variable		Total N (%)	Comorbidity	Final status		*P**
				Alive	Dead	
Age	≤30	1709 (16.3)	No	1618	16	0.535
			Yes	74	1	
	30-60	5886 (56.1)	No	4965	85	<0.001
			Yes	800	36	
	≥60	2901 (27.6)	No	1606	168	<0.001
			Yes	967	160	
Gender	Female	5592 (53.3)	No	4222	134	<0.001
			Yes	1138	98	
	Male	4904 (46.7)	No	3967	135	<0.001
			Yes	703	99	
PO_2	<93	5816 (55.4)	No	4336	220	<0.001
			Yes	1089	171	
	≥93	4680 (44.6)	No	3853	49	<0.001
			Yes	752	26	
ICU admission	No	9957 (94.9)	No	7943	138	<0.001
			Yes	1769	107	
	Yes	539 (5.1)	No	246	131	<0.001
			Yes	72	90	

**P*-value of the chi-square test

Table 2. Distribution of comorbidities by age group

Comorbidity	Total (N=10496)	≤30 (N=1709)	30-60 (N=5886)	≥60 (N=2901)	*P**
Liver	28 (0.3)	4 (0.2)	10 (0.2)	14 (0.5)	0.027
Diabetes	903 (8.6)	19 (1.1)	335 (5.7)	549 (18.9)	<0.001
Hematologic	24 (0.2)	1 (0.1)	8 (0.1)	15 (0.5)	0.001
Immunodeficiency	15 (0.1)	3 (0.2)	9 (0.2)	3 (0.1)	0.784
CVD	409 (3.9)	3 (0.2)	113 (1.9)	293 (10.1)	<0.001
CKD	53 (0.5)	8 (0.5)	19 (0.3)	26 (0.9)	0.002
Asthma	76 (0.7)	12 (0.7)	43 (0.7)	21 (0.7)	0.993
Pulmonary	153 (1.5)	6 (0.4)	52 (0.9)	95 (3.3)	<0.001
Neurological	75 (0.7)	6 (0.4)	44 (0.7)	25 (0.9)	0.125
Hypertension	1250 (11.9)	21 (1.2)	455 (7.7)	774 (26.7)	<0.001

**P*-value of the chi-square test

Table 3. Logistic regression of comorbidities as risk factors for death

Comorbidity	Crud			Adjusted*		
	OR	95% CI for OR	*P*	OR	95% CI for OR	*P*
Liver	4.72	(1.79, 12.47)	0.002	3.71	(1.34, 10.28)	0.012
Diabetes	2.51	(1.97, 3.21)	<0.001	1.61	(1.21, 2.14)	0.001
Hematologic	3.08	(0.92, 10.39)	0.069	-	-	-
Immunodeficiency	3.32	(0.75, 14.76)	0.115	-	-	-
CVD	3.83	(2.85, 5.16)	<0.001	2.26	(1.63, 3.14)	<0.001
CKD	5.75	(2.94, 11.24)	<0.001	4.27	(2.14, 8.54)	<0.001
Asthma	0.88	(0.27, 2.82)	0.834	-	-	-
Pulmonary	4.83	(3.16, 7.41)	<0.001	3.22	(2.05, 5.06)	<0.001
Neurological	3.36	(1.72, 6.59)	<0.001	3.15	(1.59, 6.25)	0.001
Hypertension	2.63	(2.12, 3.28)	<0.001	1.71	(1.32, 2.23)	<0.001

*Adjustment for Liver, Diabetes, CVD, CKD, Pulmonary, Neurological, and Hypertension

*Table 4.*Logistic regression of comorbidities and the number of comorbidities as risk factors for death by age group

Variable	Total patients			≤30			30-60			≥60		
	OR*	95% CI for OR	*P*	OR*	95% CI for OR	*P*	OR*	95% CI for OR	*P*	OR*	95% CI for OR	*P*
Comorbidity	3.26	(2.69, 3.94)	<0.001	1.37	(0.18, 10.44)	0.763	2.63	(1.77, 3.91)	<0.001	1.58	(1.26, 1.99)	<0.001
Number of comorbidities												
1	-	-	-	-	-	-	-	-	-	-	-	-
2	1.65	(1.20, 2.52)	0.002	-	-	-	1.26	(0.58, 2.76)	0.556	1.23	(0.86, 1.76)	0.253
3 and more	1.97	(1.19, 3.26)	0.009	-	-	-	1.45	(0.33, 6.37)	0.625	1.41	(0.81, 2.45)	0.222

Note: * Crude model

2(A), the number of patients with comorbidities and total deaths varied across the various age groups. Notably, patients over 60 years of age exhibited the highest proportion of total deaths and comorbidities, which aligns with the findings of most studies (5, 11, 12, 16, 18, 24, 25).

The prevalence of comorbidities was higher in women than in men, as demonstrated in Figure 2 (B). Further-

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more, there was no significant difference in the mortality rates between males and females. While some studies support this finding (6, 7), others indicate that the risk of death is greater in males (2, 3, 5, 18, 24, 26).

Conversely, the results presented in Table 1 indicate a significant relationship between mortality and comorbidities in individuals aged over 30 years, regardless of sex. Thus, mortality due to COVID-19 may be associated with sex, age, and comorbidities. Numerous studies have corroborated the association between comorbidities and mortality resulting from COVID-19 (5, 10, 12, 16, 18, 24).

Hypertension, diabetes, and cardiovascular disease (CVD) were the most prevalent comorbidities among COVID-19 patients admitted to hospitals, with the highest prevalence observed at 60 years of age, consistent with numerous studies (10, 12, 14, 15, 17, 23, 27). Furthermore, the prevalence of most comorbidities varied across different age groups (Table 2).

As shown in Table 3, liver disease, diabetes, cardiovascular disease (CVD), chronic kidney disease (CKD), pulmonary disease, neurological disorders, and hypertension are associated with mortality from COVID-19 in the total population. Most studies have reported similar findings regarding diabetes, hypertension, CVD, and CKD (28, 29). The only variation observed is in the degree of effect of each comorbidity (5, 12, 16, 18). This variation can be attributed to the studies being conducted in diverse regions of the world, which may result in differences in the prevalence of underlying diseases and health policies. Additionally, certain neurological disorders have been shown to increase the mortality rate associated with COVID-19 (30-32).

Chronic kidney disease (CKD), pulmonary disease, and liver disease exhibited the highest odds ratios in both the crude and adjusted models in our study. Several studies have indicated that CKD is associated with an increased risk of mortality in COVID-19 patients (5, 12). Although liver disease did not demonstrate a significant effect in the study conducted by Biswas, other research has shown that liver diseases elevate the risk of death among COVID-19 patients (5, 33-35).

We continued the analysis presented in Table 4 to investigate comorbidities and their effects on mortality across different age groups by considering the number of comorbidities in each patient. As indicated in Table 4, the presence of comorbidities was associated with an increased risk of death from COVID-19. The odds of mortality in patients with comorbidities were 3.26 times greater than in those without comorbidities. Specifically, the odds ratios were 2.63 for individuals aged 30 to 60 and 1.58 for those over 60.

The presence of comorbidities appears to be particularly significant in patients aged 30 to 60 years. Comorbidities did not influence mortality among patients under 30 years of age. Furthermore, the odds of death for patients with two or three or more comorbidities, compared to those with one comorbidity, were 1.65 and 1.97, respectively. While these associations were significant in the overall population, no relationship between the number of comorbidities and mortality was observed in age groups over 30 years. Some studies have reported a correlation between the number of comorbidities and the risk of death in COVID-19 patients (16, 24).

The comorbidity status was self-reported, which may represent a limitation of this study. Additionally, due to the high false-negative rate of the test, some individuals were excluded from the study. Also, the presence of only one death among 75 people with comorbidities in people under 30 years of age makes the obtained estimate OR (in Table 4) unreliable, which is another limitation of the present study.

Conclusion

It seems that having comorbidities affects COVID-19 mortality, especially among those between 30 and 60 years of age. Although the number of comorbidities significantly affected mortality in the total population, this influence was not observed across different age groups.

Acknowledgment

Not applicable.

Conflict of Interests

The authors declare that they have no competing interests.

Authors' Contributions

All authors contributed to the design and implementation of the study. Design of the study: MRM and MMA. Preparing data: RS. Statistical analysis: MMA. Manuscript drafting: MMA and RS. All authors read and approved the final manuscript.

Ethical Considerations

The names and addresses of the patients were kept confidential. The study received the approval code from the Ethics Research Committee as IR.SIRUMS.REC.1400.023.

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Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

AI Use Statement

The authors did not use artificial intelligence or AI-assisted technologies in the preparation of this manuscript

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