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Evaluation of Clinical Features and Outcomes of Patients with Coronavirus (COVID-19) Admitted to ICU in Southeastern Iran in 2020

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Abstract

Background: Coronavirus, coronavirus disease 2019 (COVID-19), in humans, mainly causes respiratory and gastrointestinal manifestations that can range from a simple cold to severe clinical symptoms or death. On the other hand, COVID-19 patients' hospitalization in the intensive care unit (ICU) have serious problems, which can affect their mortality; therefore, the awareness of these problems has a main role in decision-making in the early stages.
Objectives: This study aimed to evaluate the clinical features and outcomes of patients with COVID-19 admitted to the ICU.
Methods: This cross-sectional (descriptive-analytical) study was conducted on patients with COVID-19 pneumonia admitted to the ICU of Valiasr Hospital, Birjand, Iran, in 2020. A total of 111 patients, including 51 female and 63 male subjects, were enrolled in this study using convenience sampling. Demographic data, comorbidities, signs and symptoms, radiological findings, supportive methods of oxygen therapy, and clinical outcomes were collected using a checklist and compared between two groups (i.e., survivors and nonsurvivors).
Results: Among 111 patients (including 59 nonsurvivors and 52 survivors), the numbers of mortalities within the age ranges of $\geq$ 75 and $\leq$ 44 years were the highest and lowest, respectively. In the survived patients, hypertension (50.8%), diabetes mellitus (47.5%), heart disease (44.1%), and chronic obstructive lung disease (23.7%) were the most common comorbidities. Moreover, dyspnea (81.1%), fever and chills (73%), cough (64.9%), muscle pain (45%), and weakness, and lethargy (42.3%) were the most common symptoms of the patients. Based on the comparison of survived and nonsurvived groups, diarrhea ($P < 0.001$), sore throat ($P < 0.001$), nausea ($P < 0.001$), and vomiting ($P < 0.0001$) were significantly higher in the group of survived patients. Among the radiological findings (i.e., chest X-ray and high-resolution computed tomography), bronchoalveolar markings ($P = 0.05$) and pleural effusion ($P = 0.02$) were higher in the nonsurvived patients. The average Acute Physiology and Chronic Health Evaluation II (APACHE II) score $\geq$ 16 was reported with a higher mortality rate.
Conclusions: Risk factors, including dyspnea, older age, comorbidities, and high APACHE II score, could increase the risk of poor clinical outcomes and help identify ill patients with a poor prognosis at the beginning of ICU admission.

Keywords: Intensive Care Unit, COVID-19, Coronavirus, Clinical Features, Outcomes

1. Background

Coronaviruses are a large family of viruses that can cause anything from a simple cold to more severe illnesses, such as Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome coronavirus (1). On January 30, 2020, the World Health Organization declared the new coronavirus, coronavirus disease 2019 (COVID-19), a Public Health Emergency of International Concern and as the sixth public health threat emergency that needs international attention (2). The prevalence of COVID-19 in Iran began in March 2019 with the identification of two positive cases in Qom, and the number of total cases reached 6 million and 128000 mortalities by November 2021 (3).

The most important clinical signs of admitted patients with COVID-19 t the hospital are fever, dry cough, respiratory problems, headache, vomiting, diarrhea, fatigue, rhinorrhea, and chest pain (4). In more severe cases, the infection can cause pneumonia, acute respiratory syndrome, kidney failure, and even death (5). The current epidemiological data show that the mortality rate of COVID-19 patients with severe symptoms is about 20 times higher than that of those with mild symptoms (6).

The patients develop dyspnea after the onset of the disease, and severe cases can quickly suffer from dysfunction of some organs. Acute respiratory dyspnea syndrome, septic shock, acute heart and kidney damage, blood clotting disorders, and even death might be the symptoms (7). The awareness of the prevalence of these symptoms is of particular importance for the initial identification and screening of patients. The standard laboratory method for the current diagnosis of the disease is a real-time polymerase chain reaction (PCR). In addition, laboratory and radiological findings are used to diagnose the disease, especially in the early stages (8). Patients admitted to the intensive care unit (ICU) usually have serious problems and various underlying diseases that can affect patient mortality (9).

2. Objectives

This study investigated the clinical features, and outcome of patients with CIVID-19 admitted to the ICU of Valiasr Hospital, Birjand University of Medical Sciences, Birjand, Iran, in 2020 (March to December).

3. Methods

3.1. Study Design and Participants

In the beginning, the code of ethics was received from the Vice-Chancellor for Research and Technology of Birjand University of Medical Sciences. All patients with COVID-19 admitted to the ICU of Valiasr Hospital (n = 157) were the statistical population. The inclusion criterion was a positive real-time PCR, and the exclusion criterion was the lack of patient's electronic file. In this cross-sectional study, 111 of 157 patients were entered the study using convenience sampling. After designing the study checklist, the following information was collected: (1) demographic characteristics (e.g., age and gender); (2) comorbidities; (3) vital signs when admitting to the ICU [e.g., temperature, heart rate, arterial oxygen saturation with and without oxygen therapy, respiratory rate (RR), and blood pressure]; (4) clinical symptoms (e.g., fever, cough, dyspnea, sore throat, sputum, rhinorrhea, muscle pain, weakness and lethargy, chest pain, abdominal pain, headache, nausea and vomiting, hemoptysis, anosmia, seizures, anorexia, skin lesions, and conjunctivitis); (5) radiological findings [e.g., chest X-ray (CXR) and high-resolution computed tomography (HRCT)]; (6) oxygen therapy (e.g., high flow nasal cannula, simple facial mask, facial mask with reserve bag, noninvasive ventilation, and invasive mechanical ventilation (IMV)]; (7) patient outcomes (e.g., the length of hospital stay before ICU, ICU stay, and length of hospital stay after ICU); (8) two clinical scores for ICU (i.e., acute physiology and chronic health evaluation II (APACHE II) and Glasgow Coma Scale (GCS)] (10-12).

3.2. Data Analysis Method

The data were entered into SPSS software (version 22) for analysis, and then statistical tests were performed for comparing the survived and nonsurvived groups. The data were expressed as mean (standard deviation) or median (interquartile range) for continuous variables and number (%) for class variables. If continuous variables have a normal distribution according to the Kolmogorov-Smirnov test, the mean, and otherwise the median was used in the tests (13, 14). The independent *t*-test, chi-square test, Mann-Whitney U test, and Fisher's exact test were used to compare the survived and nonsurvived groups at 95% confidence level where appropriate.

4. Results

The findings showed that out of 111 patients admitted to the ICU, 59 (53.2%) subjects died, and 52 (46.8%) cases were discharged from the ward. The mean age of all patients was 65.15 $\pm$ 15.37 years, with a minimum and maximum of 24 and 94 years, respectively. Furthermore, the mean age values of the survivors and nonsurvivors were 71 $\pm$ 11.87 and 58.4 $\pm$ 15.9 years, respectively; therefore, there was a difference between the age of the two groups ($P < 0.001$).

By categorizing the age of patients into five groups based on Yang et al.' study (12), the highest frequency was related to patients over 75 years of age. Table 1 shows that the numbers of mortalities within the age ranges of over 75 and under 44 years were the highest and lowest, respectively. In the case of patients discharged from the ICU, the highest and lowest numbers were related to the ranges of under 44 and 45 - 54 years, respectively (Table 1). Therefore, there was a relationship between the age group and mortality. In other words, there was a higher mortality rate in the older age groups and a greater improvement in the younger age groups. Table 2 shows that there is no significant difference in the number of male and female patients in total ($P = 0.40$), survived ($P = 0.57$), and nonsurvived ($P = 0.51$).

Table 3 shows that clinical symptoms, including diarrhea ($P < 0.001$), sore throat ($P < 0.001$), and hemoptysis ($P < 0.001$), statistically differ between the two groups. In addition, regarding the symptoms, there was a significant difference in coronary heart disease ($P < 0.001$), chronic obstructive lung disease (COPD) ($P = 0.03$), history of influenza vaccine ($P < 0.001$), and cerebrovascular accident ($P = 0.03$) between the two groups. Moreover, the frequency of RR ($\geq$ 26 breaths/minute) in nonsurvivors was significantly higher than in survivors ($P = 0.01$). On the other hand, five methods of supportive oxygen therapy were considered for patients admitted to the ICU. The results showed that in the group of survivors, 52 patients

Table 1. Characteristics of Age Groups of Patients [a]

Variables	All Patients (n = 111)	Survivors (n = 59)	Nonsurvivors (n = 52)	P-Value
Age	65.15 ± 15.37	71 ± 11.87	58.4 ± 15.9	< 0.001
Age range (y)				< 0.001
< 44	14 (12.6)	13	1	
45 - 54	14 (12.6)	7	7	
55 - 64	20 (18.0)	12	8	
65 - 74	28 (25.2)	9	19	
> 75	35 (31.5)	11	24	

[a] Values are expressed as No. (%) or mean ± standard deviation.

Table 2. Gender Frequency of Studied Patients [a]

Gender	All Patients	Survivors	Nonsurvivors
Female	51 (46)	24 (46)	27 (45)
Male	60 (54)	28 (54)	32 (55)
P-value	0.40	0.57	0.51

[a] Values are expressed as No. (%).

needed to use supportive methods (P < 0.001). Accordingly, at the time of ICU admission, only one patient (1.7%) in the nonsurvivors used IMV; however, 54 patients (91%) of this group needed to use IMV at the time of death. Therefore, out of the total number of patients, 60 patients needed to use IMV, and 6 intubated patients were recovered and extubated (Table 3). The comparison of the two groups showed that hospitalization duration before the ICU (P = 0.15) and ICU stay duration (P = 0.43) were significantly different between the groups. The mean values of APACHE II scores among all patients at the time of ICU admission and discharge were 14.65 and 20.18, respectively. Furthermore, the GCS scores were 14.44 and 9.27 at the time of ICU admission and discharge, respectively (Table 4).

Table 4. Comparison of Acute Physiology and Chronic Health Evaluation II and Glasgow Coma Scale Scores on Admission and Intensive Care Unit Discharge [a]

Variables	ICU Admission		ICU Discharge	
	Survivors	Nonsurvivors	Survivors	Nonsurvivors
APACHE II	12.63 (7.3)	16.44 (5.92)	10.46 (6.10)	28.76 (17.7)
GCS	14.46 (2.34)	14 (1.45)	14.38 (2.3)	4.69 (3.17)

Abbreviations: ICU, intensive care unit; APACHE II, acute physiology and chronic health evaluation ii; GCS, Glasgow Coma Scale.
[a] Values are expressed as scores (standard deviation).

5. Discussion

This study investigated various variables of patients with COVID-19 who have been hospitalized in the ICU of Valiasr Hospital since 2020. Among 111 patients, 53.2% died, and 46.8% were discharged safely. The numbers of nonsurvivors in the age groups of ≥ 75 and ≤ 44 years were the highest and lowest, respectively. Moreover, there was a higher mortality rate in the older age groups. In previous studies, old age has been reported as an important independent predictor of mortality in severe acute respiratory syndrome (SARS) and MERS (15, 16). The mean age of the present study sample was 65.15 years; nevertheless, in a study performed on 164 patients admitted to the ICU of several medical centers in Mexico, the mean age of patients was 57.3 years, which was lower than the average age of the current study patients. Additionally, 69.5% of patients in the aforementioned study were male (17).

Out of 111 patients, 46 and 54% were female and male, respectively. Furthermore, 52.9% of women and 54.2% of men died. There was no significant relationship between gender and mortality variables that is inconsistent with the findings of Jin et al.'s study, in which male subjects had a higher than three times mortality rate, compared to female cases (18). The findings of the present study showed that hypertension (49.5%), diabetes (41.4%), heart disease (31.5%), COPD (17.1%), and hyperlipidemia (20.7%) had the highest prevalence of comorbidities in COVID-19 patients. The present study results are not consistent with the findings of Alamdari et al.'s study performed on 459 COVID-19 patients admitted to Shahid Modarres Hospital in Tehran, Iran, whose diabetes was significantly associated with COVID-19 mortality (19). In addition, in a study involving 140 patients admitted to Wuhan Hospital in China, no significant difference was observed in the proportion of patients with hypertension, diabetes, and coronary heart disease between severe and nonsevere patients (20).

Previous studies evaluating the mortality rates of MERS, SARS, and most recently COVID-19 have shown no signs of immunodeficiency as a risk factor for death. Furthermore, there is no history of higher mortalities related to chemotherapy, transplantation, or other disorders that require immunosuppression at any age (21, 22), which is

similar to the present study findings. Moreover, a history of influenza vaccination had no significant effect on mortality (23) that is consistent with the results of the present study.

The most commonly reported clinical symptoms were dyspnea (81.1%), fever and chills (73%), cough (64.9%), muscle pain (45%), weakness and lethargy (42.3%), anorexia (36%), and headache (25.2%). Yang et al. observed that dyspnea was more common in ICU patients, similar to the current study results (12). Contrary to the findings of the present study, muscle pain was not common in patients with COVID-19 and was reported in only two clinical trials. Muscle pain was observed in 11% of the 99 COVID-19 patients admitted to Wuhan Jinyintan Hospital in China (11) and 14% of the 28 confirmed COVID-19 cases in South Korea (23). Zhang et al. showed that dyspnea (29%) is the least common symptom in COVID-19 patients (22). Based on the results of the current study, it was concluded that the patients did not refer to the hospital in the early stages of the disease, compared to the Chinese patients.

Among the radiological findings, only bronchoalveolar markings in CXR and pleural effusion in HRCT were significant between the two groups of survivors and nonsurvivors, which is inconsistent with the results of a study by Zhou et al. They observed that consolidation and ground-glass opacity were significantly different between the two groups (11).

The mean values of APACHE scores among survivors at the time of ICU admission and discharge were 12.6 and 10.46, respectively. Moreover, the mean values of APACHE scores in nonsurvivors at the time of ICU admission and discharge were 16.44 and 28.7, respectively. Additionally, the GCS scores at the time of admission and discharge were 14.4 and 14.3 in survivors and 14 and 4 in nonsurvivors. Yang et al. showed an APACHE II score of 17 in nonsurvivors similar to that of the present study (12). Contrary to the findings of the current study, Halim et al. demonstrated an APACHE II score of 22 for nonsurvivors (24). The APACHE II score was significantly increased in the group of patients who died. In a study conducted by Rahimzadeh et al. in Tehran (1986), it was shown that the mortality rate highly met the standards in the APACHE II scores less than or equal to 15; however, in scores above 16, the mortality rate was significantly higher than expected (25). Studies by Hosseini and Ramezani conducted in Bojnourd, Iran, (1991) and Zimmerman et al. (2013) showed that APACHE II is a suitable criterion for predicting mortality. Patients who are more severe and have a higher APACHE II score need longer hospitalization (26, 27).

Except for heart rate, there was a significant difference in vital signs between the two groups of patients; nevertheless, Zhang et al. showed the heart rates of the two groups were different, although their findings of other vital signs are similar to those of the present study (22). In the current study, in the group of survivors, 52 patients needed to use supportive oxygen therapy methods ($P < 0.001$), which is almost similar to those of Yang et al.'s (94%) and Li et al.'s (100%) studies (12, 28). Naved et al. in Pakistan in 2011 and Bahtouee et al. in 2012 showed a relationship between the duration of hospital stay and mortality (29, 30). Nonetheless, the present study obtained no significant data regarding ICU stay in two groups, contrary to the results of Halim et al.'s study reporting 11 days in the nonsurvived group (24).

5.1. Conclusions

The most common clinical symptoms of COVID-19 were dyspnea, fever and chills, cough, muscle pain, weakness and lethargy, anorexia, and headache in patients at the time of admission. Some variables might increase the risk of poor clinical outcomes, such as older age, comorbidities, bronchoalveolar markings, pleural effusion on HRCT, higher RR $\geq$ 26 breaths/minute, and APACHE II score $\geq$ 16. The aforementioned risk factors can help detect ill patients with a poor prognosis at the beginning of ICU admission.

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Footnotes

Authors' Contribution: Hanieh Hosseinnezhad, study concept and design, acquisition of data, and drafting of the manuscript; Seyyed Morteza Hozhabrossadati, interpretation of the data, statistical analysis, and drafting of the manuscript; Alireza Khalesi, administrative, technical, and material support and study supervision; Mahmud Ganjifard, critical revision of the manuscript for important intellectual content.

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Table 3. Symptoms, Comorbidities, Radiologic Findings, Vital Signs, Oxygen Therapy Methods, and Intensive Care Unit Duration Between Survivors and Nonsurvivors

Symptoms (%)	All Patients	Survivors	Nonsurvivors	P-Value
Fever and chills	81	41 (51)	40 (49)	0.91
Cough	72	38 (52)	34 (48)	0.63
Fatigue	13	4 (30)	9 (70)	0.16
Sputum	15	6 (40)	9 (60)	0.43
Myalgia	50	24 (48)	26 (52)	0.77
Diarrhea	16	11 (68)	5 (34)	< 0.001
Nausea	22	11 (50)	11 (50)	0.08
Vomiting	15	12 (80)	3 (20)	< 0.001
Vertigo	13	5 (38.6)	8 (61.5)	0.40
Dyspnea	90	44 (48)	46 (52)	0.83
Sore throat and rhinorrhea	8	7 (87)	1 (13)	< 0.001
Headache	28	17 (60.6)	11 (39.4)	0.25
Chest pain	12	7 (58)	5 (42)	0.56
Abdominal pain	12	8 (75)	4 (25)	0.24
Hemoptysis	15	3 (20)	12 (80)	< 0.001
Rectorrhagia	0	0	0	-
Anosmia	10	6 (60)	4 (40)	0.57
Seizure	5	1 (20)	4 (80)	0.18
Malaise	47	26 (55)	21 (45)	0.46
Anorexia	40	20 (50)	20 (50)	1.00
Decrease of conciseness	13	5 (38)	8 (62)	0.40
Conjunctivitis	2	1 (50)	1 (50)	1.00
Comorbidities (%)				
Hypertension	55	25 (45)	30 (55)	0.50
Hyperlipidemia	23	15 (65.2)	8 (34.8)	0.14
Coronary heart disease	35	9 (25.7)	26 (74.2)	0.00
Diabetes mellitus	46	18 (39.1)	28 (60.8)	0.14
COPD	1	5 (26.3)	14 (73.6)	0.03
Asthma	3	2 (66.6)	1(33.3)	0.56
Malignancy	10	2 (20)	8 (80)	0.05
Chronic kidney disease	8	2 (25)	6 (75)	0.15
Chronic liver disease	3	0	3 (100)	-
Smoking	4	2 (50)	2 (50)	-
Drug addiction	14	8 (57.1)	6 (42.8)	0.59
Rheumatoid arthritis	2	2 (100)	0	-
Malnutrition	2	1 (50)	1 (50)	1.00
Androgenic alopecia	12	5 (8.3)	7 (91.7)	0.56
Influenza vaccination history	12	1 (1.9)	1 (18.6)	0.00
Anticoagulant therapy	3	2 (66)	2 (66)	0.56
Psychological disease	13	3 (23)	3 (23)	0.05
CVA	11	2 (18)	2 (18)	0.03
Gastrointestinal disease	15	7 (46)	7 (46)	0.79
Hepatitis	2	1 (50)	1 (50)	1.00
Tuberculosis	2	1 (50)	1 (50)	1.00
Anemia	2	1 (50)	1 (50)	1.00
Thyroid dysfunction	8	5 (62)	5 (62)	0.48
Paralysis	2	1 (50)	1 (50)	1.00
HRCT				

Consolidation	60	45 (44)	33 (56)	0.60
Ground glass	90	42 (47)	48 (53)	0.40
Patchy infiltrates	78	37 (48)	41 (52)	0.20
Lymphadenopathy	50	23 (46)	27 (54)	0.32
Pleural effusion	38	12 (32)	26 (68)	0.02
Pleural thickness	24	9 (37)	15 (63)	0.16
		CXR		
Unilateral infiltrates	3	1 (34)	2 (66)	0.56
Diffuse bilateral infiltrates	88	41 (47)	47 (53)	0.52
Pneumothorax	5	-	5 (100)	-
Increased bronchovascular markings	26	8 (30)	18 (70)	0.05
		Vital Sings		
Temperature	37.2	37.5 (1.3	37.4 (1.0)	< 0.001
SPO2 without oxygen therapy	84.5	86.3 (6.7)	82.7 (8.6)	< 0.001
SPO2 with oxygen therapy	92.2	93.4 (5.0)	91.3 (6.3)	< 0.001
RR	21.4	19.2 (3.0)	23.7 (9.1)	< 0.001
SBP	124.0	124.0 (19.3)	123.3 (20.9)	< 0.001
DBP	76.1	76.9 (13.7)	75.4 (13.7)	< 0.001
MAP	92.1	92.8 (14.3)	91.3 (13.5)	< 0.001
HR	91.9	92.6 (12.7)	91.2 (17.0)	0.52
		Oxygen Therapy on Admission		
High flow nasal cannula	54	24 (45)	30 (55)	0.49
Facial mask	16	12 (75)	4 (25)	0.46
Mask with reserve bag	25	13 (37.2)	22 (62.8)	0.17
NIV	3	1 (33.4)	2 (66.6)	0.56
IMV	3	2 (66.6)	1 (33.4)	0.56
		Oxygen Therapy on Discharge		
High flow nasal cannula	16	16 (100)	-	-
Facial mask	7	6 (85.7)	1 (14.3)	0.37
Mask with reserve bag	23	22 (95.6)	1(4.4)	< 0.001
NIV	5	2 (40)	3 (60)	0.65
IMV	60	6 (10)	54 (90)	< 0.001
		Hospitalization Duration		
Hospital stay duration before ICU admission	4.9	5.7 (4.0)	3.5 (3.7)	0.15
ICU stay	8.4	8.1 (9.5)	8.1 (6.5)	0.43
Hospital stay duration after ICU	4.9	4.91 (3.3)	-	-

Abbreviations: ICU, intensive care unit; CVA, cerebrovascular accident; COPD, chronic obstructive lung disease; HRCT, high-resolution computed tomography; CXR, chest X-ray; SpO2, oxygen saturation; RR, respiratory rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; HR, heart rate; NIV, noninvasive ventilation; IMV, invasive mechanical ventilation.