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Research Article

Predictors of Mortality for Severe COVID-19: A Descriptive Analysis from an Intensive Care Unit of a Tertiary Care Center

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ABSTRACT

Background: This study aimed to investigate mortality risk factors among severe COVID-19 patients admitted to the intensive care unit (ICU) to inform better management strategies and reduce mortality rates.

Methods: A descriptive-analytical, cross-sectional, and retrospective study was conducted between March 2022 and April 2023 at the intensive care unit of Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran. The study included patients admitted to the ICU with severe COVID-19. The main variables were demographic factors (age, gender), pre-existing medical conditions (smoking, diabetes, hypertension), disease severity markers (CT-scan scores, inflammatory and coagulation parameters), and mortality outcomes.

Results: The study included 395 eligible patients. The mortality rate was 57.72%, with no significant difference in hospital stay duration between deceased and survived patients. Smoking, diabetes mellitus, and hypertension were significantly associated with higher mortality. Males exhibited a higher mortality rate, although not statistically significant. Patients over 65 years old had significantly higher mortality. Winter showed a significant increase in mortality, likely due to the Omicron subvariant. Higher CT scan scores and elevated inflammatory/coagulation markers correlated with increased mortality risk.

Conclusion: Pre-existing conditions, demographic factors, and disease severity markers are crucial predictors of mortality in severe COVID-19 patients. Tailored interventions targeting these risk factors are essential to improve outcomes.

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Introduction

The COVID-19 pandemic brings enormous challenges to global healthcare systems, requiring an in-depth analysis of the variables impacting patient outcomes, notably in severe cases requiring intensive care.

Research indicates a correlation between COVID-19 severity and underlying diseases, potentially leading to cerebrovascular consequences like cerebral venous sinus thrombosis, hemorrhagic stroke, and ischemic stroke, and more likely to die from COVID-19 [1-2]. These findings emphasize the need to consider pre-existing medical issues when predicting COVID-19 patient outcomes [3-4].

A higher risk of developing a severe illness from COVID-19 is associated with those who already have a medical history (PMH) as opposed to those who do not. These conditions include diabetes mellitus (DM), hypertension (HTN), obesity, cardiovascular disease (CVD), chronic kidney disease (CKD), liver disease, cancer, chronic obstructive pulmonary disease (COPD), hyperlipidemia (HLP), heart failure (HF), and anxiety disorders [5-6].

Besides the pre-existing illnesses, other risk factors affecting the mortality rate in hospitalized COVID-19 patients include advanced age, male gender, tachypnea, low systolic blood pressure, low peripheral oxygen saturation, acute kidney injury (AKI), elevated D-dimer, and respiratory distress [7-8].

Several studies have examined various factors like length of hospitalization and intensive care unit (ICU) stay, survival rates, and intubation need in COVID-19 patients. One study found that time of intubation didn't significantly impact clinical outcome benefits, such as length of mechanical ventilation, hospital and ICU stays, and 28-day mortality [9-11]. Conversely, another study suggested postponing intubation beyond the initial 24-hour period could potentially increase mortality risk in severe COVID-19 patients [12]. According to some studies, the extent of lung involvement observed in CT scans of COVID-19 patients was linked to a range of laboratory indicators, so that higher levels of CRP, ESR, D-dimer and lactate dehydrogenase (LDH), along with lower levels of lymphocytes, were associated with increased severity of lung damage at radiological findings [13-15].

Based on these articles, the presence of underlying medical conditions has been identified as a contributing factor to the hospitalization of individuals with COVID-19 in ICU and is also recognized as a significant determinant of patient mortality.

Consequently, this study aims to explore the mortality risk factors among severe COVID-19 patients admitted to ICU, with the ultimate goal of managing the disease and reducing daily mortality rates by potentially controlling these risk factors.

Methods

Study Design

This study is a descriptive-analytical, cross-sectional, and retrospective study in which the demographic, clinical, and laboratory findings of severe COVID-19 patients were analyzed to find outcome-correlating factors. The research was conducted at the ICU of Sina Hospital, Tehran University of Medical Sciences (TUMS), Tehran, Iran, between March 21, 2022, and April 1, 2023.

Ethical Consideration

Before patient enrollment, ethics approval from the TUMS ethics committee was obtained (ethics code: IR.TUMS.SINAHOSPITAL.REC.1401.052), and by adhering to the Helsinki declaration, written consent form was obtained from the legal guardian.

Inclusion and Exclusion Criteria

Inclusion criteria included patients over 18 years old with a confirmed diagnosis of COVID-19 by RT-PCR and chest CT scan, admitted to the ICU, and meeting severe stage criteria (SpO_2 <94% on room air, PaO_2/FiO_2 <300 mmHg, a respiratory rate (RR) >30 breaths/min, or lung infiltrates >50% on chest CT scan).
In cases where demographic or clinical data were lacking and patient outcome information was inaccessible due to file deficiencies, patients were excluded from the study.

Demographic and clinical data

Comprehensive demographic, clinical, and paraclinical data, containing age, sex, body mass index (BMI), habitual history, past medical history (PMH), length of hospitalization, length of ICU stays, survival status, the need for intubation, laboratory, and imaging findings, were documented in an Excel sheet.

Imaging assessment

Initially, the CT scans were reviewed to determine if the characteristic features of COVID-19 pneumonia, including subpleural unilateral or bilateral grand glass opacities (GGOs) in the lower lobes with a peripheral or posterior distribution that further developed into the crazy-paving pattern and subsequent consolidation, were present or not.

The study used visual severity scoring on a chest CT scan [16] to determine lung involvement. A semiquantitative CT severity grading was computed for each of the 5 lobes, with different categories such as Score 1 (less than 5% area involved), Score 2 (5-25% area involved), Score 3 (25-50% area involved), Score 4 (50-75% area involved), and Score 5 (more than 75% area involved), resulting in a total score of 25 [17].

Statistical analysis

Data were analyzed by SPSS statistical software (version 16) with T-test and Chi-square tests. P value less than 0.05 was considered significant, and P value between 0.05 and 0.06 was considered almost significant.

Results

Background Information of Patients

This research was conducted for the statistical analysis of data from 395 eligible patients, comprising 177 (44.36%) females and 218 (55.64%) males with a mean age of 66.47 ± 4.3 and a mean BMI of 21.98 ± 4.21 Kg/m^2, which were not statistically different between deceased and alive participants. A total of 21.01% of patients were cigarette smokers. The most prevalent underlying conditions were DM (34.17%), IHD (31.89%), HLP (27.59%), and HTN (18.73%). Notably, 35.54% of participants had no underlying disease. Supplementary data is summarized in (Table 1).

Relationship Between Underlying Conditions and Mortality

The study found a strong relationship between smoking and mortality rates (P value=0.051). Deceased patients showed a higher incidence of HTN and DM compared to survivors (P value=0.043 and 0.01, respectively). Although surviving patients had a greater proportion of patients without underlying diseases, this difference did not reach statistical significance (N=83 vs. 36; P value=0.083). No patient, whether alive or dead, met the criteria for obesity based on BMI, so this parameter was not included in the analysis as a potential risk factor. The relationship between underlying conditions and mortality outcomes is illustrated in (Table 1).

Relationship Between Gender and Mortality

A significant association was found between gender and mortality in severe cases of COVID-19. The cohort consisted of 55.64% males, with a mortality rate of 77.52% and a P value of 0.048, implying a significantly higher mortality rate compared to women, which is shown in (Table 1).

Relationship Between Age of Patients and Mortality

In this study, participants were categorized by age: 86 were ≤ 44 years, 170 were 45-65 years, and 139 were > 65 years. The analysis exhibited that in the ≤ 44 years category, the number of recovered patients was significantly higher than those who died (P value=0.043). Conversely, in the patients >65 years category, the number of deceased patients was significantly greater (P value=0.003). These data are summarized in (Table 1).

Investigating the Relationship Between Outcomes

The mean duration of hospital stay was 11±13.14 days, with a non-statistical variation between deceased and survived ones (10.96±13.08 vs. 22.64±15.28 days; P value=0.631). The mortality rate within the cohort was 57.72%, which was statistically significant (P value=0.043). A comparison of outcomes is illustrated in (Table 2). The initial CT-scan score for deceased patients was 18.32 ± 4.57 out of 25, compared to 15.72 ± 15.57 for survivors, which was statistically significant (P value= 0.042). The relationship between CT-scan scores and mortality outcomes is shown in (Table 2).

Table 1- Demographic Factors and Background Information of Patients

Parameters		Total (n=395)	Deceased (n=228)	Alive (n=167)	P value
Age; (Mean ± SD)		66.47 ± 4.3	67.39 ± 3.6	65.09 ± 5.9	0.061
Age	< 44 years	86 (21.77%)	21 (9.21%)	65 (38.92%)	0.043
Category;	45-65 years	170 (43.03%)	79 (34.64%)	91 (54.49%)	0.961
N(%)	> 65 years	139 (35.18%)	128 (56.14%)	11 (6.58%)	0.003
Sex; N(%)	Male	218 (55.64)	169 (77.52)	49 (29.34)	0.048
	Female	177 (44.36)	59 (33.33)	118 (70.65)	0.086
BMI (kg/m^2); (Mean ± SD)		21.98 ± 4.21	21.11 ± 5.47	22.76 ± 3.27	0.081
COVID-19 Vaccination		392 (99.24)	2(0.87)	2(1.19)	0.059
Smoking		83 (21.01)	51 (36.4)	32 (19.16)	0.051
DM		135 (34.17)	99 (43.42)	36 (21.55)	0.036
HTN		74 (18.73)	58 (25.43)	16 (11.85)	<0.01
CKD		45 (11.39)	18 (7.89)	27 (16.16)	0.751
IHD		126 (31.89)	84 (36.84)	42 (25.14)	0.639
Cancer		21 (5.31)	15 (6.58)	6 (3.59)	0.053
HLP		109 (27.59)	67 (29.38)	42 (25.14)	0.962
HF		39 (9.87)	27 (11.84)	12 (7.18)	0.063
COPD		11 (2.78)	4 (1.75)	7 (4.19)	0.073
Without PMH		119 (35.54)	36 (15.78)	83 (49.70)	0.083

DM: Diabetes mellitus; HTN: Hypertension; CKD: Chronic Kidney Disease; IHD: Ischemic Heart Disease; HLP: Hyperlipidemia; HF: Heart Failure; COPD: Chronic Obstructive Pulmonary Disease; PMH: Past Medical History

Table 2- Comparison of Outcomes between Groups

Parameters	Deceased	Alive	P value
CT-Scan Score (out of 25); Mean ± SD	18.32 ± 4.57	15.72 ± 15.57	0.042
Length of ICU Stay (days); Mean ± SD	13.08 ± 10.96	15.28 ± 22.64	0.631
Mortality Rate; N (%)	228 (57.72)	167 (37.2)	0.043

Investigating the Relationship Between Season of Disease and Mortality Outcome

The study analyzed hospitalization data from 31 patients in spring, 137 in summer, 78 in fall, and 149 in winter. Results showed a significant difference in mortality compared to the winter season (P value=0.049). However, the summer had more deaths than recoveries; this difference was not statistically significant. In spring and fall, recoveries were more common than deaths. (Table 3) provides further details on the relationship between disease season and mortality outcome.

Table 3- The Relationship Between Season of Disease and Mortality Outcome

Season of Admission	Total (n=395)	Deceased (n=228)	Alive (n=167)	P value
Spring	31 (7.84%)	9 (3.94%)	22 (13.17%)	0.087
Summer	137 (34.68%)	98 (42.98%)	39 (23.35%)	0.063
Fall	78 (19.74%)	14 (6.14%)	64 (38.32%)	0.064
Winter	149 (37.72%)	107 (46.92%)	42 (25.14%)	0.049

Relationship Between Blood Tests at Admission and Mortality Outcomes

The study investigated the correlation between the initial blood test results of patients upon hospitalization and their mortality outcomes. Results showed no statistically significant differences in organ function biomarkers, except for higher troponin levels in the deceased group (P value=0.054).

The analysis of inflammatory variables revealed no significant differences in WBC counts between died and recovered patients (10.2 vs. 10.1, P value=0.703). The deceased had lower platelet counts, but the difference was not statistically significant (199±82.2 vs. 280±203, P value=0.587). While lymphocyte percentages increased in survivors, neutrophil percentages slightly increased in deceased individuals, both approaching statistical significance (P value=0.058, and 0.061, respectively). At admission, ESR and CRP levels were markedly elevated in dead patients (P value=0.018, and 0.051, respectively), whereas LDH levels were similarly higher but not substantially different from those of survivors (P value=0.277).

The analysis of coagulation factors indicated that deceased patients had lower platelet levels compared to survivors, although this difference was not statistically significant (P value=0.587). Additionally, while PT and INR levels were higher in deceased patients, these differences were also not statistically significant (P value=0.248 and P value=0.132, respectively). In contrast, ferritin and D-dimer levels were significantly elevated in deceased patients (P value=0.057 and P value=0.047, respectively). (Table 4) illustrates the relationship between blood tests and mortality outcomes.

Table 4- The relationship between laboratory findings at the beginning of hospitalization and the outcome of mortality.

Variables		Deceased (n=228)	Alive (n=167)	P value
Organ function parameters				
Cr (mg/dl) (n=395)	Mean (SD)	1.57 (1.17)	1.49 (1.08)	0.271
	MD [Min, Max]	1.11 [0.600, 6.73]	1.12 [0.800, 3.89]	
AST (U/L) (n=389)	Mean (SD)	121 (430)	78.4 (68.5)	0.627
	MD [Min, Max]	53.0 [10.0, 3460]	58.0 [24.0, 217]	
ALT (U/L) (n=389)	Mean (SD)	61.4 (143)	38.0 (26.8)	0.275
	MD [Min, Max	31.0 [10.0, 1140]	24.0 [15.0, 77.0]	
Troponin (ng/ml) (n=393)	Mean (SD)	120 (344)	65.3 (120)	0.054
	MD [Min, Max]	11.0 [0.0100, 2090]	10.0 [1.00, 332]	
Bilirubin Total (mg/dl) (n=395)	Mean (SD)	0.980 (0.978)	0.955 (0.508)	0.064
	MD [Min, Max]	0.735 [0.300, 7.20]	0.835 [0.420, 1.92]	
Inflammatory parameters				
WBC($\times 10^3$/m3) (n=395)	Mean (SD)	10.1 (5.51)	10.2 (6.00)	0.703
	MD [Min, Max]	8.80 [1.40, 25.6]	6.80 [4.70, 19.0]	
Neutrophil (%) (n=395)	Mean (SD)	89.2 (11.3)	83.3 (11.2)	0.061

	MD [Min, Max]	93.4 [26.0, 96.0]	81.1 [64.4, 100]	
Lymphocyte (%) (n=395)	Mean (SD)	8.97 (9.40)	14.5 (8.46)	0.018
	MD [Min, Max]	7.70 [0.300, 71.0]	14.5 [4.10, 29.3]	
CRP (mg/l) (n=395)	Mean (SD)	92.2 (41.9)	73 (43.5)	0.051
	MD [Min, Max]	102 [3.50, 251]	96.0 [12.0, 245]	
ESR (mm/hr) (n=395)	Mean (SD)	69.4 (23.1)	54.1 (29.0)	0.018
	MD [Min, Max]	61.0 [43.0, 96.0]	51.0 [7.00, 125]	
LDH (U/L) (n=366)	Mean (SD)	982 (468)	897 (347)	0.277
	MD [Min, Max]	905 [0, 2440]	886 [408, 1390]	
Coagulation parameters				
PLT ($\times 10^3$/m3) (n=395)	Mean (SD)	199 (82.2)	280 (203)	0.587
	MD [Min, Max]	185 [62.0, 401]	219 [120, 719]	
PT (s) (n=395)	Mean (SD)	15.1 (3.89)	14.3 (2.14)	0.248
	MD [Min, Max]	14.0 [11.7, 33.2]	13.4 [12.0, 18.0]	
INR (n=395)	Mean (SD)	1.19 (0.300)	1.12 (0.169)	0.132
	MD [Min, Max]	1.10 [1.00, 2.79]	1.00 [1.00, 1.40]	
Ferritin (ng/ml) (n=378)	Mean (SD)	927 (1690)	470 (52.2)	0.057
	MD [Min, Max]	759 [0, 10700]	500 [710, 800]	
D-Dimer (mg/l) (n=378)	Mean (SD)	1820 (2570)	965 (1060)	0.047
	MD [Min, Max]	829 [14.3, 11600]	659 [331, 3330]	
Fibrinogen (g/l) (n=73)	Mean (SD)	4.25 (3.41)	1.25 (2.23)	0.093
	MD [Min, Max]	3.51 [0, 8.53]	0 [0, 5.46]	

Abbreviation-MD: Median; Cr: creatinine; AST: Aspartate transaminase; ALT: Alanine transaminase; WBC: White blood cell; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; LDH: Lactate dehydrogenase; PLT: platelet; PT: prothrombin time; INR: International normalized ratio.

The correlation between organ dysfunctions and pulmonary involvement in deceased individuals

Based on deceased patients' data analysis in this study, a significant connection between pulmonary involvement severity and specific organ dysfunctions was found. The study revealed a significant correlation between the extent of pulmonary involvement and specific organ dysfunctions like decreased consciousness (P value=0.003), hypotension (P value=0.041), acute lung injury (ALI) (P value=0.000), acute liver injury (0.053), and AKI (P value=0.057) in deceased patients, which is shown in (Table 5).

Table 5- Correlation between pulmonary involvement and organ dysfunction in deceased patients.

Organ dysfunction		Death (n=228)					P value
		CT-score 0-5, N=0	CT-score 5-10, N=3	CT-score 10-15, N=29	CT-score 15-20, N=65	CT-score 20-25, N=131	
GCS	<13	0 (0%)	0 (0%)	16 (50.0%)	21 (75.0%)	123 (93.89%)	0.003
MAP	<65 mmHg	0 (0%)	0 (0%)	23 (79.31%)	51 (78%)	87 (66.41%)	0.041
PaO2/FiO2	<300	0 (0%)	3 (100%)	29 (100)	65 (100%)	131 (100%)	0.000
Bilirubin total	>1.2 mg/dl	0 (0%)	0 (0%)	6 (20.68%)	43 (66.15%)	112 (85.49%)	0.053
Creatinine	>1.5 mg/dl	0 (0%)	2 (66.66%)	18 (62.06%)	26 (40%)	107 (81.67%)	0.057
platelet	<150 (×1000/m3)	0 (0%)	1 (33.33%)	14 (48.27%)	16 (24.61%)	86 (65.64%)	0.079

Abbreviation: GCS: Glascow Coma Score; MAP: Mean Arterial Pressure; PaO2: partial pressure of oxygen in arterial blood; FiO2: fraction of inspiratory oxygen concentration.

Discussion

This study crucially emphasizes the mortality risk variables linked to severe COVID-19 patients hospitalized in the intensive care unit. The pandemic's total mortality rate of 57.72% highlights the severity of the illness and the issues that healthcare systems encountered.

Pre-existing Conditions and Mortality

The findings indicate a clear correlation between higher mortality rates and pre-existing illnesses, particularly diabetes and hypertension, which aligns with previous studies highlighting the increased susceptibility of individuals with underlying diseases to catastrophic COVID-19 outcomes [18-22]. Since none of the participants in our study met the obesity criteria, we did not include this factor in the analysis. Together with the other research findings [23-25], this one also suggests

that although obesity is considered by most to be a major risk factor, the effect might differ depending on the specific population being researched. Future studies ought to examine this disparity further, since knowing how various comorbidities interact might help guide focused therapies.

Demographic Factors

The study also shows that there is a gender disparity in mortality rates, with men having a much higher death rate than women. This result aligns with research investigations that have documented gender variations in COVID-19 results, potentially due to physiological, behavioral, and social factors [26]. Gender-specific interventions may benefit from more research into the processes behind this discrepancy.

Age as a Predictor

Age became a significant predictor of mortality in severe COVID-19 patients, especially in individuals over 65 years of age. The markedly elevated mortality rate in this age group underscores the necessity for increased awareness and proactive treatment in elderly patients. This data is consistent with global patterns reported throughout the pandemic, indicating that severe COVID-19 has more frequently affected older people [27-28].

Seasonal Variations

The observed changes in mortality rates, especially the rise during winter, indicate that environmental variables may affect the severity and consequences. Numerous variables could be responsible for this, such as seasonal respiratory infections and the possibility of enhanced viral transmission during the colder months. In order to develop initiatives for public health that have been more successful, future studies should look at these seasonal trends.

Radiological and Laboratory Findings

Pulmonary involvement severity is a significant risk factor for fatality in COVID-19 patients, and chest CT-scans are crucial in diagnosing, assessing disease severity, and monitoring treatment response [29]. The strong relationship shown between mortality outcomes and CT-scan severity ratings highlights the role radiological examinations play in prognosticating patients. Greater CT severity ratings in deceased patients show the importance that early imaging may be for risk assessment. Additionally, the fact that deceased patients showed higher levels of inflammatory markers (CRP and ESR) and coagulation indicators (ferritin and d-dimer) supports the idea that systemic inflammation and coagulation contribute to COVID-19 mortality. These findings underscore the necessity for ongoing surveillance of inflammatory and coagulopathy indicators to identify patients at elevated risk for poor outcomes.

Limitations and Future Directions

Even though this study offers valuable data, it is important to note its limits. The retrospective approach and single-center setup may limit the generalizability of the findings. Multicenter prospective studies should be the main focus of future research in order to verify these findings and investigate other risk variables. Moreover, comprehensive patient treatment also requires knowledge of the long-term consequences of survivorship and the influence of post-acute sequelae of SARS-CoV-2 infection (PASC).

Conclusion

In conclusion, our study highlights the importance of pre-existing medical conditions, demographic factors, and disease severity markers in predicting mortality risk in severe COVID-19 patients. Risk Notable mortality risk factors include advanced age, male gender, diabetes, high blood pressure, smoking history, the severity of pulmonary involvement, and coagulation/inflammatory markers. This highlights the need for tailored interventions and proactive management strategies.

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