

## Clinical, Laboratory and Risk Factors for COVID-19 Mortality in the Elderly Population of Iran: A Three-year Cross-sectional Study

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### ABSTRACT

**OBJECTIVE:** To investigate the clinical characteristics, laboratory findings, and risk factors associated with COVID-19 mortality among elderly patients in Khoy, West Azerbaijan, Iran.

**METHODOLOGY:** This retrospective cross-sectional study analyzed data from 447 confirmed COVID-19 patients over 60 years old hospitalized in Khoy's referral hospital between March 2020 and December 2022. The diagnosis was confirmed via RT-qPCR based on Iran's national protocol. Demographic, clinical, and laboratory data were extracted from hospital records and the city health centre using a standardized checklist.

**RESULTS:** Significant risk factors for mortality included patient gender, hospital admission route, and the presence of severe clinical symptoms such as dyspnea, hypoxia, myalgia, altered consciousness, and high fever. Among comorbidities and lifestyle factors, diabetes, neurological disorders, smoking, and lung diseases were significantly associated with increased mortality risk. Except for platelet count and alanine aminotransferase (ALT) levels, all other laboratory parameters demonstrated significant differences between recovered and deceased patients.

**CONCLUSION:** This study highlights the importance of considering age, gender, clinical presentation, and pre-existing conditions when managing elderly COVID-19 patients to mitigate complications and reduce mortality. Targeted interventions and enhanced monitoring strategies for high-risk individuals are essential to improve outcomes in this vulnerable population.

**KEYWORDS:** COVID-19, elderly, laboratory outcomes, clinical characteristics, risk factors, SARS-CoV-2

**INTRODUCTION**

COVID-19 is a global pandemic caused by the SARS-CoV-2. This virus can produce a wide range of clinical symptoms, ranging from mild to severe, requiring hospitalization and even resulting in death<sup>1</sup>. The pathophysiology of SARS-CoV-2 infection shares significant similarities with the SARS-CoV virus, where a severe host inflammatory response plays a critical role in respiratory system damage. Therefore, the severity of the disease depends not only on the viral infection itself but also on the host's immune response. One known factor that exacerbates the severity of the disease is increasing age<sup>2</sup>. Among COVID-19 patients, acute respiratory distress syndrome (ARDS) is one of the leading causes of respiratory failure and mortality, accounting for approximately 70% of COVID-19-related deaths<sup>3</sup>.

Furthermore, a cytokine storm caused by the uncontrolled release of cytokines in response to viral infection and secondary infections is responsible for death in about 28% of severe COVID-19 cases. In such instances, widespread systemic inflammation leads to multi-organ damage, including heart, liver, and kidney failure<sup>4</sup>. Although individuals of all ages can contract COVID-19, existing evidence from similar pandemics such as SARS and MERS indicates that older adults are particularly at risk for more severe forms of the disease and related complications. The Centers for Disease Control and Prevention (CDC) has reported that while individuals over 65 years old represent 17% of the U.S. population, this age group accounts for 31% of COVID-19 cases, 45% of hospitalizations, 53% of intensive care unit admissions, and 80% of deaths due to the disease<sup>6,5</sup>.

These statistics demonstrate that older adults are not only at greater risk of contracting COVID-19, but they also have a significantly higher likelihood of experiencing fatal outcomes. Additionally, a study found that 31% of elderly patients with COVID-19 developed severe or critical illness, while only 1.4% remained asymptomatic. In this study, severe symptoms included any of the following criteria: (a) shortness of breath and an increased respiratory rate of over 30 breaths per minute, (b) oxygen saturation below 93% at rest, (c) a ratio of arterial oxygen partial pressure to inspired oxygen fraction (PaO<sub>2</sub>/FiO<sub>2</sub>) less than 300 mmHg, and (d) rapid progression of lung lesions (<50%) within 24 to 48 hours<sup>7</sup>.

Several risk factors are associated with adverse outcomes of COVID-19 in older adults. Advanced age, male gender, and underlying conditions such as diabetes, cardiovascular diseases, and chronic respiratory diseases are among these factors. Various studies have shown that the most common clinical symptoms in COVID-19 patients include fever, cough, shortness of breath, fatigue, and muscle pain. Additionally, laboratory findings, such as elevated CRP, lactate dehydrogenase, and decreased lymphocytes, are associated with poorer prognosis<sup>8</sup>.

This study examines the typical clinical and laboratory symptoms in elderly patients with COVID-19 and the risk factors associated with adverse outcomes<sup>9</sup>. Understanding these factors can facilitate more appropriate medical care and improve patient prognosis. Research indicates that adults aged 60 years and older, particularly those with underlying health conditions such as cardiovascular diseases, respiratory diseases, diabetes, or cancer, are more vulnerable to this disease<sup>10</sup>. Given the absence of comprehensive studies focusing on older adults in this specific region, and considering the unique phenotypes of the local population along with the high proportion of elderly patients and the severity of the disease in this group, this study is designed to investigate clinical symptoms, paraclinical factors, and risk factors in older adults during the COVID-19 pandemic.

## **METHODOLOGY**

This retrospective study was conducted on clinical and laboratory data of elderly patients hospitalized with COVID-19 at Ayatollah Khomeini Hospital in Khoy, Iran, during March 2020 and December 2022. Patients were diagnosed using the reverse transcription real-time PCR (RT-qPCR) method, following the Iranian Ministry of Health and Medical Education's national diagnostic protocol for COVID-19<sup>11</sup>. Information regarding infection symptoms, laboratory results, underlying diseases, and mortality was extracted from the hospital's patient registration system. A total of 447 elderly patients (aged  $\geq 60$  years) were included in this study, comprising 268 deceased and 179 recovered patients. **This research received ethical approval from the Ethics Committee of the Khoy University of Medical Sciences (approval code: IR.KHOY.REC.1402.045).**

### **Statistical Analysis**

Statistical analysis was performed using SPSS software version 22. Descriptive statistics were calculated for demographic variables and risk factors. To compare the means of quantitative characteristics related to elderly patients with COVID-19 across different levels of categorical demographic variables, such as gender and disease symptoms, independent samples t-tests and Mann-Whitney U tests were employed. A p-value of less than or equal to 0.05 was considered statistically significant.

## RESULTS

In this study, 447 elderly patients with COVID-19 were analyzed. Data analysis indicated that laboratory and clinical factors significantly influenced disease outcomes in this age group. The average age of the patients was 75 years, and an older age was significantly associated with the occurrence of more severe complications and a higher mortality rate ( $p \leq 0.01$ ). Among the 447 patients, 225 were male (including 146 deceased and 79 recovered), and 222 were female (including 122 deceased and 100 recovered). The results showed that males were at a higher risk for severe complications compared to females ( $p \leq 0.05$ ). Analysis of clinical variables indicated that patient gender, hospital admission method, and the presence of severe clinical symptoms such as shortness of breath (dyspnea), low oxygen saturation, myalgia (muscle pain), decreased consciousness, and high fever were associated with an increased risk of mortality ( $p \leq 0.05$ ). Among the underlying diseases and lifestyle factors (**Table I**), diabetes, neurological diseases, smoking, chronic lung disease, and the need for oxygen therapy were significantly more prevalent in patients who died ( $p \leq 0.05$ ). Among the laboratory results obtained from recovered and deceased elderly patients (**Table II**), only platelet count and the liver enzyme alanine aminotransferase (ALT) did not show a significant difference between the two groups ( $p > 0.05$ ); this indicates that other laboratory parameters measured, including white blood cell count, hemoglobin level, hematocrit, neutrophil, lymphocyte, monocyte counts, blood glucose, urea, creatinine, calcium, magnesium, phosphorus, sodium, potassium, liver enzyme aspartate aminotransferase (AST), alkaline phosphatase, lactate dehydrogenase, creatine phosphokinase, ferritin, PT, PTT, INR, ESR, and direct and total bilirubin, showed statistically significant differences between the groups of recovered and deceased elderly patients due to COVID-19 ( $p \leq 0.05$ ).

**Table I: Demographic Characteristics, Underlying Diseases, and Clinical Symptoms of Recovered and Deceased Elderly COVID-19 Patients**

Variable		Deceased (n = 268)	Recovered (n = 179)	p-value
<b>Gender</b>	Male	146	79	0.03
	Female	122	100	
<b>Hospital admission method</b>	outpatient	174	163	0.0
	Hospitalized	94	16	
<b>Fever</b>	Negative	195	150	0.008
	Positive	73	29	
<b>Cough</b>	Negative	137	83	0.3
	Positive	131	96	
<b>Myalgia</b>	Negative	178	83	0.0
	Positive	90	96	
<b>Respiratory distress</b>	Negative	74	79	0.0
	Positive	194	100	
<b>Decreased consciousness</b>	Negative	243	175	0.003
	Positive	25	4	
<b>Abdominal pain</b>	Negative	263	175	1.0
	Positive	5	4	
<b>Vomit</b>	Negative	230	152	0.7
	Positive	38	27	
<b>Nausea</b>	Negative	261	174	1.0
	Positive	7	5	
<b>Headache</b>	Negative	250	159	0.1
	Positive	18	20	
<b>Brain Fog</b>	Negative	264	177	1.0
	Positive	4	2	
<b>Chest pain</b>	Negative	261	174	0.9
	Positive	7	5	
<b>po2</b>	Negative	208	99	0.0
	Positive	60	80	
<b>Smoke</b>	Negative	261	179	0.04
	Positive	7	0	
<b>Cancer</b>	Negative	263	177	0.7
	Positive	5	2	
<b>Liver disease</b>	Negative	265	179	0.2
	Positive	3	0	
<b>Diabetes</b>	Negative	188	140	0.05
	Positive	80	39	
<b>Cardiovascular disease</b>	Negative	217	156	0.09
	Positive	51	23	
<b>Renal disease</b>	Negative	258	177	0.1
	Positive	10	2	
<b>Respiratory disease</b>	Negative	254	177	0.03
	Positive	14	2	
<b>Neurological diseases</b>	Negative	252	178	0.002
	Positive	16	1	
<b>Oxygen therapy</b>	Negative	46	23	0.04
	Positive	131	119	
<b>Blood pressure</b>	Negative	161	109	0.9
	Positive	107	70	
<b>Hospitalization (day)</b>		47.7	7.70	0.6

**Table II: Laboratory Results of Recovered and Deceased Elderly COVID-19 Patients**

	<b>Deceased (n = 268)</b>	<b>Recovered (n = 179)</b>	<b>p-value</b>
<b>WBC</b>	13181.59	9536.99	0.0
<b>Hb</b>	12.66	13.38	0.001
<b>HCT</b>	39.70	40.93	0.03
<b>PLT</b>	288657.28	223591.24	0.8
<b>N</b>	88.84	75.99	0.0
<b>L</b>	10.15	20.08	0.0
<b>Mono</b>	2.54	2.85	0.02
<b>BS</b>	189.69	163.42	0.02
<b>Urea</b>	120.88	44.62	0.0
<b>Cr</b>	2.68	1.21	0.0
<b>Ca</b>	8.42	8.75	0.0
<b>Mg</b>	2.38	2.15	0.02
<b>Phos</b>	4.37	3.19	0.0
<b>Na</b>	141.27	138.85	0.0
<b>K</b>	4.49	6.72	0.0
<b>AST</b>	116.58	40.57	0.0
<b>ALT</b>	89.22	44.12	0.2
<b>Alk</b>	256.57	197.87	0.0
<b>LDH</b>	871.67	552.42	0.0
<b>CPK</b>	422.19	211.77	0.03
<b>Ferritin</b>	668.04	442.08	0.0
<b>PT</b>	12.33	13.36	0.0
<b>INR</b>	1.17	1.16	0.0
<b>PTT</b>	41.76	29.44	0.0
<b>ESR</b>	46.55	40.11	0.0
<b>Billi total</b>	1.09	0.74	0.0
<b>Billi direct</b>	0.486	0.294	0.0

WBC: White Blood Cell count, Hb: Hemoglobin, HCT: Hematocrit, PLT: Platelet count, N: Neutrophils, L: Lymphocytes, Mono: Monocytes, BS: Blood Sugar, Cr: Creatinine, Ca: Calcium, Mg: Magnesium, Phos: Phosphorus, Na: Sodium, K: Potassium, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, Alk: Alkaline Phosphatase, LDH: Lactate Dehydrogenase, CPK: Creatine Phosphokinase, PT: Prothrombin Time, INR: International Normalized Ratio, PTT: Partial Thromboplastin Time, ESR: Erythrocyte Sedimentation Rate, Billi: Bilirubin.

## DISCUSSION

This retrospective study of 447 elderly patients with COVID-19 revealed that both clinical and laboratory parameters significantly influence disease outcomes in this vulnerable population. The average age of the patients was 75 years, and increasing age was independently associated with a higher incidence of severe complications and mortality. This observation aligns with the established understanding that older adults are disproportionately affected by COVID-19, mainly due to immunosenescence and the increased prevalence of comorbidities. For instance, **Nikolich-Žugich et al. (2021)** demonstrated the heightened susceptibility of older adults to viral infections, including COVID-19, stemming from age-related immunological decline, which correlates with disease severity and associated complications<sup>12</sup>. Our findings corroborate this, underscoring the imperative for proactive identification and management of high-risk elderly individuals.

Sex emerged as another critical determinant of COVID-19 outcomes. Males demonstrated a significantly elevated risk of severe complications compared to females. This disparity may be attributed to a combination of biological and social factors. Studies suggest that females exhibit a more robust immune response than males, potentially contributing to the observed sex differences in mortality<sup>13</sup>.

Moreover, behavioral risk factors such as smoking and alcohol consumption, often more prevalent in males, may further exacerbate these disparities. **Hernández and colleagues (2022)** reported similar findings, highlighting the increased mortality risk in elderly males with COVID-19, further supporting the role of biological and social influences<sup>14</sup>.

Beyond demographic factors, the severity of clinical presentation was strongly predictive of mortality. Symptoms such as shortness of breath decreased oxygen saturation, muscle pain, altered consciousness, and high fever were significantly associated with increased mortality risk. These findings emphasize the importance of early symptom recognition and prompt intervention, particularly in elderly patients prone to rapid clinical deterioration, which can ultimately improve the survival outcomes of these patients.

The presence of underlying diseases and lifestyle factors also significantly impacted disease outcomes. Diabetes and neurological disorders emerged as prominent risk factors, reinforcing the need for comprehensive management of comorbidities in this population. Diabetes, a well-established risk factor for severe COVID-19, necessitates meticulous glycemic control<sup>15</sup>. Additionally, smoking history and chronic lung diseases were significantly associated with mortality, highlighting the importance of smoking cessation and respiratory management. **Pérez et al. (2023)** similarly reported a strong correlation between dyspnea, fever, and mortality in elderly COVID-19 patients, alongside an increased risk in those with diabetes and cardiovascular diseases<sup>16</sup>. Our results corroborate these findings, emphasizing the critical role of managing acute symptoms and underlying conditions in elderly patients. **Dessi et al. (2021)** observed a cumulative mortality rate of 17.62% in hospitalized elderly COVID-19 patients, with pre-existing conditions like chronic obstructive pulmonary disease (COPD), cardiovascular disease, diabetes, hypertension, obesity, cancer, and acute kidney injury significantly influencing mortality risk<sup>17</sup>, further supporting our observations regarding diabetes and pulmonary obstruction.

Analysis of laboratory parameters revealed significant differences between recovered and deceased patients for most markers. Among the various laboratory parameters measured, including white blood cell count, hemoglobin levels, hematocrit, neutrophils, lymphocytes, monocytes, blood glucose, urea, creatinine, calcium, magnesium, phosphorus, sodium,

potassium, liver enzyme AST, alkaline phosphatase, lactate dehydrogenase, creatine phosphokinase, ferritin, PT, PTT, INR, ESR, and direct and total bilirubin, a statistically significant difference was observed between the two groups of elderly patients who recovered and those who died. Only platelet count and liver enzyme ALT did not show significant differences between the two groups; this suggests that while most laboratory parameters reflect disease severity, these specific markers may not be as informative in predicting outcomes in this population.

**Kirkland et al. (2023)** found that changes in platelet levels and inflammatory markers could predict severe complications in elderly COVID-19 patients.<sup>18</sup>, contrasting with our findings. This discrepancy may be attributed to differences in study design, patient populations, or the timing of laboratory measurements.

Lifestyle factors also played a role in determining COVID-19 outcomes. **Cohen et al. (2023)** demonstrated that older adults with healthier lifestyles had a significantly lower risk of severe complications and mortality from COVID-19<sup>19</sup>; this underscores the importance of promoting healthy lifestyle behaviors in older adults as a preventative strategy against infectious diseases.

Overall, our findings are consistent with the growing body of literature highlighting the multifaceted impact of COVID-19 on older adults. They underscore the importance of considering age, sex, clinical presentation, underlying diseases, and lifestyle factors in managing this vulnerable population. Our study reinforces the need for a multidisciplinary approach to managing elderly COVID-19 patients. It emphasizes the necessity for continued research to elucidate further these factors' complex interplay to refine treatment strategies and improve patient outcomes.



## **CONCLUSION**

The findings of this retrospective study on 447 elderly patients with COVID-19 underscore the significant influence of age, sex, clinical presentation, and pre-existing comorbidities on disease outcomes. Considering all these results, it can be concluded that to reduce complications and mortality in elderly patients with COVID-19, targeted interventions focusing on age, sex, clinical symptoms, and underlying diseases are crucial. Additionally, age-specific preventive and therapeutic measures should be explicitly designed, including optimized management of comorbidities and enhanced public health education regarding COVID-19 risks in older adults. Furthermore, the critical need for early screening and vigilant monitoring of elderly COVID-19 patients, particularly those with pre-existing health conditions, is highlighted. Overall, the findings of this study highlight the importance of a comprehensive approach in managing elderly patients with COVID-19 and emphasize the necessity for continued research to refine treatment strategies and improve outcomes in this vulnerable population. Identifying and managing these key factors can improve treatment outcomes in this age group.

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**Conflict of Interest:** No conflicts of interest, as stated by authors.

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**Data Sharing Statement:** The corresponding author can provide the data proving the findings of this study on request. Privacy or ethical restrictions bound us from sharing the data publicly.

## **AUTHOR CONTRIBUTION**

All authors equally contributed to the study design, methodology, and writing of all research sections.

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