

Baseline demographic, clinical and laboratory risk factors for predicting admission to intensive care unit in patients diagnosed with COVID-19 in the emergency department

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Cite this article as: Güngörer B. Baseline demographic, clinical and laboratory risk factors for predicting admission to intensive care unit in patients diagnosed with COVID-19 in the emergency department. Anatolian Curr Med J 2021; 3(4); 279-283.

ABSTRACT

Aim: The COVID-19 pandemic has caused very significant morbidity and mortality throughout the world. Predicting the need for intensive care in these patients is important in terms of proper planning of health services and developing cost-effective management strategies. In this study, we sought to investigate the predictability of whether patients with COVID-19 would need intensive care by looking at some clinical, hematological and biochemical parameters.

Material and Method: All of the patients who applied to the adult emergency department of our hospital with the diagnosis of COVID-19 and were hospitalized were included in the study. The age, physical examination findings, comorbidities, and first laboratory parameters of the patients admitted to our hospital between March 2020 and June 2020 were retrospectively analyzed. A multivariable logistic regression model was constructed to determine the significant predictors of admission to ICU.

Results: A total of 1,005 patients were included in the study. Logistic regression analyses revealed that age (OR: 1.094, $p<0.001$), chronic renal failure (OR: 4.735, $p=0.036$), cancer diagnosis (OR: 3.957, $p=0.021$), higher levels of lactate dehydrogenase (OR: 1.006, $p<0.001$), and ferritin (OR: 1.001, $p=0.001$), and lower levels of lymphocyte count (OR: 0.879, $p=0.021$) were the independent risk factors in predicting the intensive care unit admission of the patients

Conclusion: Age, chronic renal failure, cancer, higher levels of LDH and ferritin, and lower levels of lymphocyte are found to be independent risk factors in predicting intensive care admission for patients admitted to the emergency department with the diagnosis of COVID-19.

Keywords: COVID-19, emergency department, intensive care unit

INTRODUCTION

The coronavirus 2019 disease (COVID 19) caused by a new strain of coronavirus, SARS-CoV 2, has caused a pandemic. It led to millions of people being hospitalized and being hospitalised in intensive care unit (1,2). For a long time, health systems caused serious problems in many countries due to lack of space and intensive care beds, and people were unable to access health services. Emergency services became the most important actor of this pandemic and had to decide which patients will have a poor prognosis and which patients will be treated as outpatients, and doing this in a very short time has become an important approach for the management of patients (3). In some studies, clinical clues such as the age of the patients, underlying diseases, some hematological parameters and radiological findings were investigated whether the patients should be

hospitalized and whether they needed intensive care (4,5). During the pandemic in Turkey, especially large hospitals were accepted as pandemic hospitals and took an active role in the management of the pandemic. In this regard, *** has become a very important center in Turkey with the number of patients admitted, the number of beds and the number of intensive care units. We planned this retrospective study with the thought that with the decrease in the number of applications today, there are clues about which patients will have a poor prognosis and which patients may need intensive care, and it will be of great help to the clinician. With this research, we investigated the predictability of whether patients with COVID-19 would need intensive care by looking at some clinical, hematological and biochemical parameters.

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Received: 26.08.2021 **Accepted:** 14.09.2021



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MATERIAL AND METHOD

The study was carried out with the permission of Ankara City Hospital No. 2 Clinical Research Ethics Committee (Date: 14.07.2021, Decision No: E2-21-739). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patients

All of the patients who applied to the adult emergency department with the diagnosis of COVID-19 and were hospitalized were included in the study. The ages, examination findings, comorbidities, and first laboratory parameters of the patients admitted between March 2020 and June 2020 were retrospectively analyzed. All hospitalized patients older than 18 years with positive polymerase chain reaction (PCR) tests were included. Patients whose laboratory findings were missing and clinical information could not be reached were excluded from the study. The patients were separated into two groups as those admitted to the normal service and those requiring intensive care, and compared in terms of these parameters. The patients' ages, pregnancy status, presence of hypertension, diabetes, coronary artery disease, chronic obstructive pulmonary disease, chronic kidney failure, cancer, immunodeficiency, pneumonia, and whether the patient was a healthcare worker were recorded. Hematological data of the patients, hemoglobin levels, white blood cell counts, lymphocyte count, platelet count were obtained from the hospital data system. Among the biochemical parameters, creatinine level, sodium, potassium, lactate dehydrogenase, erythrocyte sedimentation rate, c reactive protein, interleukin 6 level, procalcitonin level, ferritin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase and troponin levels were recorded on patient follow-up forms.

Admission to intensive care unit was done according to current guidelines (6). Severe illness, severe respiratory tract infection (severe pneumonia; respiratory rate $\geq 30/\text{min}$ and/or severe respiratory distress (dyspnea, use of extra respiratory muscles) and/or oxygen saturation in room air $\leq 90\%$), hypotension (systolic blood pressure $< 90 \text{ mmHg}$ and more than 40 mmHg decrease from normal systolic blood pressure and mean arterial pressure $< 65 \text{ mmHg}$, tachycardia $> 100/\text{min}$, troponin elevation, presence of skin disorders such as capillary return disorder and cutis marmoratus, acute respiratory distress syndrome, sepsis, septic shock, myocarditis, arrhythmia and cardiogenic shock, metabolic acidosis, coagulation disorder and multiple organ failure.

Statistical Analysis

All statistical analysis entered to Stata computer based programme (version16.0 MP; StataCorp). The

distribution of continuous variables was determined using Kolmogorov-Smirnov. Of the continuous data, those with normal distribution were presented as mean \pm standard deviation (SD), and data without normal distribution were presented as median (range). Categorical data were defined as the number of cases. Statistical analysis differences in variables those with normal distribution were compared.

Student's t-test was used for two different groups (ICU and non-ICU patients) with normal distribution, Mann-Whitney U test was used for data not normally distributed. Categorical variables were compared using Pearson's Chi square test. A univariate logistic regression model was constructed for each variable to show significant predictors of ICU admissions, and then those with $p<0.1$ values were tested in the multivariate logistic regression model. Odds ratios (ORs) and their 95% confidence intervals (CI) for ICU admission are presented. $p<0.05$ was considered significant in all statistical analyses.

RESULTS

A total of 1,005 patients were included in the study. While 847 patients were admitted to the normal inpatient service, 158 of them were hospitalized to the intensive care unit. The mean age of the patients admitted to the intensive care unit was higher than the patients admitted to the normal service (42.9 ± 15.7 vs 67.3 ± 14.5 , $p <0.001$). There was no difference between the groups in terms of gender and pregnancy. Hypertension, diabetes, chronic obstructive pulmonary disease, chronic kidney failure, cancer, pneumonia and being a healthcare worker differed significantly between the groups. These data are summarized in **Table 1**.

When the laboratory data were compared between the two groups, it was seen that all other laboratory data were statistically different between the two groups, except for platelet, sodium and potassium levels. All these parameters are also summarized in **Table 2**.

Table 1. Baseline clinical and demographical findings of the study population

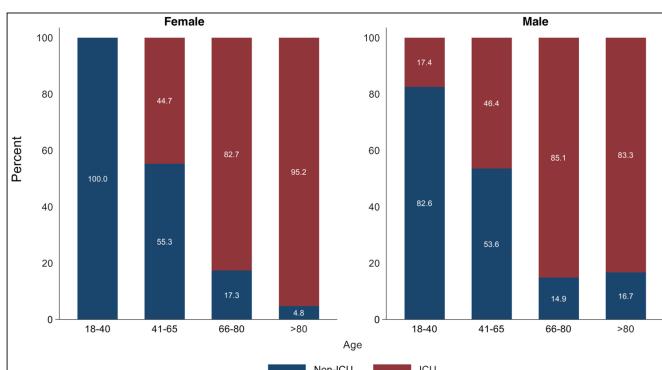
	Non-ICU (n=847)	ICU (n=158)	p-value
Age, mean (SD)	42.9 (15.7)	67.3 (14.5)	<0.001
Male, n (%)	438 (51.7%)	88 (55.7%)	0.36
Pregnancy, n (%)	16 (9.8%)	0 (0.0%)	0.083
Hypertension, n (%)	79 (9.3%)	48 (30.4%)	<0.001
Diabetes mellitus, n (%)	56 (6.6%)	19 (12.0%)	0.017
Chronic obstructive pulmonary disease, n (%)	16 (1.9%)	18 (11.4%)	<0.001
Coronary artery disease, n (%)	11 (1.3%)	4 (2.5%)	0.24
Chronic renal failure, n (%)	5 (0.6%)	7 (4.4%)	<0.001
Cancer, n (%)	9 (1.1%)	13 (8.2%)	<0.001
Immun deficiency, n (%)	2 (0.2%)	1 (0.6%)	0.40
Pneumonia, n (%)	359 (42.4%)	88 (55.7%)	0.002
Health-care workers, n (%)	44 (5.2%)	1 (0.6%)	0.011

Table 2. Initial laboratory findings of the study population

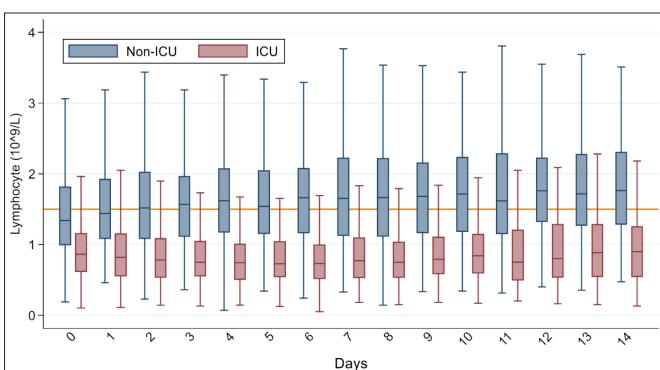
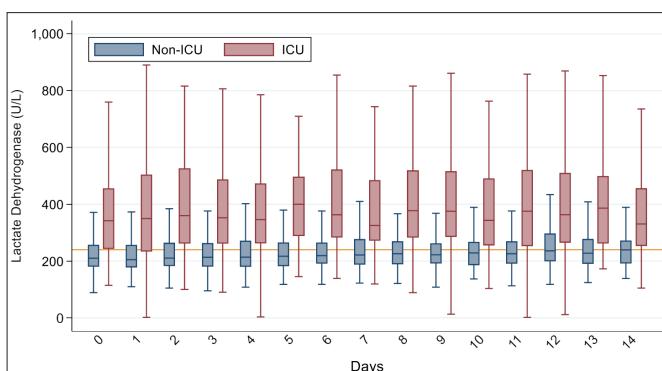
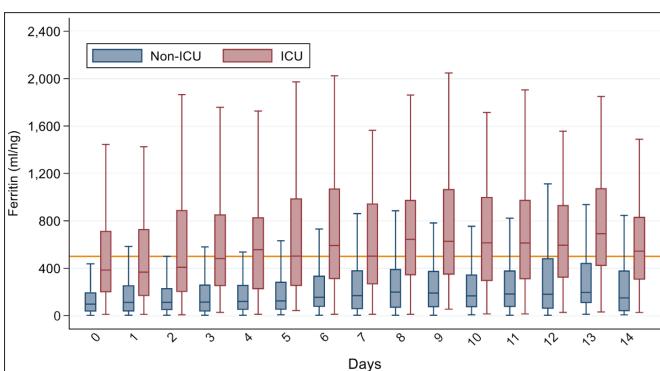
	Non-ICU (n=847)	ICU (n=158)	p-value
Hemoglobin, mean (SD)	13.8 (1.7)	12.7 (2.1)	<0.001
White blood cell, mean (SD)	5.6 (2.5)	7.5 (6.3)	<0.001
Neutrophil, mean (SD)	3.6 (2.1)	5.7 (4.9)	<0.001
Lymphocyte, median (IQR)	1.4 (1.0, 1.9)	0.9 (0.5, 1.2)	<0.001
Platelet, mean (SD)	226.8 (80.4)	217.9 (102.3)	0.23
Creatinine, mean (SD)	0.8 (0.5)	1.1 (0.7)	<0.001
Sodium, mean (SD)	139.1 (3.2)	138.6 (7.3)	0.15
Potassium, mean (SD)	4.1 (0.4)	4.0 (0.5)	0.19
Lactate dehydrogenase, median (IQR)	214.0 (181.8, 270.5)	331.3 (234.5, 424.0)	<0.001
C-reactive protein, median (IQR)	5.0 (1.1, 25.6)	86.9 (25.9, 165.0)	<0.001
Erythrocyte sedimentation rate, mean (SD)	24.9 (23.5)	52.5 (40.4)	<0.001
Interleukin-6, median (IQR)	8.1 (1.1, 37.9)	41.7 (12.9, 90.4)	<0.001
Procalcitonin, mean (SD)	0.1 (0.3)	0.4 (0.9)	<0.001
Ferritin, median (IQR)	112.9 (26.7, 293.4)	380.2 (187.0, 721.2)	<0.001
Alanine aminotransferase, mean (SD)	32.5 (29.5)	47.5 (74.5)	<0.001
Aspartate aminotransferase, mean (SD)	26.3 (20.9)	52.0 (61.8)	<0.001
Alkaline phosphatase, mean (SD)	73.3 (32.8)	91.5 (77.5)	<0.001
Troponin, median (IQR)	3.4 (0.4, 6.3)	13.1 (5.4, 20.7)	0.011

IQR: Interquartile Range, SD: Standard deviation

When we look at the results of the logistic regression analysis, it was seen that the clinical demographic parameters, age, chronic renal failure and cancer diagnosis, high lactate dehydrogenase and ferritin levels, and low lymphocyte count were the only independent risk factors in predicting the intensive care unit admission of the patients (**Table 3**). The bars showing the relationship between age and gender distribution and the intensive care unit are presented in **Figure 1**, and the trends of LDH, lymphocyte count and ferritin levels are presented in **Figure 2A, 2B, 2C**.

**Figure 1.** Non-intensive care unit (ICU) vs ICU patients' distributions according to sex and age subgroups**Table 3.** Predictors of ICU patients according to multivariable logistic regression analysis

	Adjusted odds ratio (95% confidence interval)	p value
Age	1.094 (1.077-1.112)	<0.001
Chronic renal failure	4.735 (1.117-20.067)	0.036
Cancer	3.957 (1.225-12.776)	0.021
Lactate dehydrogenase	1.006 (1.003-1.008)	<0.001
Lymphocyte	0.879 (0.789-0.980)	0.021
Ferritin	1.000 (1.000-1.001)	0.001

**Figure 2B.** Dynamic trends of Lymphocyte count according to Non-intensive care unit (ICU) and ICU patients up to 14-days**Figure 2A.** Dynamic trends of Lactate Dehydrogenase according to Non-intensive care unit (ICU) and ICU patients up to 14-days**Figure 2C.** Dynamic trends of Ferritin according to Non-intensive care unit (ICU) and ICU patients up to 14-days

DISCUSSION

According to the results of this study, age, additional morbidities such as chronic kidney failure and cancer, and laboratory data, high lactate dehydrogenase and ferritin and low lymphocyte count alone are independent risks in predicting whether patients who are admitted to the emergency department with the diagnosis of COVID-19 and hospitalized will need intensive care or not. factor was found. The fact that it included a fairly sufficient number of patients and that different parameters were found to be independent risk factors in predicting intensive care admission are the peculiarities of our study.

In the literature, there are different studies on the parameters taken during the intensive care unit admission of COVID-19 patients. In some studies, diabetes and HbA1c are predictive, and some studies have shown that pneumonia and chronic lung problems are important in ICU admission (7,8). Age is also seen in the studied and published data among these parameters. Many parameters can be used to decide on the hospitalization of patients in adverse situations such as in cases where there are too many patient admissions, the number of beds is insufficient, and the limited usage conditions. Some of these can be added as troponin, lung radiology and clinical findings (8,9). Although clinical findings are at the forefront in intensive care admission, it may be useful to look at additional parameters and make decisions based on independent risk factors in places with limited number of beds. For this reason, the results of our study can support healthcare professionals serving the emergency department in their decision-making and can be used during practical applications in predicting intensive care admission.

In the study of Luo et al. (10), age, neutrophil and platelet count were found to be significantly correlated with CRP and severe disease and poor prognosis. Similarly, in the study of Marin et al. (11), increased age was shown to be associated with lymphopenia and chronic renal failure suffocation, mortality and poor prognosis. In the same study, an increase in LDH, which indicates cellular injury, is associated with mortality and poor prognosis. Covino et al. (12) similar to other studies in the literature, it was shown that advanced age is closely related to intensive care unit admission and mortality. Wu et al. (13) found a close relationship between ferritin level and the development of ARDS in patients with COVID-19 pneumonia. Similarly, Şan et al. (14) found that the complete blood count parameters can help to identify and classify COVID-19 patients into non-severe to severe groups.

In the study conducted by Carlino et al. (5), a significant relationship was found between patients with a history of cancer and admission to intensive care unit. In the study of Hu et al. (15), no significant difference was found between

comorbidities (anemia, cancer, hypertension, diabetes, coronary heart disease, chronic obstructive pulmonary disease, cerebral infarction) and serious disease. We attributed this situation to the small number of patients included, unlike our study. Lee et al. (16) in his study, a significant correlation was found between patients with a history of lymphopenia, cancer, and chronic renal failure and mortality. Similarly, Bhargava et al. (17) found a significant relationship between chronic renal failure and severe disease in their study.

This study may have some limitations, one of them being a retrospective study, but the sufficient number of cases is an important factor in closing this gap. The high number of patients in our hospital, the high number of emergency service applications and the large bed capacity can be counted as the strengths of our study.

CONCLUSION

This study revealed that age, chronic renal failure, and cancer are the only independent risk factors in predicting intensive care admission for patients admitted to the emergency department with the diagnosis of COVID-19, and that high LDH, ferritin levels, and low lymphocyte count are laboratory independent risk factors.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara City Hospital No. 2 Clinical Research Ethics Committee (Date: 14.07.2021, Decision No: E2-21-739).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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