Advanced Medical Journal, Vol.9, No.3, P.98-107,2024 https://doi.org/10.56056/amj.2024.282

Mortality Predictors among COVID-19 Patients Admitted to the Intensive Care Unit in Sulaymaniyah City, Iraq: A Cross-Sectional Study

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Abstract

Background and objectives: On February 22, 2020, Iraq confirmed the first case of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The number of confirmed cases in Sulaimaniyah city reached 152,846, with 3,178 deaths. Our objective was to assess the clinical characteristics and identify variables that may predict mortality of COVID-19 cases in the intensive care unit.

Methods: Our cross-sectional study involved patients who were diagnosed with laboratory-confirmed Covid-19 and admitted to the intensive care unit of Shaheed Dr. Hemn Hospital/ Sulaymaniyah/ Iraqi Kurdistan from January 15, 2021, to April 29, 2022. Collected data included the patient's demographic characteristics, vital signs, hematological parameters, and management as documented in the patient's medical records. Patients were separated to two groups: those who were discharged and those who were dead. The binary logistic regression model was used to identify independent factors that predict mortality.

Results: During the study period, 403 patients were admitted to the intensive care unit. Case fatality rate was high 69.2%. The patient's average age was 61.42 ±13.17 years, and 249 (61.8%) of them were men. The majority of the patients 319 (79.2%) had comorbidities. Lymphocytopenia was observed in 306 (75.9%) of the patients and there was a statistically significant difference between discharged and death groups (p value 0.021). Remdesivir was given to 185 patients (45.9%) and there was a statistically significant difference between discharged and death groups, p-value <0.001.

Conclusions: Critically ill patients with COVID-19 had a high mortality rate in the intensive care unit. low SBP, GCS<15, high D. dimer, and poor oxygen saturation were considered predictor factors of mortality.

Keywords: Covid19, ICU, Iraq, Mortality Predictors, Sulaymaniyah

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Introduction

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is the source of the novel coronavirus infection known as COVID-19, which was initially identified in Wuhan, China, in December 2019 as a result of the appearance of several pneumonia cases with unknown origins.[1] On March 1, 2020, the city of Sulaymaniyah recorded the first COVID-19 infected case in Kurdistan. The patient was an old man who had traveled to Iran for medical treatment. Through the same month, the World Health Organization (WHO) declared this virus' rapid expansion to be a pandemic.[2] Over 600,000,000 COVID-19 patients were confirmed globally, which led to approximately 6,000,000 deaths.[3] Some patients may have the signs and symptoms of a severe respiratory infection together with a quickly progressing acute respiratory distress syndrome (ARDS) with other significant consequences, which might finally result in organ failure and fatalities. Therefore, it is essential to diagnose serious situations quickly and treat them correctly.[4]According to epidemiological research, around 6-10% of the cases have severe COVID-19 and need admission to an intensive care unit (ICU) for respiratory failure due to acute hypoxia.[5] Another study by Huang, et al. revealed that 29% of individuals acquire ARDS and necessitate hospitalization.[6] Research in Wuhan estimated that mechanized ventilation would be needed by 2-12% of patients, and fatality rates would range from 26% to 97%. [7] Initial research from China and Italy revealed that COVID-19-positive critically sick individuals had death rates ranging from 26% to 62%.[8,9] Studies from Seattle and New York stated that total mortality ranged from 23% to 50%.[10,11] Among 344 hospitalized patients in another Chinese study, 38.7% have died within 28 days of intensive care unit admission.[12] Depending on data gathered from various nations, fatality rates in COVID-19 patients are really quite different. Identifying causes and predictive factors that lead to ICU fatality in cases of COVID-19 referred to ICU is still challenging problem. [13] More specifically, there is a lack of knowledge regarding the clinical characteristics of Middle Eastern patients in critical care who have been diagnosed with COVID-19. It is crucial to have more data to guide the management of intensive care unit cases of COVID-19, that's why more research is required to monitor and summarize their features and results and for efficient use of limited critical care unit resources. The study aimed to characterize the critical cases of COVID-19 admitted to the intensive care unit and to identify the possible predictors of mortality.

Patients and methods

Our cross-sectional study was carried out at the intensive care unit of Shaheed Dr. Hemn Hospital, a 164-bed tertiary teaching hospital located in Sulaimaniyha city, Kurdistan region, Iraq. In the hospital admitting all patients confirmed with COVID-19, severely ill patients are referred to the ICU with 20 beds for COVID-19 patients. Enrolled patients were those cases 18 years of age or older proved to have COVID-19 infection and were admitted to the hospital's intensive care unit (ICU) for at least 24 hours or more during the period from January 15, 2021, to April 29, 2022. Patients with incomplete data and pregnant women were excluded. The diagnosis of the patients was confirmed by using real-time reverse transcription polymerase chain reaction (RT-PCR) of nasopharyngeal swap.[14] The outcome of the patients was categorized as either being discharged (cured) group or the death group. The Research Protocol Ethics Committee of the Kurdistan Higher Council of Medical Specialties has given approval to the study protocol, NO. (4573) on February 16, 2022. Moreover, permission was obtained from the Directorate of Health in Sulaimaniya.Hospital files were used to collect the following data: Age, sex, medical comorbidities, vital signs that include diastolic and systolic blood pressure temperature, respiratory rate, heart rate, saturation of peripheral oxygen (SpO_2), and Glasgow Coma Scale (GCS). The GCS consists of three

https://doi.org/10.56056/amj.2024.282 https://amj.khcms.edu.krd

distinct examinations: eye responses, verbal and motor responses. The score values ranged from three to fifteen, with three being the worst and fifteen being the best.[15] Laboratory parameters at admission (C-Reactive Protein, D. dimer, total white blood cell count and lymphocyte count). The type of oxygen therapy in ICU (non-rebreathing face mask, non-invasive ventilation c-pap, invasive ventilation). Other data including medical treatment (favipiravir, remdesivir), the days that the patients stayed in ICU, and the patient's outcome (discharged or death) were collected. Calculation of the qSOFA scoring (quick Sequential Organ Failure Assessment) was determined on hospitalization based on criteria established by the definitions of sepsis and septic shock international consensus task force.[16] The (qSOFA) is capable of predicting significant disease at the beginning of hospitalization in those infected with COVID-19.[17]Descriptive analysis of the data was presented as the median interquartile range (IQR) for parameters with non-normal distribution while mean and standard deviation were used for normally distributed variables. Data normality was assessed by using the Shapiro-Wilk test. Numbers and percentages were used to describe categorical variables. The Chi-square test was used to analyze categorical variables and Fisher's exact test was utilized in small sample analysis. Differences between continuous variables were analyzed by using a student's t-test if the data were normally distributed and the Mann-Whitney U test when the data were non-normal distributed. To determine independent variables that predict mortality, a binary logistic regression model was used. P-values of ≤0.05 were considered to be statistically significant. For all data analysis, the Statistical Package for the Social Sciences (SPSS, IBM) version 25 was utilized.

Results

From January 15, 2021, to April 29, 2022, 403 COVID-19 cases were sent to ICU in Dr. Shaheed Hemn hospital / Sulaimaniya city/ Iraqi Kurdistan. Out of 403 individuals with COVID-19, 124 (30.8%) were sent home and 279 (69.2%) died with an overall fatality rate of 69.2%. The mean age of the patients was 61.42±13.17 years (range: 27-88 years). About two third of them 61.8% (249/403) were males. One or more comorbidities were found in the majority of the patients 319 (79.2 %); hypertension was the most common chronic disease 221(54.8%) followed by diabetes 154(38.2%), and cardiovascular disease 128(31.8%). The discharged group had lower mean age of 54.37±13.37 years than the death group, the difference was statistically highly significant (p value <0.001). Table (1).

https://doi.org/10.56056/amj.2024.282 https://amj.khcms.edu.krd

Table (1): Study sample by Demographic characteristics and comorbidity

Demographic characteristics and comorbidities	All patients N = 403	Discharged group N = 124	Death group N=279	p value
Age, years Mean ± SD	61.42±13.17	54.37±13.37	64.55±11.83	<0.001
Age groups, n (%) <41 41-50 51-60 61-70 >71	 34(8.4) 57(14.1) 74(18.4) 123(30.5) 115(28.5)	 18(14.5) 32(25.8) 30(24.2) 25(20.2) 19(15.3)	 16(5.7) 25(9.0) 44(15.8) 98(35.1) 96(34.4)	 <0.001
Sex, n (%) Male Female	 249(61.8) 154(38.2)	 62(50.0) 62(50.0)	 187(67.0) 92(33.0)	 0.001
Comorbidities, n (%) Yes No	 319(79.2) 84(20.8)	 71(57.3) 53(42.7)	 248(88.9) 31(11.1)	 <0.001
Hypertension, n (%) Yes No	 221(54.8) 182(45.2)	 47(37.9) 77(62.1)	 174(62.4) 105(37.6)	 <0.001
Diabetes mellitus, n (%) Yes No	 154(38.2) 249(61.8)	 25(20.2) 99(79.8)	 129(46.2) 150(53.8)	 <0.001
Cardiovascular disease, n (%) Yes No	 128(31.8) 275(68.2)	 15(12.1) 109(87.9)	 113(40.5) 166(59.5)	 <0.001
Respiratory disease, n (%) Yes No	 93(23.1) 310(76.9)	 20(16.1) 104(83.9)	 73(26.2) 206(73.8)	 0.027
Renal disease, n (%) Yes No	 46(11.4) 357(88.6)	 10(8.1) 114(91.9)	 36(12.9) 243(87.1)	 0.159 (NS)
Cerebrovascular disease, n (%) Yes No	 36(8.9) 367(91.1)	 2(1.6) 122(98.4)	 34(12.2) 245(87.8)	 0.001
Malignancy, n (%) Yes N0	 41(10.2) 362(89.8)	 9(7.3) 115(92.7)	 32(11.5) 247(88.5)	 0.197 (NS)

Regarding the hematological parameters, 306 patients (75%) had lymphocytopenia, lymphocyte count less than 1 $\times 10^9$/L, and was dominant in the death group (79.2% versus 68.5%, P-value 0.021). The median values of D. dimer and CRP were higher in dead patients 1960 (IQR 1400-2993), 140 (IQR88-210) than in discharged patients 1114 (IQR 780-1605), 130 (IQR 84-169) respectively, and these differences were statistically significant, Table (2).

Table (2): Hematological parameters of COVID-19 patients at admission to ICU

Hematological parameters	All patients	Discharged group	Death group	p value
WBC*, $\times 10^9$ /L, median (IQR)	16.5 (12-21.8)	18 (12-22.7)	16 (12-21)	0.152 (NS)
Lymphocytes, $\times 10^9$ /L, median (IQR)	0.6 (0.3-1)	0.6 (0.3-1.2)	0.6 (0.6-0.9)	0.081 (NS)
Lymphocytes<1, n (%)	306 (75.9)	85 (68.5)	221 (79.2)	0.021
D. dimer, ng/ml, median (IQR)	1655(11002670)	1114 (780-1605)	1960(14002993)	<0.001
CRP**, mg/l, median (IQR)	138 (86-192)	130 (84-169)	140 (88-210)	0.008

*White blood cells, ** C-reactive proteins

In total, the median oxygen saturation was 84% (IQR 80-88) at admission to the ICU; compared to the Death group, the discharged group had a higher oxygen saturation (SpO_2) of [88 (IQR 86-90) % versus 82 (79-87) %, P-value <0.001)]. Furthermore, the death group possessed a significantly greater qSOFA score compared to the discharged group. On admission to the ICU, 201 cases (49.9%) had GCS less than 15, yet only 14 of them (11.3%) survived, compared to 187 patients (67%) who died. This difference was statistically significant. A median duration of stay in ICU for the discharged group had been 12 (IQR 8-15) days compared to 6 (IQR3-10) days among the death group, P-value <0.001, Table (3).

Table (3): Vital signs of COVID-19 patients at ICU admission

Vital signs	All of patients	Discharged group	Death group	p value
Temperature °c, median (IQR)	37.2 (36.4-38.1)	37.3 (36.6 38.4)	37 (36.1-38)	0.017
Heart rate/min. median (IQR)	104 (76-116)	109 (84-118)	102 (68-114)	0.061
Respiratory rate/min	31 (27-36)	30 (28-34)	32 (26-36)	0.789
SBP*, mm/Hg, median (IQR)	120 (100-140)	140 (120-150)	110 (90-130)	<0.001
DBP**, mmHg, median (IQR)	70 (60-80)	70 (70-80)	70 (50-80)	<0.001
SpO2 %, median (IQR)	84 (80-88)	88 (86-90)	82 (79-87)	<0.001
GCS***<15, n (%) Yes No	 201 (49.9) 202 (50.1)	 14 (11.3) 110 (88.7)	 187 (67) 92 (33)	 <0.001
qSOFA****, n (%) 1 point 2 points 3 points	 213 (52.9) 133 (33.0) 57 (14.1)	 105 (84.7) 16 (12.9) 3 (2.4)	 108 (38.7) 117(41.9) 54 (19.4)	 <0.001 <0.001 <0.001
Days in ICU, median (IQR)	8 (4-13)	12(8-15)	6(3-10)	<0.001

* systolic blood pressure, ** diastolic blood pressure, *** Glasgow Coma Scale, **** qSOFA, quick sequential organ failure assessment

Management of COVID-19 patients including oxygen therapy and medical treatment summarized in Table (4). There were statistically significant differences between patients who survived and those who did not according to oxygen therapy. Remdesivir was administered to 185 (45.9%) individuals (200 mg as a single dose followed by 100 mg once daily), and there was a statistically significant difference between discharged and death group P-value<0.001

Table (4): Management of patients with COVID-19 in ICU

Management	All patients	Discharged group	Death group	p value
Oxygen therapy Face mask, n (%) C-pap* (NIV), n (%) IMV*, n (%)	 84 (20.8) 276 (68.5) 43 (10.7)	 46 (37.1) 73 (58.9) 5 (4.0)	 38 (13.6) 203 (72.8) 38 (13.6)	 <0.001 0.006 0.004
Favipiravir Remdesivir Didn't receive antiviral drug	72(17.9) 185(45.9) 146(36.2)	22 (17.7) 77 (62.1) 25 (20.2)	50 (17.9) 108 (38.7) 121 (43.4)	0.965 <0.001 <0.001

* Continuous positive airway pressure, ** Invasive Mechanical Ventilation

Table (5) described the binary logistic regression model where the ICU death was the dependent variable. On the other hand, low SBP, GCS<15, high D. dimer, and poor oxygen saturation were predictors of higher risk of mortality, contrasting remdesivir use, which was associated with a lower risk.

Table (5): Independent factors that predict mortality in ICU

Factors	B	P-value	OR	95%CI
Age	0.025	0.102	1.026	0.995-1.057
Sex	0.522	0.133	1.686	0.854-3.329
SBP*	-0.043	<0.001	0.958	0.939-0.978
DBP**	0.032	0.051	1.032	1.000-1.065
GCS<15***	-1.865	<0.001	0.155	0.062-0.385
CRP, mg\l****	0.000	0.874	1.000	0.995-1.005
D. dimer, ng\ml	0.000	0.035	1.000	1.000-1.001
Oxygen saturation	-0.279	<0.001	0.757	0.691-0.828
Comorbidity	0.468	0.385	1.597	0.556-4.586
Hypertension	0.670	0.134	1.955	0.813-4.703
Diabetes Mellitus	0.465	0.256	1.593	0.714-3.553
Respiratory disease	0.128	0.775	1.136	0.472-2.734
Cardiovascular disease	0.438	0.364	1.550	0.602-3.994
Cerebrovascular disease	0.512	0.587	1.669	0.262-10.614
Days in ICU	-0.060	0.044	0.942	0.889-0.998
q SOFA*****	1.205	0.192	3.336	0.547-20.359
Intubation	1.413	0.051	4.110	0.992-17.033
Remdesivir	-1.001	0.030	0.368	0.149-.908
Lymphocyte<1	-0.372	0.352	0.690	0.315-1.508
Didn't received antiviral	-0.058	0.909	0.943	0.347-2.563

* Systolic blood pressure, ** diastolic blood pressure, *** Glasgow Coma Scale; **** C-reactive protein, *****qSOFA, quick sequential organ failure assessment

Discussion

To the best of the researcher knowledge, this is the first study that described the baseline characteristics and the independent factors that predict the mortality of COVID-19 patients admitted to the ICU in Sulaymaniyah city /Iraqi Kurdistan. Patients' demographic, hematological parameters, comorbidities, and management were analyzed for their association with death. According to the findings of this study, male patients above 61 years with preexisting chronic diseases, such as hypertension, diabetes, and cardiovascular diseases are extremely vulnerable to COVID-19 and exhibit a highly significant association with fatal outcome which is similar to the trend that has been reported by several studies.[9,18,19] Previous investigations revealed that although most of the occurrences of Covid-19 are rather mild, the disease can be critical and fatal in elderly patients who already have comorbidities.[6] The studied sample showed higher mortality than earlier published data by Richardson S, and Grasselli G[3,9]According to multicenter cohort research done in China, over fifty percent of patients had co-morbidities. Hypertension was reported as the most common chronic disease, followed by Diabetes and cardiovascular disease in the China study. These results were likewise consistent with our findings.[7] Regarding the hematological parameters of COVID-19 patients at admission to the ICU, lymphopenia (lymphocyte $<1 \times 10^9$/ L) was reported in the majority of patients at admission to the ICU and was significantly associated with death. This is in line with previous studies done by Jiménez-Ibáñez EO and Liu Q. [20,21] Another important finding in the present study was an increase in D. dimer and CRP, these increases were significantly associated with the death group. In addition, we found that high D. dimer at admission to the ICU may be a predictor of death for COVID-19 cases in ICU. A number of studies and meta-analyses have reported the significance of these biomarkers as risk factors and predictors of mortality and deteriorating COVID-19 severity.[21,22] It is worth mentioning that we found the temperature in the discharged group was significantly higher than the temperature in the death group. This is consistent with a study conducted by Tharakan who found that increased temperature at initial presentation was not significantly related to death.[23]Another study has shown that 20%-30% of elderly individuals with life-threatening viral or bacterial infections initially had no fever. This is most likely due to the lowered core body temperature associated with aging. [24] In addition, we revealed that low systolic blood pressure, GCS<15, and low SpO_2 at admission to the ICU were regarded as predictors of mortality. The qSOFA score system is used to evaluate organ dysfunction. In the present study, higher qSOAF scores at admission to the ICU were significantly associated with mortality. Previous literature found that early therapies and rapid identification of critical patients utilizing qSOFA scores could enhance the clinical outcomes of COVID-19 patients.[18] For survivors, the median length of stay in the ICU was significantly greater than non-survivors (12 days versus 6 days). Additionally, the death group had a short staying in ICU compared to the discharged group and there was a statistically significant difference between these groups. A similar result was also reported in Italy[9]. Based on the finding of our research, most of cases (68.5%) treated with NIV (c-pap), whereas (20.8%) required an oxygen face mask and only (10.7%) have been treated with IMV. This is contradictory to prior studies stated by Grasselli G and Arentz M where the majority of patients required IMV.[9,25] This could be because IMV was the preferred mode of ventilation during the initial days of the pandemic when guidelines for the best mode of ventilation were still being developed. [26] Only late after the pandemic, NIV was supported as the preferable option, especially for individuals without severe comorbidities. Moreover, it's essential to mention the risks of prolong mechanical ventilation, such as lung injury, acquired

pneumonia, and trouble weaning off the machine.[26] As to antiviral therapy, (63.8%) of the patients were treated with antiviral drugs. Favipiravir was given to (17.9%) and Remdesivir was given to (45.9%) of the patients. Remdesivir use was associated with decreased mortality in COVID-19 critical patients. Remdesivir is recommended for use in treating critical patients by the governments of several countries, including Taiwan, the United States, the European Union (EU), and Japan.[27] On 22 October 2022 Remdesivir was approved by FDA for the management of hospitalized COVID-19 patients.[28] In our research, the total mortality rate was 69.2% and it is consistent with previous studies from China 61.5%,[8] and Washington 67%,[25] Nonetheless, low mortality rates have been published in Italy 26%,[9] and in Belgium 36%.[13] Three variables may be responsible for these differences between countries. Infrastructure comes first (because to a high patient load, there is a shortage of resources, including ventilators and ICU beds), followed by host variables (old age, obesity, smoking, and chronic illness), and finally environmental factors (temperature and rainfall).[29] There were several limitations in our study. This is a single-center study with limited sample size. Also, there are some missing data from the ICU, such as mechanical ventilation settings, imaging results, and some laboratory tests (serum ferritin, pro-inflammatory interleukins, and procalcitonin).

Conclusions:

In our ICU, the mortality among COVID-19 is high; older patients and men with comorbid conditions had a much higher risk of dying from COVID-19. The following factors are thought to be predictors of COVID-19 mortality in the ICU: low SBP, GCS<15, high D. dimer, poor oxygen saturation. whereas treated those cases with Remdesivir lower that risk in ICU.

Acknowledgments

The author would like to thank Dr. Maath Mohammed Hashim who helped with the data collection and all the staff of Dr. Shaheed Hemin hospital.

Conflict of interest

The author reports no conflicts of interest.

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