Original Article

Demographic features, laboratory findings and outcomes of ICU patients with COVID-19 in Ahvaz, Iran: A single-centered prospective study

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Abstract

Background: COVID-19 can lead to severe acute respiratory syndrome so that some patients need to be admitted to the Intensive Care Unit (ICU). The aim of the current study is to investigate the frequency of demographic, laboratory and imaging findings and type of treatment and their relationship with disease outcomes in patients with COVID-19. **Material and Methods:** This prospective cross-sectional study was conducted on all patients with COVID-19 who were admitted in the ICU of Razi Hospital in Ahvaz, Iran from January 20 to February 20, 2021. Patient information including demographic features, laboratory and imaging findings and clinical outcomes was recorded. **Results:** One hundred and thirty-three patients were recruited in the present study, out of which 74 patients (55.6%) were males and 59 patients (44.4%) were females. The overall mortality rate of patients was 35.3% (47 patients) and was higher in patients over 65 years of age. There was a significant difference in terms of thrombocytopenia (*P* value: 0.001), lymphopenia (*P* value: 0.004), progression of lung involvement in imaging, shock, disseminated intravascular coagulation (DIC), sepsis and receiving invasive respiratory support in living and deceased patients (*P* value < 0.001). Furthermore, the difference in life status and the length of in-ICU stay in patients with hyperkalemia and renal failure was statistically significant (*P* value = 0.033, *P* value < 0.001 respectively). **Conclusion:** Mortality rate of patients with COVID- 19 admitted to ICU is generally high. According to the findings of this study, thrombocytopenia, lymphopenia, hyperkalemia and AKI are laboratory disorders associated with increased mortality. Moreover, the progression of pulmonary involvement in imaging, shock, DIC, sepsis, and need to invasive respiratory support is associated with low survival of patients.

Keywords: COVID-19, ICU, laboratory findings

Introduction

In early December 2019, the first cases of pneumonia of unknown etiology were identified in Wuhan.[1] The etiological agent of a viral disease belonging to the group of Ribonucleic acid (RNA) viruses known as acute coronavirus syndrome 2 (SARS-COV-2). Coronavirus infections are commonly mild, but two beta-coronavirus epidemics (β-CoV), Acute Respiratory Syndrome (SARS) and Acute Middle East Respiratory Syndrome (MERS-COV) have resulted in more than 10,000 cases and 10% and 37% deaths, respectively.[1] This disease can cause severe acute respiratory syndrome so that some patients need to be admitted to the intensive care unit.[2]

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Various studies have been conducted across the world on how to diagnose COVID-19 virus through radiography and polymerase change reaction(PCR), type of prescribed treatments, symptoms and paraclinical findings of these patients.[3] On the other hand, although COVID-19 is known as a respiratory disease, but the disease can also cause death by damaging heart, kidney, skin, neurologic system, liver, etc.

Given the high prevalence of this disease and the large number of severe cases of the disease that require special services as well as the death of patients and possible differences in patient characteristics and care provided in different areas, clinical condition assessment of critically ill patients with COVID-19 can identify possible new clinical aspects and improvements in the provision of intensive care services. Therefore, reviewing clinical, paraclinical, and therapeutic parameters and finding the relationship between these variables and disease outcomes are of great importance in these patients.[4] In Iran, few studies have been conducted on the epidemiological, demographic, and therapeutic features of this clinical syndrome as well as its etiological factors. The aim of this study was to investigate the frequency of demographic features, laboratory and imaging findings and type of treatment and their relationship with disease outcomes in patients with COVID-19 admitted to Razi University Hospital in Iran in 2021.

Materials and Methods

Data collection and design

The study is a prospective single-center cross-sectional study conducted at Razi University Hospital in Ahvaz, Iran. Razi Hospital has been dedicated for patients with COVID-19 since the start of the pandemic. In this hospital, patients with COVID-19 were admits to routine wards, cardiac wards and intensive care units, all of which were exclusively allocated to these patients. Patients admitted to the care unit of COVID-19 are visited daily by a pulmonologist and an intensive care specialist, and in the evening and night shifts, patients need to be re-visited by a resident physician who specializes in ICU or internal medicine assistants. Before the Covid Pandemic, there were three intensive care units (surgery-internal medicine and neonatal) in this hospital, which after the start of the pandemic, their number increased to 6 COVID-19 intensive care units with 68 beds. Patient information including demographic information, laboratory disorders (e.g. routine and other required tests), cardiac dysfunction during the study, serial imaging findings, respiratory support, and clinical outcomes such as the length of stay in ICU and discharge or death was recorded. Patients with suspected sepsis were taken blood and respiratory secretions culture according to examinations and tests. Inclusion criteria included all available records of patients admitted to the intensive care unit with a definitive diagnosis of COVID-19.

The study has been approved by the Ethics Working Group of the Research Council with the code of IR.AJUMS.REC.1399.410.

Statistical analysis

After recording the data in the collection form, the data were analyzed using SPSS software version 22. Mean and standard deviation were used for data with normal distribution and mean for the abnormally distributed data. In addition, comparison of quantitative values with normal distribution was performed by Student "t-test" and quantitative values with abnormal distribution with "Mann-Whitney's score." Chi-square test and Fisher test were used to compare qualitative variables. Significance level was less than 0.05.

Results

Patient characteristics

In this study, 133 patients were recruited, of which 74 patients (55.6%) were male and 59 patients (44.4%) were female. Thirty four 34.8% of patients were in the range of 15–49 years of age, 33% were in the range of 50–64 years of age and 32.2% were over 65 years of age.

Demographic information and comparison in terms of life status in the ICU are given in Table 1.

Laboratory and radiological findings

Tables 2 and 3 show the laboratory information and comparison between living and deceased patients.

The results also showed that the number of involved lung lobes in chest Computed Tomography (CT) scan in living patients was 3.42 ± 1.2 and in deceased patients was 3.51 ± 1.4 which statistically significant difference does not exist between the two groups ($P = 0.72$). In addition, CRP above 10 was observed in

Table 1: Demographic information and comparison in terms of life status

Variable	Frequency *n*, %	Vital status		*P*
		Alive *n* (%)	Dead *n* (%)	
Age				
15-49 years old	46 (34.8)	40 (88.6)	6 (11.4)	<0.001
50-64 years old	44 (33.0)	30 (68.9)	14 (31.1)	
≥65 years old	43 (32.2)	16 (36.4)	27 (63.6)	
Smoking status				
Never	105 (79.2)	72 (68.3)	33 (31.7)	0.252
Currently	14 (10.5)	6 (46.2)	8 (53.8)	
Before	14 (10.5)	8 (58.3)	6 (41.7)	
Sex				
Male	74 (55.6)	45 (60.3)	29 (39.7)	0.243
Female	59 (44.4)	41 (70.0)	18 (30.0)	
DM	41 (32.8)	28 (68.2)	13 (31.8)	0.55
Heart failure	16 (12.03)	10 (64.7)	6 (35.3)	0.997
HTN	40 (32)	26 (65.9)	14 (34.1)	0.848
CAD	23 (18.5)	-	-	-
Cancer	7 (5.3)	3 (42.9)	4 (57.1)	0.215
CKD	6 (4.5)	2 (33.3)	4 (66.7)	0.10
Undergoing dialysis	1 (0.8)	1 (100.0)	0 (0)	0.458

n, number of patients; DM, diabetes mellitus; HTN, hypertension; CAD, coronary artery disease; CKD, chronic kidney disease; SD, standard deviation

Table 2: Laboratory findings of patients infected with COVID-19

Variable	Total patients	Alive patients	Deceased patients	*P*
Absolute neutrophil count per microliter Mean	8147.03	8742.73	7605.02	0.182
Absolute lymphocyte count per microliter Mean	1239.05	1367.6	891.57	0.004*
Absolute platelet count per microliter Mean	207630.3	226838.37	165426.09	0.001*
Hb (gr/dL) Mean	12.4	12.36	11.99	0.369
Cr (mg/dL) Mean	1.4	1.06	2.01	0.031*
NEWS2 score Mean	4.2	4.67	5.02	0.276
Number of pulmonary lobes having lesion in chest CT scan Mean	3.46	3.42	3.51	0.72
CRP (>10mg/L) N,%	123 (92.5)	80 (65)	43 (35)	0.494
AST (>40U/L) N,%	70 (52.6)	40 (57.1)	30 (42.9)	0.065
ALT (>40U/L) N,%	48 (36.1)	29 (60.4)	19 (39.6)	0.474

SD, standard deviation; Hb, hemoglobin; Cr, creatinine; NEWS2, The National Early Warning Score; CRP, C-Reactive Protein; AST, Aspartate aminotransferase; ALT, Alanin aminotransferase

92.5% of patients (123 patients), aspartate aminotransferase above 40 in 52.6% (70 patients) and alanine aminotransferase above 40 in 36.1% (48 patients). There was no significant difference in terms of NEWS score between living and dead patients ($P = 0.276$). The most pulmonary involvement in CT scan was ground glass with 45.9% (61 patients). Consolidation was reported in 21.1% of patients, patchy in 26.3%, pneumothorax in 6.8% and nodules in 0.8% of patients [Table 4].

Out of 58 cultures, 12.1% (7 patients) were positive blood and 24.1% (14 patients) were positive respiratory secretions cultures. The highest respiratory secretion microorganism was related to Enterobacter with 10.3% (6 patients) and the highest positive blood culture was related to Klebsiella, Enterobacter and Streptococcus saprophyticus with 3.4%. The highest reported percentage of sensitive antibiogram was reported in positive culture of respiratory secretions, ciprofloxacin (100%), cotrimoxazole (85.7%) and then imipenem (71.5%). Furthermore, the highest reported percentage of sensitive antibiogram in positive blood culture was ciprofloxacin (100%), ceftazidime (85.7%), and then cotrimoxazole (71.4%).

Treatment modalities

Table 5 shows the treatment modalities in the studied patients. There was a significant difference in the length of ICU hospitalization between patients who received Remdesivir and those who did not received it ($P = 0.002$) and Patients with Remdesivir injection were hospitalized in the ICU for a longer period of time. But life status was not different between the two groups of patients ($P = 0.227$).

The length of hospital stay in patients using high doses of corticosteroids and patients who did not receive it was significantly different ($P < 0.001$), but mortality was not significantly different between the two groups ($P = 0.442$). There was a significant difference in terms of ICU length of stay and life status between patients with broad-spectrum antibiotics and non-broad-spectrum antibiotics ($P = 0.013$ and $P = 0.003$, respectively). No significant difference in terms of ICU length of stay and life condition existed between the group of patients receiving therapeutic anticoagulant and the group of patients receiving prophylactic anticoagulants ($P = 0.288$ and $P = 0.442$, respectively). There was no statistically significant difference between the method of ventilator support and the length of in-ICU hospitalization ($P = 0.057$). However, in terms of life status, a significant difference was observed between the three groups of patients ($P < 0.001$) and mortality rate was higher in intubated patients [Figure 1].

Table 3: Comparison of laboratory information of living and deceased patients

Variable	Frequency *n*, %	Vital status		*P*
		Alive *n* (%)	Dead *n* (%)	
Leukocytosis	70 (53.2)	44 (62.9)	26 (37.1)	0.088
Leukopenia	26 (19.6)	9 (36.4)	17 (63.6)	0.058
Lymphocytopenia	106 (80.0)	63 (59.8)	43 (40.2)	0.048
Hypokalemia	2 (1.6)	1 (50.0)	1 (50.0)	0.662
Hyperkalemia	5 (3.7)	1 (20.0)	4 (80.0)	0.033
Hyponatremia	38 (28.2)	21 (55.3)	17 (44.7)	0.152
Hypernatremia	1 (0.8)	1 (100.0)	0 (0)	0.458

n, number of patients; SD, standard deviation

Table 4: Imaging findings of admitted patients with COVID-19

Parameter	Result (*n*, %)
Grand glass	61 (45.9)
consolidation	28 (21.1)
patchy	35 (26.3)
pneumothorax	9 (6.8)
Atelectasis	0 (0)
Nodule	1 (0.8)
Mass	0 (0)

Outcome

Table 6 illustrates the information about the clinical condition of the studied patients. The results of statistical analysis indicated that there was a significant difference in terms of ICU length of stay and life expectancy in patients with and without acute renal failure ($P = 0.046$, $P < 0.001$, respectively). Patients with DIC or shock or sepsis were significantly different from the opposite group in terms of life status ($P < 0.001$) but the lengths of hospitalization in the ICU was not different. Also, life condition in patients with and without lung parenchymal involvement was different ($P < 0.001$), although there was no significant difference in the length of hospitalization between the two groups ($P = 0.357$).

Table 5: Treatment options in patients during hospitalization

Variable	Frequency *n*	Mean (SD) of ICU admission period, day	*P*	Vital status		*P*
				Alive *n* (%)	Dead *n* (%)	
Remdesivir injection	103 (77.4)	8.56±4.6	0.002	69 (67.3)	34 (32.7)	0.227
High dose systemic corticosteroid injection	55 (41.9)	10.12±5.4	<0.001	34 (62.0)	21 (38.0)	0.442
Narrow-spectrum antibiotic injection	71 (53.2)	7.45±3.9	0.376	53 (75.3)	18 (24.7)	0.004
Broad-spectrum antibiotic injection	78 (58.9)	8.70±5.3	0.013	42 (54.4)	36 (45.6)	0.003
Therapeutic anticoagulant injection	87 (65.3)	8.17±4.6	0.288	59 (67.1)	28 (32.9)	0.442
Use of high flow oxygen	62 (46.6)	7.03±4.3	0.057	61 (98.4)	1 (1.6)	<0.001
Use of non-invasive mechanical ventilation	21 (15.8)	10.17±5.6		21 (100)	0 (0)	
Use of invasive mechanical ventilation	50 (37.6)	7.96±5.2		4 (8)	46 (92)	

n, number of patients; SD, standard deviation

Table 6: Information about the clinical condition of the studied patients

Variable	Frequency, *n*	Vital status		*P*
		Aive *n* (%)	Dead *n* (%)	
Shock	25 (18.5)	1 (4.0)	24 (96.0)	<0.001
ARF	18 (13.7)	2 (11.1)	16 (88.9)	<0.001
DIC	9 (6.5)	0 (0)	9 (100.0)	<0.001
Sepsis	20 (15.3)	6 (31.6)	14 (68.4)	<0.001
Expansion of lung parenchymal lesions in imaging	34 (25.8)	6 (17.1)	28 (82.9)	<0.001

n, number of patients; ARF, acute renal failure; DIC, disseminated intravascular coagulation; SD, standard deviation.

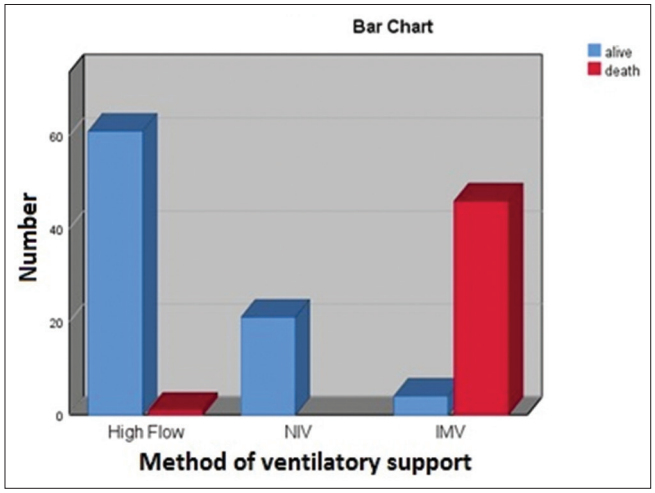

Figure 1: Relationship between life status and method of ventilatory support

Figure 2 BOX PLOT regarding the relationship between mortality and length of hospitalization of patients shows that the mean duration of hospital stay in deceased patients (7.95 ± 5.2) and surviving patients (7.77 ± 4.8) is not significantly different ($P = 0.97$).

Moreover, in the present study, the mortality rate of patients with COVID-19 was 35.3% (47 patients). Table 7 illustrates the final status of the studied patients.

Table 7: Outcome of patients admitted with COVID-19

Parameter	Result (*n*, %)
Heart attack	1 (0.8)
Cardiopulmonary arrest for unknown reasons	1 (0.8)
Respiratory failure	39 (29.2)
Shock	6 (4.5)

Discussion

In the present study, 133 patients were enrolled, of which 74 patients (55.6%) were male and 59 patients (44.4%) were female. There was a significant difference in life status between the three defined age groups and the mortality rate was higher in patients over 65 years. Also in this study, there was a significant difference in terms of thrombocytopenia, lymphopenia and the occurrence of shock, sepsis, DIC, the need for invasive mechanical ventilation and the development of pulmonary involvement in imaging among survived and dead patients. In addition, mortality and the length of ICU stay were statistically significant in patients with hyperkalemia and renal failure.

In general, in most studies, the incidence and mortality rate was higher among older people compared to the younger people. In a study conducted by Yang *et al.*,[5] the mean age of COVID-19 deaths was 69.8 years, which is consistent with the findings of the present study. Similarly, in another study by Bhatraju *et al.*,[6] the mortality rate in elderly patients was higher than young patients. Studies have shown that older age is related with further involvement by the virus, because old age is associated with a large number of abnormalities in immune function and an increased risk of viral infection is associated with reduced or altered immune function.[7]

Laboratory data

Analysis of laboratory data of the current study demonstrated that the length of in-ICU hospitalization in patients with lymphopenia was not different from those without lymphopenia ($P = 0.101$),

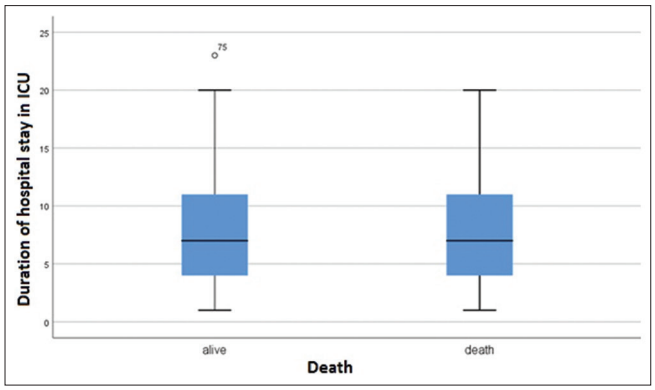

Figure 2: Relationship between duration of hospital stay in ICU and death cases

however, in terms of life status, there was a significant difference between the two groups ($P = 0.048$).

A cohort study on 201 patients indicated that the disease triggers a number of immune responses and, as a result, alters immune components such as peripheral blood leukocytes and lymphocytes.[8] In the two separate studies, which included 41 patients and 150 patients in Wuhan, China, respectively, a large association was observed between lymphopenia and the need for in-ICU hospitalization.[9,10] Chen *et al.* reported that a significant reduction in total lymphocyte numbers indicates that coronaviruses affect immune cells and inhibit the function of the immune system.[11]

Consistently, in the present study, platelet count was significantly different between living and deceased patients and platelet count in deceased group was significantly lower than living patients. In a meta-analysis of 9 studies involving 1779 patients, it was found that thrombocytopenia was significantly associated with the severity of the disease. Despite the heterogeneity between the studies, a significant reduction in platelet count (thrombocytopenia) was observed, particularly in the deceased,[3] which is consistent with the results of the current study. In the study by Chen *et al.*,[11] out of 99 hospitalized patients with Covid infection, 12% had thrombocytopenia. Also, another study on blood samples of patients infected with COVID-19 from different provinces of China showed that 2.36% of patients had lower than normal platelets confirming the results of the current study.[12]

Also, a significant increase in the creatinine level of deceased patients, which was observed in our study is consistent with the results of a study by Mardani *et al.*[13,14] In addition, in a study conducted by Cao *et al.*[15] in Shanghai, China, examining the clinical and laboratory characteristics of 198 patients with COVID-19, the results demonstrated that patients admitted to the intensive care unit also had a slight increase in creatinine compared to other hospitalized patients (15.8% vs. 4.1%) and they indicated increased creatinine as criteria for general dysfunction. The results of their study are in line with those of the current study. Conversely, in a study by Khoshnoud *et al.*,[16] creatinine levels were not significantly different between deceased and living patients with COVID-19, which are in contrast with the results of current study. The reason for this discrepancy may be the sample size. Other reports of elevated serum creatinine in severely deceased patients with COVID-19 have been reported[17] that are similar to the results of our study. The exact mechanism of renal involvement is unclear, however hypothetical mechanisms include sepsis that lead to cytokine storm or direct cell damage due to SARS-CoV-2.[18]

Electrolyte abnormalities particularly potassium disorders are common among COVID-19 patients. In the study conducted by Noori *et al.*,[19] based on the analysis, hypokalemia and hyperkalemia were observed in 24.3% and 4.15% of patients with COVID-19, respectively. In their study, they stated that hypokalemia and hyperkalemia can deteriorate cardiac outcomes and indicate a poor prognosis for COVID-19 disease. In our study, the mortality rate in patients with a history of hyperkalemia was significantly different from patients without hyperkalemia and mortality was higher in patients with hyperkalemia, too. Wu *et al.*'s[20] study also reported that high levels of blood potassium (due to kidney failure) and heart disease were the leading causes of death in patients with COVID-19, and that none died from pneumonia. They stated that the high mortality rate in patients may not be due to the virus but also to the exacerbation of the existing disease.

Mortality rate

The results of statistical analysis in this study illustrated that the mortality rate in patients with sepsis and septic shock was higher and there was a significant difference compared to patients without sepsis and shock ($P < 0.05$). Similarly, Zafer *et al.*[21] also reported that a higher mortality rate was observed in COVID-19 patients with sepsis. Studies have shown that respiratory infections cause an increase in pro-inflammatory cytokines in the blood, creating a cytokine storm that can cause severe sepsis, septic shock, and ultimately increase mortality.

Imaging findings

In a retrospective study in which data from 225 patients were examined, the most common radiological manifestations observed in patients admitted to the ICU were consolidation.[22] In addition, the mortality rate in patients with and without the spread of lung parenchymal lesions in imaging was different ($P < 0.001$) and in deceased patients, the severity of the lung parenchymal lesions was higher, which is consistent with the present study. Accordingly, in a study by Yun *et al.*,[23] it was found that in people with more severe primary disease, the pulmonary parenchymal lesions are more sever and the process of radiological healing of the lesions is slower.

In the present study, the need for invasive mechanical ventilation in 37.6%, the need for non-invasive mechanical ventilation in 15.8% of patients, acute renal failure in 13.7% of patients, shock in 18.5% of patients, DIC in 6.5%, and Sepsis were observed in 15.3% of patients.

Clinical condition

In a study by Guan *et al.*,[3] Which performed clinical trials on 1,099 patients with COVID 19, the results showed that out of the 1,099 patients, 1% had shock, 3.4% had severe acute respiratory syndrome, and 0.5% had acute kidney damage, 2.3% needed invasive mechanical ventilation, and 5.1% needed invasive mechanical ventilation. The result of their study is in contrast with the results of the present study. This difference may be due to the fact that in the present study, all patients were admitted to the intensive care unit, but in the Guan's study, outpatients were also included in the study.

Due to the high incidence of deaths in people with higher age and underlying diseases, precautionary and preventive measures are required to be taken into account regarding these groups. Further research is needed to identify the underlying pathogenesis in these patients. The present study has some limitations that can be related to being cross-sectional, single center, as well as a limitation of similar studies in these areas, which makes it difficult to communicate and compare well in society. Therefore, the design of multicenter and comparative studies with a larger sample size is recommended in order to determine the most influential factors and to obtain comprehensive information and insight in general.

Conclusion

Mortality rate of patients with COVID-19 admitted to ICU is generally high. According to the findings of this study, thrombocytopenia, lymphopenia, hyperkalemia, and creatinine increase are laboratory disorders associated with increased mortality. Moreover, the progression of pulmonary involvement in imaging, shock, DIC, sepsis, and invasive respiratory support is associated with low survival of patients.

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Conflict of interest

The authors declare that they have no conflict of interest.

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