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TANAFFOS

Clinical Features and Outcomes of ICU Patients Confirmed with COVID-19 Infection in Bandar Abbas, Iran: A Single-Centered Retrospective Study

Hamideh Estabraghnia Babaki [1], Hashem Jarineshin [1], Fateme Saljoughi [2], Mehdi Hassaniazad [3], Shideh Rafati [4], Shahla Sohrabipour [5, 6]

[1] Anesthesiology, Critical Care and Pain Management Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran, [2] Student Research Committee, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran, [3] Infectious and Tropical Diseases Research Center, Hormozgan Health Institute, Hormozgan University of Medical Sciences, Bandar Abbas, Iran, [4] Social Determinants in Health Promotion Research Center, Hormozgan Health Institute, Hormozgan University of Medical Sciences, Bandar Abbas, Iran, [5] Endocrinology and Metabolism Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran, [6] Molecular Medicine Research Center, Hormozgan Health Institute, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

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Correspondence to: Sohrabipour S
Address: Endocrinology and Metabolism Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
Email address: Sh.sohrabipour@gmail.com

Background: The clinical characteristics of COVID-19 are diverse from a simple common cold symptom to acute respiratory distress syndrome (ARDS). In the present study, we attempted to identify the associated factors in surviving COVID-19 intensive care unit (ICU) patients based on their clinical characteristics.

Materials and Methods: This retrospective study was performed on 114 laboratory-confirmed COVID-19 patients admitted to the intensive care units of Hormozgan University of Medical Sciences, Iran. Demographic, medical, clinical manifestations at admission time, and outcome data were obtained from the patient's medical records.

Results: Of 114 participants included in this study, 64.9% were men. Their mean age was approximately 54 years old, 69.3% of them died and 30.7% of them were discharged. The mortality rate was 2.96 times higher in people who had ARDS compared to their counterparts, 1.37 times higher in people under non-invasive ventilation, and 3.56 times higher in people under invasive mechanical ventilation.

Three common underlying diseases among them were hypertension in 34.2%, diabetes in 23.7%, and cardiovascular diseases in 17.5% of them. Alive and dead patients significantly differed only in the following laboratory tests: D-dimer, urea, troponin, Procalcitonin, and ferritin.

Conclusion: The mortality rate among COVID-19 patients admitted to ICU is generally high. Dyspnea, as the initial presentation and comorbidity, especially hypertension, diabetes, and cardiovascular diseases, may be associated with a higher risk of developing severe disease and consequent mortality. Therefore, D-dimer, urea, troponin, Procalcitonin, and ferritin at the time of hospital admission could predict the severity of the disease and its probable mortality.

Keywords: Intensive Care Unit; Mortality; SARS-CoV-2; Survival Rate

INTRODUCTION

Until August 2, 2021, more than 198,234,951 confirmed cases and 4,227,359 confirmed deaths due to COVID-19 were reported worldwide (1). In Iran, according to the latest epidemiological data, at least 3,940,708 laboratory-confirmed cases and 91,407 deaths due to COVID-19 were reported until August 2, 2021(2). Since August 22, 2021, COVID-19 cases in Hormozgan province have surpassed 20890 people. Moreover, the mortality rate has reached 2051 patients (3).

The severity of this disease ranges from asymptomatic to death (4). The clinical characteristics of COVID-19 are

diverse and unspecific, ranging from mild to a simple common cold symptom, and gastrointestinal signs and symptoms, which may subsequently progress to acute respiratory distress syndrome (ARDS). The rapid spread of this disease and increasing number of new cases implies the need for a better understanding of the clinical and paraclinical characteristics of COVID-19, which then helps in prompting triage and management of the affected patients (5). Based on the clinical symptoms and results of laboratory tests, patients are categorized into mild, moderate, severe, and critical groups. Mild/moderate cases include most of the affected patients with this disease (81%). Although severe and critical patients comprise only 14% and 5% of all the infected cases, respectively, they mainly need hospitalization. Moreover, almost 20% of hospitalized patients need an intensive care unit (ICU). So, the mortality rate among ICU-admitted COVID-19 patients is reported quite high, as nearly 61.5% of them die due to many different reasons that have been used in some settings to show the hyperinflammation state (6). It is still unclear why some patients have no symptoms and some others need ICU care. Accordingly, several reasons were proposed such as the presence of 13 genes determining specific proteins in the lungs or immune system (7). In this regard, some routine tests can predict the probable severity. These combinations include neutrophil to lymphocyte ratio (NLR) and lymphocyte to C-reactive protein ratio (LCR); the decreased lymphocytes and normal or the increased monocytes;(6) and the elevated lactate dehydrogenase (LDH), D-dimer, and ferritin concerning (8), which are associated with a high fatality rate. Some factors such as age; presence of comorbidities (8); male sex (9); and underlying diseases such as hypertension, cardiovascular diseases (10), and type 2 diabetes (11), are associated with a high fatality rate.

The most asked question is how we can guess which patients need more caution and are more prone to show critical diseases and maybe those who need ICU care. So, we performed this retrospective, observational study on 114 consecutive critically ill patients who were laboratory-confirmed COVID-19 individuals referred for ICU admission to the coordinating center of the COVID-19 (Shahid Mohammadi Hospital, Hormozgan, Bandar Abbas, Iran). In the current study, we attempted to identify epidemiological factors, routine laboratory tests, treatments, and complications to predict mortality among critically ill patients with COVID-19 at the time of their admission.

MATERIALS AND METHODS

Study design and patients

This single-center, retrospective, and observational study was performed on 114 patients admitted to 3 intensive care units of Shahid Mohammadi Hospital in Bandar Abbas, Iran, from 20 April to August 21, 2020. Accordingly, this hospital was the Corona Center Hospital used to treat SARS-CoV-2 patients. All the patients admitted at ICUs with the confirmed SARS-CoV-2 diagnosis according to the result of the polymerase chain reaction (PCR) test were enrolled in the study. The patients who clinically had the symptoms of COVID-19 but with negative PCR tests were excluded from the study and those who were initially admitted due to other reasons and who were later diagnosed with COVID-19 were excluded from the study as well.

The study was approved by the Ethics Committee of Hormozgan University of Medical Sciences, (IR.HUMS.REC.1398.469).

Data collection

At this stage, demographic information, preexisting comorbidities, and length of hospital stay until discharge or death were recorded. The required time from the time of their hospitalization to the need for ICU admission, has been recorded as well. Medical history of signs and symptoms; taking Angiotensin II Receptor Blockers (ARBs); Angiotensin-converting enzyme (ACE) inhibitors drugs; and vital signs and kind of respiratory support, including supplemental oxygen, invasive mechanical ventilation, and non-invasive mechanical ventilation (NIV) were obtained retrospectively from the medical records of

the patients. Drug treatments (including glucocorticoids, hydroxychloroquine, antibiotics, antiviral agents, and anticoagulants….) and causes of death were also reported. Moreover, laboratory findings related to the first day of their admission were recorded. Finally, the ICU and hospital outcomes of each patient were documented. Data collection forms were reviewed by 2 researchers independently.

The obtained data were compared between non-survivors and survivors admitted to ICUs diagnosed with SARS-CoV2.

Statistical analysis

Categorical variables were reported as number and percent (%). If a variable in the Shapiro-Wilk test has a normal distribution, it is reported as mean and standard deviation(SD), and if there is no normal distribution, it is reported as median with interquartile ranges (IQR).

The Mann-Whitney U-test (for non-normally distributed data) or t-test (for normally distributed data) was used to compare continuous variables in the two groups (dead/alive). Moreover, the Chi-square test was used to examine the association between two categorical variables. In addition, Logistic regression was used to determine the risk factors related to death due to COVID-19. All the statistical analyses were conducted using the SPSS software and a $P < 0.05$ was considered as statistically significant.

RESULTS

Of 114 participants included in this study, 74(64.9%) were men. Overall, their mean age was approximately 54 years old (SD=17.80). A median of 9 days from the admission time in the hospital until death/discharging time was calculated (IQR: 5-13) and median transfer time to ICU after hospital admission was 2 days. Among 114 cases, 79 (69.3%) died and 35 (30.7%) were discharged.

Based on Table 1, the mortality risk was 2.96 times higher in people who had ARDS compared to their counterparts (95%CI: 1.97-4.43), 1.37 times higher in people under noninvasive ventilation to receive sufficient oxygen (95%CI: 1.10-1.71), and 3.56 times higher in people under invasive mechanical ventilation (95%CI: 2.24-5.65).

Three common underlying diseases were found hypertension, diabetes, and cardiovascular diseases with a prevalence of 39(34.2%), 27(23.7%), and 20(17.5%), respectively (Table 1). There was no difference in antihypertensive drug [Angiotensin-converting enzyme inhibitors (ACEIs) and Angiotensin II receptor blockers (ARB)] administered between the two groups.

The most important Signs/symptoms at the onset of the disease were the following: dyspnea 80(70.2%), cough 70(61.4%), and fever 61(53.5%). Other histories of signs/symptoms are shown in Table 2, respectively. Of note, there was no statistical difference in signs and symptoms between alive and dead patients (Table 2).

The median (IQR) of vital signs, including temperature, respiratory rate, heart rate, systolic and diastolic blood pressures, and Pulse oximeter SPO_2 are shown in Table 2. As well, the SPO_2 was found to be lower than normal, but there was no difference between the two study groups.

Treatments

As shown in Table 3, the most prescribed medications were the followings: antibiotics (n=110, 96.5%), antivirals such as remdesivir and kaletra (n=105, 92.1%), anticoagulants(n=101, 88.6%), immune systems suppressors such as methylprednisolone and dexamethasone (n=92, 80.7%), interferon-gamma (n=81,71.1%), non-steroidal anti-inflammatory drugs(NSAID) like acetaminophen (n=67,58.8%), therapeutic plasma exchange (n=58, 50.9%), Hydroxychloroquine (n=46, 40.4%), Intravenous immunoglobulin (IVIG)(n=10, 8.8%), and vitamins. As well, no difference was found between the two groups except for IVIG, but only 10 patients received that.

Laboratory findings of the patients on the first day of their hospital admission are presented in Table 4. Alive and dead patients significantly differed only in the following laboratory tests: D-dimer, urea, troponin, Procalcitonin, and ferritin. Notably, Albumin was only reported for two patients.

Table 1. Demographics, clinical characteristics, and clinical outcomes of patients

Characteristics	All (n = 114)	Alive(n=35)	Dead(n=79)	P-value	RR (95%CI)
Age, years, mean (SD)	54.05(17.80)	47.94(17.40)	56.76(17.41)	0.014[a]	-
The total length of hospital stay/death, days, median (IQR)	9(5-13)	11(7-13.5)	8(4-12)	0.040[a]	-
Transfer time to ICU after hospital admission, days, median (IQR)	2(1-3)	3(1.75-5)	2(1-3)	0.068	-
Categorical variables; number(percent)					
Sex, n (%) Male	74(64.9)	23(20.2)	51(44.7)	0.990	0.98(0.76-1.26)
Sex, n (%) Female	40(35.1)	12(10.5)	28(24.6)		
Comorbidities					
Hypertension	39(34.2)	10(8.8)	29(25.4)	0.521	1.11(0.87-1.42)
Diabetes	27(23.7)	6(5.3)	21(18.4)	0.344	1.16(0.90-1.49)
Cardiovascular	20(17.5)	5(4.4)	15(13.2)	0.605	1.10(0.82-1.47)
Endocrine disease	9(7.9)	3(2.6)	6(5.3)	0.999	0.96(0.59-1.54)
Respiratory disease	7(6.1)	1(0.9)	6(5.3)	0.435	1.25(0.90-1.74)
Kidney disease	7(6.1)	1(0.9)	6(5.3)	0.435	1.25(0.90-1.74)
Cerebrovascular	5(4.4)	2(1.8)	3(2.7)	0.644	0.86(0.41-1.78)
Autoimmune disease	5(4.4)	1(0.9)	4(3.5)	0.999	1.16(0.73-1.83)
Malignancy	4(3.5)	1(0.9)	3(2.6)	0.999	1.08(0.60-1.93)
Hematologic disease	3(2.6)	0(0.0)	3(2.6)	0.552	-
Liver disease	2(1.8)	0(0.0)	2(1.8)	0.999	-
Nervous disease	2(1.8)	0(0.0)	2(1.8)	0.999	-
Digestive disease	2(1.8)	2(1.8)	0(0.0)	0.094	0.29(0.22-0.39)
History of antihypertensive drugs					
ACEI intake	2(1.8)	0(0.0)	2(1.8)	0.999	-
ARB intake	19(16.7)	5(4.5)	14(12.6)	0.788	1.07(0.79-1.45)
Most common cause of death					
ARDS	60(52.6)	2(1.8)	58(53.2)	<0.001[b]	2.96(1.97-4.43)
Acute renal injury	31(27.2)	0(0.0)	31(30.4)	<0.001[b]	-
Cardiac arrhythmia	8(7.0)	0(0.0)	8(8.0)	0.050	-
Thrombus	7(6.1)	0(0.0)	7(38.9)	0.013[b]	-
Septic shock	5(4.4)	0(0.0)	5(4.9)	0.166	-
VAP	3(2.6)	0(0.0)	3(2.6)	0.549	-
ICH	2(1.8)	0(0.0)	2(1.8)	0.999	-
MI	1(0.9)	0(0.0)	1(0.9)	-	-
Respiratory status					
O_2 therapy	112(98.2)	33(29.2)	79(69.9)	0.301	0.29(0.22-0.39)
NIV	34(29.8)	5(4.4)	29(25.7)	0.015[b]	1.37(1.10-1.71)
Mechanical ventilation	66(57.9)	1(0.9)	65(57.5)	<0.001[b]	3.56(2.24-5.65)

Continuous data were expressed as median (interquartile range) or mean (standard deviation), and categorical data were reported using count (%); RR (95%CI): Relative Risk (95% Confidence Interval), and Risk ratio was only computed for a 2*2 Table with no empty cells.[a]0.05 was obtained as the Significance level at using independent-samples T test/Mann-Whitney U-test; [b] Significant at 0.05 level was obtained using χ^2 test/Fisher's Exact test. ICH: Intra Cranial Hemorrhage; VAP: Ventilator associated pneumonia; NIV: Noninvasive ventilation.

Table 2. History of signs/symptoms and vital signs

Signs/symptoms	All (n = 114)	Alive(n=35)	Dead(n=79)	Pvalue	RR (95%CI)
Dyspnea	80(70.2)	20(18.3)	60(55.0)	0.060	1.35(0.95-1.93)
Cough	70(61.4)	24(22.0)	46(42.2)	0.279	0.85(0.67-1.08)
Fever	61(53.5)	21(19.4)	40(37.0)	0.401	0.88(0.68-1.12)
Myalgia	44(38.6)	15(13.8)	29(26.6)	0.527	0.91(0.70-1.18)
Malaise	44(38.6)	15(13.8)	29(26.6)	0.527	0.91(0.70-1.18)
Anorexia	30(26.3)	6(5.5)	24(22.0)	0.170	1.21(0.96-1.54)
Chills	26(22.8)	11(10.1)	15(13.8)	0.146	0.78(0.55-1.11)
Headache	25(21.9)	5(4.6)	20(18.3)	0.227	1.20(0.93-1.53)
Vomiting	23(20.2)	5(4.6)	18(16.5)	0.445	1.16(0.89-1.50)
Diarrhea	16(14.0)	6(5.5)	10(9.2)	0.559	0.88(0.59-1.31)
Chest pain	13(11.4)	5(4.6)	8(7.3)	0.528	0.86(0.55-1.36)
Abdominal pain	10(8.8)	3(2.8)	7(6.4)	0.999	1.00(0.65-1.53)
Decrease level of consciousness	9(7.9)	1(0.9)	8(7.3)	0.274	1.3(0.99-1.69)
Confusion	8(7.0)	2(1.8)	6(5.5)	0.999	1.08(0.71-1.64)
Sore throat	5(4.4)	1(0.9)	4(3.7)	0.999	1.15(0.73-1.82)
Rhinorrhea	5(4.4)	0(0.0)	5(4.4)	0.320	-
Dizziness	2(1.8)	0(0.0)	2(1.8)	0.999	-
Perspiration	2(1.8)	0(0.0)	2(1.8)	0.999	-
Arthralgia	1(0.9)	0(0.0)	1(0.9)	0.999	-
Vital signs at the time of hospital admission					
Temperature, °C	37(36.6-37.4)	37(36.7-37.3)	36.9(36.6-37.5)	0.861	-
Respiratory rate, breaths/min	20(18-24)	19 (18-24.5)	20 (18-24.5)	0.557	-
Heart rate, /min	87.5(80-100.7)	87.5(81-99.5)	87.5(80-101.75)	0.866	-
O2 saturation, %	91.0(86-94)	90.5(88-93)	91 (82-94)	0.845	-
Systolic blood pressure, mmHg	120.0(110-120)	120(110-137)	120 (115-130)	0.416	-
Diastolic blood pressure, mmHg	80.0(70-80)	70(70-80)	80 (70-80)	0.388	-

Continuous data were expressed as median (interquartile range) and categorical data were reported using count (%)

Based on Table 2, there was no significant difference between the proportions/means of signs and symptoms in the two study groups, including alive and dead people (P-value>0.05).

Table 3. The treatments that patients received during their hospitalization

Treatments	All (n = 114)	Alive(n=35)	Dead(n=79)	P-value	RR (95%CI)
Antibiotics	110(96.5)	33(29.2)	77(68.1)	0.226	2.10(0.42-10.45)
Antivirals	105(92.1)	34(30.1)	71(62.8)	0.431	0.77(0.57-1.03)
Anticoagulants	101(88.6)	31(28.4)	70(64.2)	0.703	1.10(0.68-1.92)
Immune systems suppressor	92(80.7)	32(28.3)	60(53.1)	0.074	0.76(0.60-0.95)
Interferon gamma	81(71.1)	29(26.1)	52(46.8)	0.167	0.80(0.63-1.02)
NSAID	67(58.8)	20(18.0)	47(42.3)	0.680	1.06(0.81-1.38)
Therapeutic plasma exchange	58(50.9)	20(18.0)	38(34.2)	0.543	0.91(0.71-1.17)
Hydroxychloroquine	46(40.4)	10(9.1)	36(32.7)	0.064	1.28(1.00-1.64)
IVIG	10(8.8)	0(0.0)	10(8.8)	0.03[a]	-

[a] 0.05 as the Significance level was obtained using χ 2 test/Fisher's Exact test; RR (95%CI): Relative Risk (95% Confidence Interval), and Risk ratio was only computed for a 2*2 Table with no empty cells.

Based on Table 3, there was a significant association between IVIG intake and mortality (P-value=0.03).

Table 4. Laboratory findings of the patients

Laboratory values	All (n = 114)	Alive(n=35)	Dead(n=79)	P-value
WBC count (× 10^3 per µl; normal range: 3·5–9)	6.25(4.82-9.47)	6.3(4.4-9.5)	6.2(4.9-9.5)	0.688
Neutrophil count (%; normal range: 40-70)	79(69.9-86.7)	76.6(65.1-83.4)	81.2(72.2-87.2)	0.074
Lymphocyte count (%; normal range: 20-50)	15(8.3-23.6)	17.4(9.6-23.8)	13.6(8.2-21.4)	0.274
Neutrophil/lymphocyte	5.3(2.8-10.0)	4.2 (2.5-8.5)	5.7(3.3-10.5)	0.124
Platelet count (× 10^3 per µl; normal range 150–450)	187(140-245.5)	195(148.5-309)	185(138-226)	0.210
Hemoglobin (g/dl; normal range 13.5-18)	12.1(10.6-13.7)	12.1(10.9-14.2)	12.1(10.2-13.6)	0.390
Prothrombin time (s; normal range 12-14)	13(12.27-14.02)	13(12.2-13.4)	13(12.2-14.1)	0.602
Partial thromboplastin time (s; normal range 25-45)	31.7(28-37.78)	31(29-39.1)	32(28-37)	0.906
Fibrinogen (mg/dL; normal Range 200 - 400)	366(198-440)	179(179-179)	375(218.2-442.7)	0.206
D-dimer (ng/L; normal Range <500)	943.3(423.8-2419.4)	494.5(300.7-936)	1416(620.8-3047)	0.007[a]
INR (normal Range< 1.1)	1.02(1-1.02)	1(1-1.1)	1.1(1-1.2)	0.331
ESR (mm/h; normal Range 0·0–15·0)	50(32-62)	43.5(33-61.2)	50(32-62.5)	0.528
CRP (mg/L; normal Range<10)	37.4(14.5-66.8)	52.1(21-69)	33.2(8.9-62.3)	0.272
Procalcitonin (ng/ml; normal range:<0.15)	0.25(0.05-0.5)	0.04(0.04-0.04)	0.3(0.1-2.1)	0.044[a]
Ferritin (ng/ml; normal range: 4.63-204)	817.1(281.6-1783.5)	474(237.8-1189.3)	1035(358.2-2131.1)	0.033[a]
Albumin (gr/dl; normal range 3.5-5) n=3	2.95(2.8-3.4)	3.8(3.6 [b])	2.9(2.8-3.1)	0.036[a]
Urea (mg/dl; normal range: 11-55)	40(28.5-63)	32(27-44)	44(32.7-89.2)	0.003[a]
Serum creatinine (mg/dl; normal range 0.6-1.3)	1.1(1-1.4)	1.05(0.9-1.3)	1.15(1-1.4)	0.134
Troponin (ng/l; normal range<19)	6.7(3.1-37.5)	4.2(1.9-14.4)	9.5(3.9-67.4)	0.026[a]
Potassium (mEq/L; normal range: 3.5-5.3)	4.3(4-4.7)	4.2(3.9-4.5)	4.4(4-4.7)	0.412
Calcium (normal Range 8.5-10.5 mg/dl)	8.7(8.3-8.9)	8.8(8.5-9)	8.6(8.3-8.8)	0.150
ALT (U/L; normal range: up to 41)	44(31-64)	47(31-66.5)	43.5(31-61.7)	0.637
AST (U/L; normal range: up to 37)	51(36-73)	47(30.5-69.7)	51(38-76.7)	0.234
ALP (U/L; normal range: 98- 279)	160(129-219)	152(129.5-242)	164.5(128.2-217.5)	0.606
Total bilirubin (mg/dl; normal range 0·1–1.2)	0.9(0.6-1.3)	0.85(0.7-1.1)	0.9(0.6-1.3)	0.799
CPK (mg/dl; normal range 24-195)	126.5(64.5-232.5)	127(65-153)	126(63-240)	0.840
LDH (U/L; normal range 120–460)	812(584-1051.5)	714(502.5-1061.5)	823.5(589.2-1047.2)	0.248
Blood glucose (mg/dl; normal range <140)	125.5(99.7-173.5)	143.5(102.7-174.2)	121.5(97-174.5)	0.198
Serum PH (normal range 7.35-7.45)	7.4(7.3-7.44)	7.4(7.3-7.5)	7.3(7.2-7.4)	0.069
$PaCO_2$ (mmHg; normal range 35-45)	38.1(31.9-44.7)	37.8(35.8-43.2)	38.2(30.6-48.1)	0.836
HCO_3 (mmol/l; normal range 24)	23.7(19.7-27.1)	25.9(22.6-28.1)	23.2(18.5-26.3)	0.063

The obtained data were expressed as median (interquartile range); [a] 0.05 was gained as the significance level using test/Mann-Whitney U-test; significant albumin value has been reported only for 2 patients, so quartile 3 (Q3) was not calculated.

As shown in Table 4, the means of D-dimer, urea, troponin, procalcitonin, and serum ferritin in the two groups were statistically different (P-value<0.05).

The total length of hospital stay/death, as days were obtained from our available data, the median (IQR) duration of hospitalization was 9(5-13) days in total ,and it was 11(7-13.5) and 8(4-12) days in survivors and non-survivors, which was significantly higher in survivors compared to non-survivors ($p<0.05$), respectively. However ,the duration of hospitalization until ICU admission in the current study was not significantly different between survivors and non-survivors.

Notably, two patients were pregnant women, and one of them died.

DISCUSSION

Herein, we described 114 ICU patients with the confirmed SARS-CoV-2 tests. Of 114 participants included, 64.9% were men. Overall, their mean age was approximately 54 years old (SD=17.80). As well, 69.3% of them died and 30.7% were discharged. Similar to most studies performed previously, men were found to be more prone to infection and dying (5,9,10,12) due to having higher ACE2 as the coronavirus's receptor, poor immunology because of X chromosome, their poor lifestyle such as more drinking and smoking, and less caring

related to the prevention procedures during COVID-19 pandemic, especially in wearing a mask (13,14).

The mortality rate of patients admitted to ICU is generally high. Although there was no statistical difference in the underlying diseases between the living and dead groups, in the dead patients, the number of underlying diseases was higher except for gastrointestinal diseases. A study performed in Shiraz showed that COVID-19 diabetic patients when infected with SARS-CoV-2 have worse conditions, longer ICU admission duration, and worse laboratory tests compared to other underlying diseases such as hypertension and cerebrovascular diseases (11). In a study conducted on critically ill mechanically-ventilated patients, diabetes mellitus was recorded to have a moderate correlation with the fatal outcome (12). There is insufficient evidence regarding the effect of hypertension on the rate of mortality due to COVID-19. Some studies considered this as an effective prognosis for the disease, while others did not (15). In the present study, 34.2% of all the included patients had hypertension and 25.4% of them died. Among critically-ill patients who were ventilated, the most common comorbidity was hypertension which was found to have a positive correlation with the fatal outcome (12).

Of 7 patients with renal insufficiency, 6 cases died. In Stefan et al.'s study on 37 hemodialysis patients infected with COVID-19, 19% died during their hospitalization time, mostly due to cardiovascular diseases and respiratory distress syndrome (15). Of 7 patients with a history of underlying respiratory disease, 6 died.

Šabanović Adilović et al. in their study on mechanically ventilated patients reported that 14.1% of patients with COPD had a moderate correlation with the fatal outcome (12).

Of 20 (17.5%) underlying cardiovascular patients, 15 cases died. Moreover, in another study, 16.3% of patients were reported with chronic heart disease, which had a correlation with the fatal outcome (12). In Phelps et al., it was presented that among 22.1%patients, (16).

History of cerebrovascular disease was recorded in 4.4% of them. Some studies reported 11.9 % (17) and 12% with a moderate correlation with the fatal outcome (12).

The most organ damages that caused death after infection with SARS-CoV-2 include ARDS, acute renal injury, cardiac arrhythmia, and thrombus, respectively.

Of 114 patients, 60 had ARDS, of whom 58 patients died. Mortality is high in ARDS patients, especially in those with invasive mechanical ventilation, which is up to 40.5 % (12). In Vahedi et al.'s study, this rate was reported as 57.89 % (5). In our study, it was more than 96%.

The second cause of death was found as acute renal failure (ARF). In this study, 31 patients developed ARF after COVID-19 infection, and all of them died. A retrospective observational study previously performed in London showed that of 313 patients, 240 cases (76.7%) developed ARF within 14 days after their ICU admission. Correspondingly, mechanical ventilation was found as one of the risk factors to develop ARF, but steroid therapy led to a reduction in ARF progression and they had a higher mortality rate among the non-ARF patients. After 3-month follow-up in survivors, 16% of all ARF survivors had developed chronic kidney disease (CKD); among those with no renal recovery, the CKD incidence rate was 44% (18). So, monitoring renal function post-discharge is essential as well. ARF pathogenesis is multifactorial (18), and the kidneys are very rich in ACE2 as a coronavirus receptor. So, direct viral invasion may possibly damage kidneys (19) due to some other factors, including, hypovolemia, inflammation, and coagulopathy (18).

Cardiac arrhythmia was the third leading cause of death in our study, and eight of our patients developed cardiac arrhythmia, all of whom died. Some studies have previously reported cardiac complications resulting from COVID-19 in patients with and without any prior cardiovascular disease. Accordingly, these complications include arrhythmias because direct virus invasion and myocardial inflammation lead to myocarditis, heart failure, cardiogenic shock, coronary artery thrombosis, and even death (20,21). Another reason for the development of

cardiac complications is the administration of drugs with the potential cardiac effect on the treatment of SARS-COV2 (22).

The fourth cause of death was vascular thrombosis, in which seven patients became thrombosis and all died. In Helms et al.'s study thromboembolic events were evaluated between non-COVID-19 ARDS and COVID-19 ARDS patients in ICU. In this study, they performed on 150 ARDS patients, 64 clinically relevant thrombotic complications were diagnosed mainly as pulmonary embolisms, most of which had D-dimer and fibrinogen raising. Despite performing the treatment with anticoagulants, a great number of COVID-19 ARDS-related patients were found to be prone to thrombotic complications (23). In Tang et al.'s study on 183 patients, 71.4% of non-survivors had coagulopathy (24). In ICU patients, in wang et al study, the increased D-dimers and prothrombin time (PT) at admission time were reported (25). Moreover, in our study, there was a significant difference between the two study groups in terms of D-dimers, but not PT, PTT, or fibrinogen. There was a probable difference in fibrinogen as well, but because there was missing data in this study, it did not make any sense.

Coagulation abnormalities, including low platelet count, increased fibrinogen, D-dimer level, and PT in severe patients at the ICU admission time, were reported (6).

After all, the most common cause of death was found as septic shock, ventilation-associated pneumonia, cerebral hemorrhage, and MI.

The most common history of symptoms in our study was dyspnea (70.2%), which is in agreement with other studies conducted on SARS-CoV-2 ICU patients in Tehran that reported its rate as 84.2% (5), followed by cough (61.4%) and fever (53.5%) in the second and third places, respectively. However, at the time of admission, the study patients were afebrile, which may be due to the use of antipyretic drugs in advance. In other studies, it was shown that fever starts a few days later when the lungs are involved (26). Shortness of breath, fever, and cough are the three most important factors in most of the studies that have previously predicted a patient's possible need for an ICU (14).

Our patient's median respiratory rate was 20 (18-24). Of note, the respiratory rate has been identified as an important predictor of ICU admission in COVID-19(14).

Since ARDS is the leading cause of death, shortness of breath was mostly observed among deceased patients.

The median of blood urea was significantly higher among non-survivals . As well, the second cause of death was acute renal failure; however, the median creatinine at the admission time did not differ between the two groups.

Inflammatory markers such as ESR, CRP, ferritin, PCT, and LDH as organ damage factors, were found to be positively associated with COVID-19 severity in patients (5). In our study, ESR and LDH levels in dead patients were higher, but CRP level was lower. In addition, Serum ferritin and PCT significantly increased in dead patients.

In our study, Troponin was significantly higher among expired patients. Of our patients, eight cases had arrhythmias and one had myocardial infarction. As well, ACE2 was highly expressed in hearts, which consequently led to the susceptibility of the heart to SARS-CoV-2 infection. Rising troponin, as a myocardial enzyme, was associated with myocardial injury and led to severe illness and mortality (27). Unfortunately, all of our patients with cardiac arrhythmias and myocardial infarction died.

In a meta-analysis study by Ghahramani et al., it was shown that in severe cases of COVID-19, a significant decrease in lymphocyte, monocyte, eosinophil, hemoglobin, platelet, albumin, serum sodium, lymphocyte to C-reactive protein ratio (LCR), leukocyte to C-reactive protein ratio (LeCR), and leukocyte to IL-6 ratio (LeIR) can be observed as well as the increased neutrophil ,alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, blood urea nitrogen (BUN), creatinine(Cr), Erythrocyte Sedimentation Rate (ESR), C-reactive protein (CRP), Procalcitonin (PCT), lactate dehydrogenase (LDH), fibrinogen, prothrombin time (PT), D-dimer, glucose level, and neutrophil to lymphocyte ratio (NLR). No significant

changes were detected in white blood cells (WBC), Creatine Kinase (CK), troponin I, myoglobin, IL-6, and potassium between the two groups (6). But these tests were at the time patients entered the ICU. But our study tests were performed at the time of hospital admission.

Almost all the included patients (112 out of 114) received oxygen at their hospital admission time. Only 5 patients used NIV and only one patient receiving invasive mechanical ventilation survived. In Kovačević et al.'s study, some factors predicting the failure of NIV weaning in COVID-19 critically ill patients were introduced, including the presence of dyspnea at the time of hospital admission, higher lung edema on the day of starting NIV, higher length of NIV, and higher urea on the day of starting NIV (28). Correspondingly, Dyspnea is one of the most common symptoms among COVID-19 critically ill patients. Jiang et al. reported dyspnea in more than 50% of patients with COVID-19 (29) and a significantly higher incidence rate has been also found in patients who need ICU care (12), as 70.2%in accordance with our study. This is a critical sign and of 80 patients with this symptom, 60 patients died.

Out of 66 patients under mechanical ventilation, only one person survived. The mortality rate among COVID-19 critically ill patients under ventilator is as high as 40.5% (12). In our study, this rate was more than 98%.

The median O_2 saturation in the two groups was about 91%, which is lower than normal.

The median of O_2 saturation in Vahedi et al.'s study in ICU patients was 77%, lower than that of our study (5). In Estedlal et al.'s study on non-diabetic COVID-19 patients, it was 92% and in diabetic patients, it was 88% (11).

It was shown that patients with severe anorexia are more likely to die (28). In our study, of 30 patients with anorexia, 24 cases died. Because hypoxia due to COVID-19 increases the need to use the respiratory accessory muscles and these patients are not able to provide enough energy (28), it is important to pay more attention to the nutrition of these patients.

In this study, there was no difference between the two study groups in terms of treatment strategies, except for IVIG.

The duration of time from the Hospital admission to discharge or death was significantly lower among the patients who died from the disease, and also ICU length of stay, in terms of days, was lower.

Limitation

This study has certain limitations. Firstly, not all patients had all laboratory tests, which may reduce the reliability of the statistical analysis. Secondly, the sample size was small. This study has a single-centered, retrospective nature.

CONCLUSION

The mortality rate of patients admitted to ICU is generally high. The comorbidity, especially hypertension, diabetes, and cardiovascular diseases, may also be associated with a higher risk of developing severe disease and its consequent mortality rate. Additionally, a history of dyspnea, cough, and fever, as the initial presentations, may indicate more diffuse and severe SARS-CoV-2 infections.

In summary, our evidence regarding the differentiation of severe and non-severe cases of COVID-19 based on their laboratory test results at the time of hospital admission, was as follows: D-dimer, PCT, serum ferritin, urea, and Troponin. However, to confirm the results obtained in this study, further studies, particularly on other populations, are needed.

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