#### **ORIGINAL ARTICLE**



# Predictors of COVID-19 related death in elderly patients hospitalized due to COVID-19 infection: a cross-sectional study in the west of Iran

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#### Abstract

**Aim** Identifying risk factors associated with mortality in elderly patients hospitalized with COVID-19 can be helpful in managing the disease in this age group. Therefore, the aim of this study was to determine the risk factors of death in elderly patients hospitalized with COVID-19 in Hamadan in 2020.

**Subject and methods** This cross-sectional study was performed on the medical records of 1694 patients aged 60 years and older who were diagnosed with COVID-19 disease between March and August 2020 and were admitted to Shahid Beheshti and Sina Hospitals. A researcher-made checklist included demographic information, clinical information, laboratory results, type of procedures performed for the patient in the hospital, and the number of hospitalization days.

**Results** The results showed that 30% of the elderly patients died due to COVID-19 complications. The results of adapted logistic regression showed that the variables of gender, age, inpatient ward and laboratory indices of albumin, hemoglobin, ESR, and LDH were the main predictors of COVID-19 related death in elderly patients (p < 0.05).

**Conclusion** The rate of COVID-19 related death in the hospitalized elderly patients is remarkable. The death rate increased among male patients, age older than 75 years, hospitalization in the ICU, increased ESR and HDR levels, and decreased albumin and hemoglobin.

Keywords Risk factors · Death · COVID-19 · Elderly

# Introduction

Although most patients with COVID-19 are thought to have a favorable prognosis, elderly patients and those with chronic diseases may have worse outcomes (Cucinotta and Vanelli 2020;

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Wu et al. 2020). Older patients with COVID-19 show relatively higher mortality and disease severity than younger patients (Ruan et al. 2020; Wang et al. 2020). In other words, the elderly represent a special group of patients at high risk for contracting COVID-19 with rapidly progressive clinical deterioration, and their lives are in serious danger (Perrotta et al. 2020).

Compared to patients with a single disease, the hospitalization rate and mortality rate of patients with co-morbidities are higher, and the clinical prognosis is significantly poor (Dai et al. 2021; Nikpouraghdam et al. 2020; Noor and Islam 2020). This is despite the fact that the co-morbidity of chronic diseases in the elderly is a common problem in the field of global public health (Coventry et al. 2015). It has been reported that more than half of the elderly in developed countries have more than three chronic diseases, which means that a person suffers from two or more diseases with different pathologies (American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity 2012).

Elderly patients due to many reasons, including weak immune system, underlying chronic diseases of multi-drug regimen, lack of attention, and lack of ability to fully and correctly observe the principles of personal hygiene and self-care, inappropriate hygiene of the living environment, loneliness and being single, and lack of sufficient support from other family members and late visit to the doctor, are among the most vulnerable sections of the society in the face of the coronavirus epidemic (Cervellati et al. 2020; Jannat 2020; Rastad et al. 2020; Zuin et al. 2021). Patients with COVID-19 primarily have fever, dry cough, fatigue, or myalgia (Huang et al. 2020). However, the clinical characteristics of elderly patients with COVID-19 include fever, sputum and cough, and the ratio of multiple lobe involvement and pneumonia severity index score are significantly higher in elderly patients compared to middle-aged and young people (Liu et al. 2020). Considering the noticeable growth rate of the elderly population in Iran (3.9%) and 9.2% of the Iranian population are in the elderly age, as well as the high prevalence of underlying diseases in the elderly, more attention should be paid to this age group (Farokhnezhad Afshar 2020).

Nearly 9% of the worldwide population are aged 65 and over. Projections estimated that this proportion will increase to nearly 17% of the world's population by 2050 (National Institute on Aging 2016). According to the statistics of the Welfare Department, 9.8% of the population of Hamedan province is elderly, and in this respect, it ranks fourth among the provinces of the country. Due to some complexities in treatment of these patients such as non-adherence of medication, adverse effects of medication, need for a medication review, and complex medication regimen due to suffering from chronic diseases, conducting specific research in these patients is unavoidable. Identifying the risk factors related to COVID-19 related deaths in elderly patients can be helpful in the management of the disease in this age group and help the physicians to identify patients with a poor prognosis in the early stages. Therefore, the present study was conducted with the aim of determining the risk factors associated with death in elderly patients with COVID-19 in Hamadan City in the year 2020.

# **Materials and methods**

In this cross-sectional study, all elderly patients (60 years old and older) with a definite diagnosis of COVID-19 who were admitted to Shahid Beheshti Hospital and Sina Hospital (Farshchian) of Hamadan University of Medical Sciences from March 2020 to the end of 2021 were included in the study. Inclusion criteria were old patients with the definitive diagnosis of COVID-19 based on the result of PCR test and complete medical records. Patients whose treatment outcome was unclear were excluded from the study. In order to collect information, a researcher-made checklist was used, and all information was extracted from the patient's files. The checklist includes demographic information (age, gender, place of residence, marital status, education, and occupation) and clinical information (underlying disease, disease symptoms, SPO2, and vital signs), radiological symptoms (CT scan result, radiology result), laboratory results (creatinine level, ferritin, white blood cells, etc.), smoking history, drug use, the type of procedures performed for the patient in the hospital, and the number of days of hospitalization.

The independent t-test was used to compare the treatment result (recovery or death) for quantitative variables, and the chi-square test was used to compare qualitative variables. In order to simultaneously predict and examine factors affecting death in patients, crude and adjusted logistic regression models were used. Data analysis was done using Stata software version 14 and the statistical significance level was considered less than 5%.

### Results

In the present study, a total of 1694 patients with COVID-19, whose age was 60 years and older, were examined. Among them, 1180 patients recovered (69.7%) and 514 patients died (30.3%). The demographic characteristics of the patients are presented in Table 1. As shown, the results of the chi-square test showed that the outcome of the disease had a statistically significant relationship with the gender (p = 0.009) and age group (p < 0.001) of the patients. Moreover, the outcome of the disease is significantly related to heart disease (p = 0.002) and nervous system morbidity (p = 0.001).

As Table 2 shows, the outcome of the disease (recovery or death) was significantly different based on the mean of systolic and diastolic blood pressure, SPO2, ESR, BUN, BS, PT, Albumin, CPK, SGPT, Alp, hemoglobin, Troponin, LDH, and Lym (p < 0.05).

Demographic predictors of death in the hospitalized COVID-19 positive elderly are presented in Table 3. According to Table 4, the results of the crude logistic regression test showed that the odds of death in elderly males was 1.31 times higher than in women (p = 0.009) and in the age group over 75 years old was 2.43 times higher than in the age group 75–60 years old (p < 0.001).

The results of the logistic regression test showed that the clinical and biochemical variables of systolic and diastolic blood pressure, albumin, hemoglobin, troponin, SPO2, ESR, BUN, BS, PT, Cpk, SGPT, Alp, LDH, and Lym were significantly associated with death in elderly COVID-19 positive patients (p < 0.05) (Table 4).

Based on Table 5, the results of the adjusted logistic regression showed that the variables of gender, age, hospital ward and the laboratory indicators of albumin, hemoglobin, ESR and LDH in the presence of other variables in the model, were as the main predictors of death in the COVID-19 positive elderly patients (p < 0.05).

 Table 1
 Comparison of the disease outcome in the COVID-19 positive elderly according to the baseline characteristics

Variable		Remission N(%)	Death N(%)	P value
Gender	Female Male	591 (72.69) 589 (66.86)	222 (27.31) 292 (33.14)	0.009
Age group	60–75 >75	785 (77.26) 395 (58.26)	231 (22.74) 283 (41.74)	0.001>
Marital status	Married Single Bigamy	999 (70.60) 18 (66.67) 162 (64.80)	416 (29.40) 9 (33.33) 88 (35.20)	0.174
Location	Urban Rural	947 (68.92) 233 (72.81)	427 (31.08) 87 (27.19)	0.173
Smoking	Yes No	94 (69.12) 1082 (69.72)	42 (30.88) 470 (30.28)	0.884
Hookah use	Yes No	10 (83.33) 1166 (69.57)	2 (16.67) 510 (30.43)	0.301
Addiction	Yes No	93 (71.54) 1083 (69.47)	37 (28.46) 476 (30.53)	0.622
Kidney failure	No Yes	1126 (69.85) 54 (65.85)	486 (30.15) 28 (34.15)	0.442
Cancer	No Yes	1155 (69.96) 25 (58.14)	496 (30.04) 18 (41.86)	0.096
Diabetes	No Yes	896 (70.33) 284 (67.62)	378 (29.67) 136 (32.38)	0.295
Hypertension	No Yes	597 (70.48) 853 (68.83)	250 (29.52) 264 (31.17)	0.459
Heart disease	No Yes	895 (71.77) 285 (63.76)	352 (28.23) 162 (36.24)	0.002
Pulmonary disease	No Yes	1015 (70.24) 165 (66.27)	430 (29.76) 84 (33.73)	0.207
Liver disease	No Yes	1172 (69.55) 8 (88.89)	513 (30.45) 1 (11.11)	0.208
Nervous system disease	No Yes	1176 (70.0) 4 (28.57)	504 (30.0) 10 (71.43)	0.001
Other	No Yes	776 (69.97) 404 (69.06)	333 (30.03) 181 (30.94)	0.698

# Discussion

The results of the present study showed that the gender, age, hospitalization ward of the patient, and the laboratory indicators of albumin, hemoglobin, ESR, and LDH in the presence of all other investigated variables were the main predictors of COVID-19 related death in elderly patients.

In line with the results of the present study, the results of the study by Team et al. in the epidemiology team of the emergency response to the new coronavirus pneumonia showed that the death rate in the age group of 70–79 years was 8% and in the age group above 80 years was 14%, while it was less than 1% in age groups under 50 (Team 2020).

In this regard, Papadopoulos et al. and Guan et al. reported a higher rate of death in elderly male patients (Guan et al. 2020; Papadopoulos et al. 2021). Also, Leung et al.

 Table 2 Comparison of average clinical and biochemical variables according to treatment outcome

Variable	Remission Mean±SD	Death Mean±SD	P value
Temperature	$37.28 \pm 0.75$	$37.24 \pm 0.76$	0.306
Systolic blood pressure	$125.43 \pm 19.79$	$120.95 \pm 22.19$	0.001>
Diastolic blood pres- sure	77.67 ± 11.76	74.85 ± 13.19	0.001>
SPO2	$84.17 \pm 9.08$	74.79 ± 14.51	0.001>
ESR	$44.40 \pm 29.15$	48.76 ± 31.93	0.008
BUN	$22.38 \pm 15.84$	$36.50 \pm 27.0$	0.001>
BS	145.1 ± 78.31	165.18 ± 84.25	0.001>
PT	13.66 ± 3.35	$14.38 \pm 4.5$	0.001>
Albumin	$3.28 \pm 2.51$	$2.42 \pm 1.60$	0.233
Cpk	$187.57 \pm 336.08$	$289.49 \pm 424.49$	0.001>
SGPT	$34.49 \pm 90.11$	$64.04 \pm 170.83$	0.001>
Alp	$193.54 \pm 96.04$	$255.20 \pm 253.0$	0.001>
PTT	34.56 ± 13.33	35.59 ± 14.66	0.169
K	$4.24 \pm 1.14$	$4.28 \pm 0.68$	0.491
NA	$136.82 \pm 7.06$	$136.02 \pm 11.83$	0.09
Plat	197.7 ± 79.94	$190.08 \pm 99.08$	0.095
HCT	$42.04 \pm 6.0$	$41.54 \pm 7.92$	0.155
Hb	$13.76 \pm 2.31$	13.39 ± 2.73	0.004
LDH	$547.14 \pm 26.0.7$	$627.16 \pm 672.59$	0.001>
CBC	$12.95 \pm 16.96$	$10.03 \pm 6.28$	0.704
Lym	$22.15 \pm 23.96$	13.58 ± 9.59	0.001>
Mono	$3.05 \pm 2.37$	$2.80 \pm 4.04$	0.165
CR	$1.26 \pm 2.57$	$1.70 \pm 1.34$	0.001>

Table 3	Demographic	predictors	of COVID-19	related	death	in	the
elderly j	patients						

Variable		Adjusted model		
		OR	95% CI	p value
Gender	Female	1		
	Male	1.31	1.07, 1.62	0.009
Age group	60-75	1		
	>75	2.43	1.97, 3.00	< 0.001
Marital status	Married	1		
	Single	1.20	0.53, 2.69	0.657
	Bigamy	1.30	0.98, 1.73	0.066
Location	Urban	1		
	Rural	0.82	0.63, 1.08	0.173
Smoking	Yes	1		
	No	0.97	0.66, 1.42	0.844
Hookah use	Yes	1		
	No	2.18	0.47, 10.01	0.314
Addiction	Yes	0		
	No	1.10	0.74, 1.64	0.622

Variable	Crude model			
	OR	95% CI	P value	
Temperature	0.93	0.8, 1.06	0.307	
Systolic blood pressure	0.98	0.98, 0.99	0.001>	
Diastolic blood pressure	0.98	0.97, 0.98	0.001>	
SPO2	0.93	0.92, 0.94	0.001>	
ESR	1.004	1.00, 1.008	0.008	
BUN	1.03	1.02, 1.04	0.001>	
BS	1.002	1.001, 1.004	0.001>	
PT	1.04	1.01, 1.08	0.001	
Albumin	0.75	0.69, 0.83	0.001>	
Cpk	1.007	1.00, 1.01	0.001>	
SGPT	1.003	1.00, 1.005	0.001>	
Alp	1.002	1.00, 1.003	0.001>	
PTT	1.005	0.99, 1.01	0.171	
K	1.03	0.93, 1.14	0.506	
NA	0.99	0.97, 1.00	0.108	
Plat	0.99	0.99, 1.00	0.096	
HCT	0.98	0.97, 1.00	0.156	
Hb	0.93	0.89, 0.98	0.005	
LDH	1.002	1.002, 1.003	0.001>	
CBC	0.99	0.99, 1.00	0.717	
Lym	0.92	0.91, 0.93	0.001>	
Mono	0.95	0.89, 1.01	0.167	

 Table 4
 Clinical and biochemical predictors of death in hospitalized elderly due to COVID-19

concluded that age is a major risk factor for mortality among elderly patients of different ages (Leung 2020).

In line with the results of the present study, in Zali et al.'s study, the highest mortality rate was reported in patients over

 Table 5
 Adjusted logistic regression model regarding the predictors of COVID-19 related death in elderly patients

Variable	Adjusted model			
	OR	95% CI	P value	
Hospitalization ward			>0.001	
General ward	1		< 0.001	
ICU and general ward	34.68	18.0, 66.82		
ICU	36.98	17.53, 77.99		
Gender			0.005	
Female	1			
Male	2.16	1.26, 3.71		
Age group			>0.001	
60-75	1			
>75	3.23	1.90, 5.49		
ESR	0.98	0.97, 0.99	0.016	
Albumin	0.67	0.56, 0.80	>0.001	
Hb	0.84	0.74, 0.95	0.008	
LDH	1.002	1.001, 1.003	>0.001	

65 years of age and patients with diabetes, cardiovascular diseases, and cancer patients (Zali et al. 2020). In the present study, older age was identified as an independent risk factor for death, and heart disease had a significant effect on the rate of death in the elderly, although this relationship was not significant in the adjusted model. In Zali et al.'s study, contrary to the results of the present study, diabetes and cancer was reported to be among the risk factors for mortality. This difference could be due to the difference in the samples. In our study, we only investigated elderly patients and only 2.5% of the elderly were diagnosed with cancer, and therefore these results cannot be generalized to the entire population. Contrary to the results of Mendes et al.'s study, which reported lung crackle as an independent risk factor for death in patients with COVID-19, we could not observe a significant relationship in this connection (Mendes et al. 2020). Moreover, unlike the study of Sousa et al. that stated chronic obstructive pulmonary disease and cardiovascular diseases were associated with a significant increase in the risk of death in these patients (Sousa et al. 2020), in the present study, in the adjusted model, the aforementioned variables did not have a significant relationship with an increase in the risk of death in these patients.

Based on the results of the present study, albumin was among the independent risk factors for increasing the odds of death in the COVID-19 positive elderly patients. In line with the results of the present study, Violi et al. concluded that low human serum albumin and old age were independently associated with an increase in mortality rate in patients with COVID-19 (Violi et al. 2021). Also, in a review study by Acharya et al. in line with the results of the present study, low serum albumin during the onset of COVID-19 infection was associated with serious consequences such as kidney damage, cardiac damage, hypercoagulability, post-viral physical disability, and encephalopathy (Acharya et al. 2021). The results of the study by Li et al. in confirmation of the results of the present study showed that the increase in the severity of COVID-19 pneumonia had a positive relationship with the lower levels of platelets and albumin, and therefore the level of albumin can be used as an independent predictor of the risk of death in critically ill COVID-19 positive patients (Li et al. 2020).

Albumin is an important defense factor in the body that protects host cells against oxidative burst that occurs against infection or inflammation (Caraceni et al. 2013; Galley 2011; Rabbani and Ahn 2019). The plasma albumin level during acute inflammation decreases rapidly due to transcapillary leakage, and other mechanisms (Artigas et al. 2016; Caraceni et al. 2013), and in such conditions, the low level of serum albumin can make the body more vulnerable and in this field, there is a need to conduct interventional studies to reach a definite result.

The results of the present study showed that one of the independent predictors of death in the elderly with COVID-19 is ESR level. In line with the results of the present study, Alwafi et al. reported that one of the independent risk factors for increased mortality in patients with COVID-19 was an ESR level of 10 mm/h (Alwafi et al. 2021). In line with the results of the present study, in a study conducted by Tian et al., the level of red blood cell sedimentation (ESR) in people who died was higher than in those who recovered from the disease of COVID-19 (Tian et al. 2020). In the present study, the average ESR in patients who died was higher than in patients who recovered.

The results of the present study showed that a higher LDH level is an independent risk factor for increased mortality in the elderly with COVID-19. In line with the results of the present study, in the study of Li et al., the results showed that male gender, older age, and high LDH level are associated with increased death in patients with severe COVID-19, and therefore patients with older age and high LDH level need careful observation and early intervention is essential to prevent the potential progression of severe COVID-19 (Li et al. 2020). In this regard, Tian et al. reported that LDH levels were higher in deceased people compared to those who recovered from COVID-19 (Tian et al. 2020).

In the present study, the results showed that the decrease in hemoglobin level as an independent factor was associated with the increased risk of mortality in the elderly with COVID-19. In line with the results of the present study, Oh et al. reported that anemia during hospitalization was independently associated with an increased probability of death from all causes in hospitalized patients with COVID-19 (Oh et al. 2021).

Hemoglobin concentration is one of the most important indicators of oxygen-carrying capacity in the blood. In conditions of compromised breathing and an increased need for oxygen in a hypermetabolic state such as COVID-19, anemia can further reduce oxygen delivery to surrounding tissues (Chu et al. 2020).

The retrospective nature of the study and the nonexistence of the disease severity in the patient's medical records can be considered as the limitations of the study.

#### Conclusion

The results showed that the rate of deaths in the elderly with COVID-19 is high. The death rate among males, age older than 75 years, hospitalization in the ICU, increased ESR and HDR levels, and decreased albumin and hemoglobin levels is significantly higher. Therefore, it is recommended to all health care workers, especially in older patients, to take seriously the presence of any of these risk factors and take early intervention to prevent the severe progression of the disease.

**Abbreviations** Systolic BP: systolic blood pressure; *ECG*: electrocardiogram; *CRP*: c-reactive protein; *ESR*: erythrocyte sedimentation rate; *BUN*: blood urea nitrogen; *Cr*: creatinine; *PT*: prothrombin time; *PTT*: partial thromboplastin time; *WBC*: white blood cells; *HCT*: hematocrit; *Hb*: hemoglobin; *LDH*: lactate dehydrogenase; *CPK*: creatine phosphokinase; *SGOT*: serum glutamic-oxaloacetic transaminase; *SGPT*: serum glutamic-pyruvic transaminase; *Alp*: alkaline phosphatase; *BS*: blood sugar; *SPO2*: peripheral oxygen saturation with pulse oximeter; *K*: potassium; *Na*: Sodium

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#### Declarations

**Ethics approval** The ethical approval of the study was obtained from Ethics Committee of Hamadan University of Medical Sciences (ethics code: IR.UMSHA.REC.1400.165).

Consent to participate Not applicable.

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**Conflict of interest** The authors declare that they have no conflict of interest.

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