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Research Paper

Mortality Risk Factors Among Hospitalized Older Patients With COVID-19

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ABSTRACT

Background: The Coronavirus disease 2019 (COVID-19) is an infectious disease with a high mortality rate among older people.

Objective: The current study aims to investigate the death rate and related factors among hospitalized older patients with COVID-19 in Qazvin, Iran.

Methods: In this descriptive and cross-sectional study, 430 older inpatients with COVID-19 (Mean±SD age: 72.83±8.81) admitted to two hospitals in Qazvin, Iran were randomly selected. Their information was extracted from their electronic health records. Independent t-test, chi-square test, and multivariate logistic regression analysis were used for the data analysis.

Findings: Hypertension (n=234, 54.4%), diabetes mellitus (n=148, 34.4%), and cardiovascular diseases (n=127, 29.4%) were the most prevalent comorbidities. Dyspnea (n=300, 69.8%), cough (n=232, 54.0%), fever (n=186, 43.3%), and general malaise (n=168, 39.1%) were the most frequent clinical symptoms. There was in-hospital mortality in 108 (25.1%) older inpatients. Multivariate regression results showed that the risk of in-hospital death was significantly related to the inpatients' age (OR=1.037, 95%CI=1.007-1.068), white blood cell count (OR=1.187, 95%CI=1.114-1.264), hemoglobin level (OR=0.812, 95%CI=0.720-0.914), platelet count (OR=0.993, 95%CI=0.989-0.996), and oxygen saturation level (OR=0.950, 95%CI=0.967-0.932) at the time of admission.

Conclusion: Older age, white blood cell count, hemoglobin level, oxygen saturation level, and platelet count are predictors of death among older inpatients with COVID-19. Identification of these risk factors can assist the healthcare providers for timely intervention for the prevention of death.

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1. Introduction

Coronavirus disease 2019 (COVID-19) was originated in Wuhan, China in late December 2019 and spread rapidly in different countries [1]. By March 3, 2020, a total of 3,112 deaths were reported worldwide, 166 of which were from outside of China. The number of positive and death cases is still increasing [2]. According to the World health Organization report, from January 3, 2020 to January 19, 2022, there were 6,227,849 confirmed cases of COVID-19 and 132,113 deaths in Iran [3]. People of all ages are at risk for COVID-19 infection, but older adults are more vulnerable to this disease and are more likely to get severe infections [4].

A study by Liu et al. reported that the prevalence of COVID-19 and its related complications, disability, and death rates are higher in older adults [5]. Furthermore, Yang et al. found that 90% of fatal cases among 9211 confirmed patients with COVID-19 were older adults aged 60 years or over [6]. The COVID-19 has various clinical manifestations ranging from asymptomatic infections to severe illness [7]. Fever, dry cough, muscle weakness, and chest pain are the most prevalent and typical symptoms of COVID-19 [8]. However, patients might also present atypical symptoms [9] such as skin manifestation, dizziness, runny or stuffy nose, ocular manifestation, falling, and imbalance especially among older people [2]. The patients are usually recovered in 90% of cases after 10 days from onset of symptoms [10].

The risk of severe illness due to COVID-19 increases by aging. Young people are often asymptomatic and rarely require hospitalization [11]. However, older adults and immunocompromised people often get severe forms of the COVID-19 [12]. Williamson et al. observed a 20-fold increase in mortality rate of older patients aged 80 years or over in comparison with those aged 50-59 years [13]. COVID-19-related mortality mainly due to viral pneumonia-induced acute respiratory distress syndrome [14]. In older people, COVID-19 infection is a multisystem disease, particularly in those with comorbid conditions [15]. High blood pressure, ischemic heart disease, and other age-related diseases are among the important factors influencing mortality rate in older adults with COVID-19 [16].

In Iran, the pandemic started from February 19, 2020; by December 5, 2021, there were 6,134,465 infected patients and approximately 130,200 deaths [17]. Studies have reported high mortality rates among older patients hospitalized with COVID-19 in Iran [18, 19]. Few studies have assessed the risk factors for mortality in patients hospitalized with COVID-19 in Iran. We, therefore, aimed to investigate the demographic and clinical factors associated with in-hospital mortality rate among older patients with COVID-19 admitted to two hospitals in Qazvin, Iran.

2. Materials and Methods

This retrospective study was conducted. The study population consists of all older inpatients with COVID-19 in two hospitals (Velayat and Bu-Ali) in Qazvin, Iran from February 20 to August 22, 2020 (n=1061). The inclusion criteria were age ≥60 years, and having confirmed diagnosis of COVID-19. Cochran formula was used to determine the sample size. At 0.95 confidence level and considering a type I error of 0.05 and the number of population, the sample size was calculated 282. However, for increasing the test power and reducing the error rates, the sample size increased to 430. The samples were selected randomly using a random number generation software. First, the list of older patients with confirmed COVID-19 was extracted from the electronic health records and each received a number. Then, the information of 430 numbers were extracted from the health records. The information included the clinical and demographic information (age, gender, date of hospitalization), chronic comorbidities, symptoms at the time of admission, and some laboratory test results.

For statistical analysis, we divided the patients into two groups, survivors and non-survivors. Categorical and continuous variables were presented using frequency (percentage), and mean (standard deviation), respectively. Independent t-test or chi-square test was used to evaluate the differences between groups. To determine the risk factors of deaths among older inpatients, univariate logistic regression analysis was used. The normality assumption was verified by using Kolmogorov-Smirnov test. The Hosmer-Lemeshow test was used to evaluate the goodness of fit for logistic regression. All statistical analyses were performed in SPSS v. 24 software. A $P<0.05$ was considered statistically significant.

3. Results

Of 430 inpatients with COVID-19, 108(25.12%) died. The baseline characteristics of the participants are shown in Table 1. Non-survivors (Mean±SD age= 76.13±9.19 years) were significantly older than sur-

Table 1. Patients' characteristics at the time of admission

Variables		No. (%)			P
		Total (n=430)	Non-survivors (n=108)	Survivors (n=322)	
Age (y)		72.83(8.81)	76.13(9.19)	71.73(8.41)	<0.001
Gender	Female	223(51.90)	49(45.4)	174(54.0)	0.147
	Male	207(48.10)	59(54.6)	148(46.0)	-
Symptoms Fever		186(43.3)	43(39.8)	143(44.4)	0.470
Cough		232(54.0)	50(46.3)	182(56.5)	0.083
Dyspnea		300(69.8)	80(74.1)	220(68.3)	0.315
General Malaise		168(39.1)	44(40.7)	124(38.5)	0.088
Myalgia		121(28.1)	21(19.4)	100(31.1)	1.000
Sore throat		21(4.9)	6(5.6)	15(4.7)	0.907
Runny nose		0(0.0)	0(0.0)	0(0.0)	-
Headache		36(8.4)	5(4.6)	31(9.6)	0.083
Diarrhea		32(7.4)	7(6.5)	25(7.8)	0.820
Nausea & vomiting		80(18.6)	13(12.0)	67(20.8)	0.060
Nasopharyngeal discharge		29(6.7)	6(5.6)	23(7.1)	0.728
Chill		119(27.7)	30(27.8)	89(27.6)	1.000
Smell and taste		28(6.5)	6(5.6)	22(6.8)	0.810
Tachypnea		7(1.6)	3(2.8)	4(1.2)	0.514
Hemoptysis		2(0.5)	0(0)	2(0.6)	0.997

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vivors (Mean±SD age=71.73±8.41 years). The most common symptoms at admission time were dyspnea (n=300, 69.8%), cough (n=232, 54.0%), fever (n= 186, 43.3%), and general malaise (n=168, 39.1%) (Table 1).

Comorbidities were reported in most of patients (n=330, 76.7%), where hypertension was the most common comorbidity (n=234, 54.4%), followed by diabetes (n=148, 34.4%), and cardiovascular disease (n=127, 29.4%). The results of chi-square showed that there was not significant association between presence of the comorbidities and COVID-19-related mortality (Table 2).

Regarding the laboratory findings which are shown in Table 3, the mean of white blood cell (WBC) count was 10.65±6.01 in non-survivors, which was significantly higher than that in survivors (7.08±3.91) (P<0.001). Similarly, the mean of platelet count was 168.31±79.67 in non-survivors, which was significantly lower than in survivors (193.91±86.19) (P=0.005). The mean hemoglobin level in non-survivors was 11.96±2.33 that was significantly lower than in survivors (12.83±2.11) (P=0.001). Finally, the mean oxygen saturation (SaO_2) in non-survivors (76.37%) was significantly lower than in survivors (87.54%).

The findings of logistic regression analysis revealed that age (OR=1.037, 95%CI=1.007-1.068), WBC count (OR=1.187, 95%CI=1.114-1.264), Hemoglobin (OR=0.812, 95%CI=0.720-0.914), Platelet count (OR=0.993, 95%CI=0.989-0.996), and SaO_2 (OR=0.950, 95%CI=0.967-0.932) were significant predictors of mortality. With the increase of age and WBC count, and the decrease of SaO_2, Hemoglobin, and Platelet count, the risk of mortality among older inpatients increased (Table 4).

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Table 2. Frequency of comorbidities among older inpatients with COVID-19

Comorbidity	No. (%)			P
	Total (n=430)	Non-Survivors (n=108)	Survivors (n=322)	
Diabetes	152 (35.3)	37 (34.3)	115 (35.7)	0.390
Hypertension	234 (54.4)	60 (55.6)	174 (54.0)	0.895
Chronic obstructive pulmonary disease	19 (4.4)	8 (7.4)	11 (3.4)	0.140
Cardiovascular disease	127 (29.4)	36 (33.3)	91 (28.3)	0.380
Previous stroke	17 (4.0)	6 (5.6)	11 (3.4)	0.483
Cancer	10 (2.3)	2 (1.9)	8 (2.5)	0.993

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4. Discussion

This is the first study that is conducted in Qazvin, Iran to determine the correlated factors of death among older inpatients with confirmed COVID-19. The results showed 25.12% mortality rate among older inpatients. Previous studies have reported varying mortality rates; for instance, 13.92% among 25218 older adults with COVID-19 admitted to medical centers affiliated to Mazandaran University of Medical Sciences, Iran [20], 20% among 98 patients aged ≥65 years in Korea [21], 23% among 522 older patients admitted to Baharloo Hospital in Tehran, Iran [22], and 32% among 235 Caucasian older patients aged ≥65 years [23]. The discrepancies may be due to differences in the study area and time. The number of COVID-19 related deaths changes in different waves of the pandemic [24, 25].

Table 3. Laboratory findings for older inpatients with COVID-19 at the time of admission

Variables	Mean±SD			P
	Total (n=430)	Non-survivors (n=108)	Survivors (n=322)	
WBC count (×10³/L)	7.98±4.78	10.65±6.01	7.08±3.91	<0.001
Hemoglobin (gr/dL)	12.61±2.20	11.96±2.33	12.83±2.11	0.001
Platelet count (×10³/µL)	187.48±85.23	168.31±79.67	193.91±86.19	0.005
SaO_2 (%)	84.73±13.25	76.37±16.33	87.54±10.69	<0.001

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Table 4. Logistic regression analysis results for finding risk factors of mortality among older inpatients with COVID-19

Variable	B	OR	P	Wald	95% CI
Age	0.036	1.037	0.015	5.963	1.068-1.007
WBC count (×10³/L)	0.171	1.187	<0.001	28.285	1.264-1.114
Hemoglobin (gr/dL)	0.209-	0.812	0.001	11.765	0.914-0.720
Platelet count (×10³/µL)	0.007-	0.993	<0.001	14.400	0.996-0.989
SaO_2 (%)	-0.052	0.950	<0.001	30.073	0.967- 0.932

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The results of the current study showed that the most frequent comorbidities among older inpatients were hypertension, diabetes, and cardiovascular diseases. Zhou et al. [26] also found that hypertension was the most common comorbidity (30%), followed by diabetes (19%) and coronary heart disease (8%) among patients with COVID-19. In another study on 85 patients, hypertension (37.6%), diabetes (22.4%) and coronary heart disease (11.8%) were the most common comorbidities [27]. Among 140 patients with COVID-19, 30% had hypertension and 12% diabetes [28]. The comorbid diseases can weaken the immune system [29] which makes older people more vulnerable to COVID-19.

The results of our study showed that the risk of mortality related to COVID-19 was increased by the increase of age. A recent study in Italy also reported the age factor as one of the strongest predictors of mortality in patients with COVID-19 [30]. Moreover, the results of a study in China indicated a relationship between age and risk of death among patients with COVID-19 [31]. The result may be related to the immunity system of older people that are less efficient in response to COVID-19 [12]. Furthermore, older adults may have difficulty accessing to health care services [32].

In this study, increased WBC count was also associated with an increased risk of mortality rate among older inpatients with COVID-19. A study on 163 patients with COVID-19 by Zhu et al., also found a significant association between WBC count and death [33]. He et al. [34] also showed a significant increase in WBC and neutrophil counts and a decrease in lymphocytes in patients with severe COVID-19. Sepsis is one of the most common complications following COVID-19, which leads to an increase in leukocytes and mortality rate [26].

According to our results, lower SaO_2 level at the time of admission was associated with the increased mortality rate due to COVID-19. A cohort study also showed that the SaO_2 <85% on admission was independently associated with in-hospital mortality among 5279 people with COVID-19 [35]. Indeed, the major mechanism of death in patients with COVID-19 correlates to hypoxia [26]. A recent cohort study by Wang et al. showed that hypoxemia on admission was a predictor of in-hospital death in patients with COVID-19 [36].

Our findings showed a significant association between lower hemoglobin level and death among older inpatients with COVID-19. Bellmann et al. also reported that anemia at admission was an independent predictor of mortality in 259 patients with COVID-19 [37]. Tao et al. also found that anemia was the independent risk factor for severe COVID-19 in 222 patients [38]. A meta-analysis by Taneri et al. showed that the severity of disease and prognosis in patients with COVID-19 may depend on lower hemoglobin levels [39]. The hemoglobin is one of the most important markers of oxygen-carrying capacity in the blood. Anemia activates the sympathetic nervous system, which increases heart rate, blood pressure, and pulmonary capillary leakage, causing acute respiratory distress syndrome [40].

In agreement with the previous studies, we found that platelet count was associated with mortality among older inpatients with COVID-19. Yang et al. found that non-survivors had significantly lower platelet counts than survivors [41]. Lippi et al. revealed that platelet count is an independent risk factor of in-hospital mortality [42]. The results of a recent meta-analysis also revealed that a low platelet count is associated with the increased risk of severe COVID-19 [43]. Another meta-analysis study with 7,613 patients with COVID-19 revealed that the patients with severe disease had a lower platelet count than those with non-severe disease [44]. Platelet plays an important role in inflammatory responses and fighting infection [45].

This study had some limitations. Firstly, a low number of laboratory tests results were assessed due to the lack of information about the results of other laboratory tests in the medical records of many inpatients. Secondly, we included patients in two hospitals in Qazvin, which might limit the generalizability of the results.

5. Conclusions

The age, SaO_2, hemoglobin level, WBC, and platelet count at admission time are significantly correlated with death in older inpatients with COVID-19. Older age, higher level of WBC and lower level of SaO_2, hemoglobin, and platelet count should receive more attention in the treatment of older adults with COVID-19.

Ethical Considerations

Compliance with ethical guidelines

The ethical principles observed in the article, such as the informed consent of the participants, the confidentiality of information, the permission of the participants to cancel their participation in the research and the code of ethics received from the Ethics Committee of Qazvin University of Medical Sciences (Code: IR.QUMS.REC.1399.126)

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Authors' contributions

Conceptualized, Methodology, and Writing–original draft: Seyedeh Ameneh Motallebi and Fariba Abdollahi; Data collection: Mostafa Keshavarz Rad, Miaad Mirzapour, Mahdi Rajabi Yekta, Alireza Alimohammadi, Morteza Nouri; Data analysis: Seyedeh Ameneh Motallebi; Revised the manuscript: Seyedeh Ameneh Motallebi and Fariba Abdollahi; Supervision: Seyedeh Ameneh Motallebi; All authors read and approved the final manuscript.

Conflict of interest

The authors declared no conflict of interest.

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