



# How electrolyte values affect COVID-19 patients at the time of application to the hospital?

## Hastaneye başvuru sırasında elektrolit değerleri COVID-19 hastalarını nasıl etkiler?

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### ABSTRACT

**Aim:** COVID-19 disease is life threatening. we aimed to evaluated the effect of electrolyte disturbances on the course of COVID-19 disease. **Material and methods:** Patients hospitalized with the diagnosis of COVID-19 were included in the study. Demographic characteristics, comorbidities, symptoms, clinical course, and laboratory parameters were recorded. **Results:** Totally 130 COVID-19 patients, 70 (54%) of whom were female, were included in the study. The mean age was  $56.6 \pm 16.4$  years. The most common symptom was cough (57%) and the accompanying disease hypertension (45%). 68% of the patients had hyponatremia and 29% had hypocalcemia. 95% of the patients were discharged. 5% died. There was a relationship between the need for oxygen and advanced age, male gender, presence of diabetes mellitus, cardiovascular disease, bilateral involvement in chest CT, lymphopenia, CRP, low calcium level, hypocalcemia, and secondary infection ( $p = 0.024$ ,  $p = 0.001$ ,  $p = 0.030$ ,  $p = 0.045$ ,  $p = 0.002$ ,  $p = 0.010$ ,  $p = 0.000$ ,  $p = 0.022$ ,  $p = 0.048$ ,  $p = 0.001$ , respectively). There was a relationship between the need for intensive care, male gender, low calcium level, hyponatremia conclusion the presence of secondary infection. (respectively,  $p = 0.045$ ,  $p = 0.023$ ,  $p = 0.011$ ,  $p = 0.001$ ). There was a correlation between the duration of hospitalization and low calcium level and low sodium level ( $p = 0.026$ ,  $p = 0.022$ ). **Conclusion:** The severity of COVID-19 appears to be associated with low serum sodium and calcium concentrations, and regular electrolyte monitoring can be useful in follow-up.

**Keywords:** COVID-19; electrolyte; oxygen support

### Öz

**Amaç:** COVID-19 hastalığı, yaşamı tehdit etmektedir. Şiddetli hastalık seyrini ön görmek, hastalık takibinde önemlidir. Çalışmamızda elektrolit bozukluklarının COVID-19 nedeniyle hastaneye yatırılan hastaların klinik seyrine etkisini değerlendirmeyi amaçladık. **Materyal ve metod:** COVID-19 tanısı alan ve 11.03.2020-30.05.2020 tarihleri arasında yatarak tedavi gören hastalar çalışmaya alındı. Demografik özellikler, komorbiditeler, semptomlar, klinik seyir, laboratuvar parametreleri ve tedaviler kaydedildi. **Sonuç:** Çalışmaya 70'i (% 54) kadın 130 COVID-19 hastası dahil edildi. Ortalama yaş  $56.6 \pm 16.4$  yılı. En sık görülen semptom öksürüktü (% 57). En sık eşlik eden hastalık hipertansiyondu (% 45). Hastaların% 68'inde hiponatremi ve% 29'unda hipokalsemi vardı. Hastaların% 95'i tam iyileşme ile taburcu edildi, % 5'i öldü. Oksijen ihtiyacı ile ileri yaş, erkek cinsiyet, diabetes mellitus varlığı, kardiyovasküler hastalık, göğüs tomografisinde bilateral tutulum, lenfopeni, CRP, düşük kalsiyum seviyesi, hipokalsemi ve sekonder enfeksiyon arasında anlamlı bir ilişki vardı (sırasıyla  $p = 0.024$ ,  $p = 0.001$ ,  $p = 0.030$ ,  $p = 0.045$ ,  $p = 0.002$ ,  $p = 0.010$ ,  $p = 0.000$ ,  $p = 0.022$ ,  $p = 0.048$ ,  $p = 0.001$ ). Yoğun bakım ihtiyacı, erkek cinsiyet, düşük kalsiyum seviyesi, hiponatremi ve ikincil enfeksiyon varlığı arasında anlamlı bir ilişki vardı. (sırasıyla,  $p = 0.045$ ,  $p = 0.023$ ,  $p = 0.011$ ,  $p = 0.001$ ). Hastanede kalış süresi ile düşük kalsiyum seviyesi ve düşük sodyum seviyesi arasında anlamlı ilişki vardı ( $p = 0.026$ ,  $p = 0.022$ ). **Tartışma:** COVID-19'un şiddeti, düşük serum sodyum ve kalsiyum konsantrasyonları ile ilişkili görünmektedir, COVID-19 hastalarının takibinde düzenli elektrolit takibi faydalı olabilir.

**Anahtar kelimeler:** COVID 19, Elektrolit, oksijen desteği

## INTRODUCTION

The new type of coronavirus, which emerged at the end of 2019 and spread all over the world, has become a pandemic. The rapid spread of the virus infection that causes COVID-19, causing severe cases of pneumonia, incurability and fatal course make the impact of the virus important. Common symptoms of COVID-19 are fever, cough, and shortness of breath. It may cause various infection findings from asymptomatic to severe pneumonia (1). It has been shown that more than 75% of patients have kidney involvement during the course of COVID-19 disease (2). The most common forms of kidney involvement in COVID-19 are acute kidney damage, proteinuria, hematuria, and electrolyte imbalances (2, 3). In several studies, lower sodium (Na), potassium (K), and calcium (Ca) concentrations have been found to be associated with severe disease (3). However, data are limited. Therefore, we aimed to evaluate the effect of Na, K, and Ca serum concentrations on the course of COVID-19.

## MATERIALS AND METHODS

Patients diagnosed with COVID-19 in our hospital between 11.03.2020 and 30.05.2020 were included in the study. Real-time reverse transcriptase-polymerase chain reaction test (rRT-PCR) for SARS-CoV-2 was applied to all patients presenting with findings suggestive of COVID-19 disease with nasopharyngeal and oropharyngeal samples. All patients with symptoms suggestive of COVID-19 were evaluated by chest computed tomography. The presence of ground glass opacities and areas of consolidation were determined as findings consistent with COVID-19 disease. Patients with positive rRT-PCR test for SARS-CoV-2 and / or typical lung tomography findings for COVID-19 disease were included in the study.

Demographic characteristics (gender, age), chronic diseases (hypertension (HT), diabetes mellitus (DM), chronic kidney disease (CKD), asthma, chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF)), coronary vascular diseases (CVD such as myocardial infarction, angina pectoris and documented coronary heart disease, hospitalization symptoms (cough, fever, shortness of breath, diarrhea, vomiting, nausea, abdominal pain, myalgia, conjunctivitis, loss of smell / taste), need for oxygen supply (in room air) oxygen saturation <93%), history of secondary infection, need for intensive care, laboratory data (WBC, neutrophil, lymphocyte, platelet, CRP (C-reactive protein), albumin, Na, K, Ca, chest tomography, treatments, clinical outcome (death, recovery) , duration of hospitalization was evaluated.

Leukocytosis, neutrophilia, lymphopenia, increased CRP, defined according to the normal ranges given in the hospital laboratory as: white blood > 10800 u / L cells, leukocytosis; neutrophil count > 7700 u / L, neutrophilia; lymphocyte count 1300 u / L, lymphopenia; platelet count <130000 u / L, thrombocytopenia and CRP > 3 mg / L increased CRP value. The normal range of albumin was 3.5 g / dl - 5.2 g / dl, the normal range for Na was 136 mmol/L - 146 mmol/L, the normal range for K was 3.5 mmol/L – 5.1 mmol/L, the normal range for Ca was 8.4 mg/dl – 10.6 mg/dl Treatments as recommended in the COVID-19 treatment protocol of the Ministry of Health (4).

## Statistical Analysis

Data were analyzed using the SPSS 21.0 statistical program (IBM corp. Released 2012. IBM SPSS statistics for windows, Version 21.0. Armonk, NY: IBM Corp). A p-value of less than 0.05 was accepted as the statistical significance limit. Numerical variables were given as mean  $\pm$  standard deviation for normally distributed variables and as medians for skewed continuous variables. Categorical variables are shown as frequency. A Chi-square test was used to evaluate categorical data. In the analysis of continuous variables, independent sample T-test and Mann Whitney U were used appropriately considering the distribution of the data. Kartal Dr. Lütfi Kırdar City Hospital Clinical Research Ethics Committee approved. (Decision number: 2020/514/180/4)

## RESULTS

We included 130 COVID 19 patients, 70 (54%) were female and 60 (46%) were male. The mean age was  $56.6 \pm 16.4$  (median: 57.5) years. 82 patients (63%) had positive rRT-PCR. All the patients had computerized tomography findings consistent with COVID-19 disease. 79% of patients had bilateral lesions, 22% had multiple unilateral lesions and 13% had unilateral one lesion compatible with COVID-19 disease. The most common symptoms were cough (in 76 patients, 59%), and fever (in 60 patients, 46%). The most common comorbidities were HT (in 58 patients, 45%) and DM (in 53 patients, 41%).

White blood cell values were high in 14 % (18 patients), the mean white blood cell value was 7220 u/L. 48% (63 patients) were lymphopenic, the mean lymphocyte value was 1346 u/L. The neutrophil values were high in 17% (22 patients), the mean neutrophil value was 4810 u/L. Platelet values were low in 9% (in 12 patients), the mean platelet value was 204.884 u/L. CRP values were high in 85% (in 110 patients), and the average CRP value was 36.1 mg /L. Na value was low in 32% of patients (41 patients), K value was low in 4% of patients (5 patients), and Ca value was low in 26% of patients (34 patients). There was no patient with high Na level. K value was high in 4% of patients (5 patients) and Ca value were high in 1% of patients (1 patient).

Oxygen support was required in 38% of the patients (49 patients) during follow-up. The mean age and male gender were significantly higher in patients who needed oxygen than those who did not need oxygen. (60.6 years, 65% vs 52.2 years, 35%, respectively,  $p = 0.001$ ,  $p = 0.019$ ). DM and CVD were frequently accompanying patients in need of oxygen (57%, 24% versus 31%, 11%;  $p = 0.003$ ,  $p = 0.045$ ). In addition, the presence of bilateral lesions in chest tomography was significantly higher in patients who needed oxygen (94% versus 70%;  $p = 0.009$ ). Among the laboratory parameters studied, the mean lymphocyte count and Ca values of the patients who needed oxygen were significantly lower than the patients who did not need oxygen (1110 u / L, 8.6 mg / L versus 1490 u / L, 8.8 mg / L, respectively;  $p = 0.004$ ,  $p = 0.022$ ). The CRP value was

found approximately 2 times higher in patients who needed oxygen than in patients who did not need oxygen (53.7 mg / L versus 25.6 mg / L, respectively;  $p = 0.002$ ). Hypocalcemia was significantly higher in patients who did not require oxygen (63% versus 10%  $p = 0.048$ ). Secondary infections were more common in patients who needed oxygen than those who did not (27% vs 0.1%;  $p = 0.00$ ) 11% of the patients (14 patients) needed intensive care during follow-up. Male gender was more common in patients who needed intensive care than patients who did not need intensive care (71% versus 43%;  $p = 0.045$ ). Ca values were significantly lower in patients who did not need intensive care (8.4 mg / L versus 8.7 mg / L;  $p = 0.023$ , respectively). Hyponatremia and secondary infections were more common in patients who needed intensive care than patients without intensive care (27%, %42 vs 64%, 7%;  $p = 0.011$ ,  $p = 0.001$ , respectively)

The duration of hospitalization was associated with low calcium level and low sodium level. ( $p = 0.026$ ,  $p = 0.022$ ). Looking at the results, 123 patients (95%) were discharged with full recovery. Seven patients died of acute respiratory distress syndrome (ARDS) development and shock. There was no significant relationship between white blood cell, neutrophil, thrombocyte, and potassium values in terms of oxygen demand or need for intensive care. The demographic characteristics and basic clinical characteristics of the study population regarding oxygen demand are detailed in table 1.

## DISCUSSION

Since COVID-19 is a new disease that affects the whole world, data on the course of the disease are needed to help and guide clinicians. Electrolyte disturbances are a parameter that affects the course and follow-up of infectious diseases. Therefore, although the number of patients in this study is limited, it is one of the studies with a relatively high number of patients and may contribute to the limited evidence in this area (1,3,5,6).

The mean age in our study was  $56.6 \pm 16.4$  years. Average age comparable to other COVID-19 studies (51-70 years) (7,8,9). More than half (70%) of the patients in our study were women. The gender distribution varies according to the study (10,13). In addition, as in many studies, age and male gender were found to be associated with the need for intensive care and oxygen need (7,13-15).

In the first weeks of the outbreak, PCR tests were concluded within 48-72 hours due to the limited diagnostic capacity of laboratory tests. Therefore, all patients with suspected COVID 19 symptoms in our center received a CT scan to make a faster diagnosis. Most of our patients had findings consistent with COVID-19 in their radiographic images. Consistent with the literature, the findings are bilateral and the presence of consolidation has been associated with the need for intensive care (6,16,18).

The most common symptoms of COVID-19 in our study were fever and cough. This is similar to other studies (10,11). In our study, the most common accompanying diseases in the patient group were HT and DM, and in accordance with the literature, oxygen demand was significantly higher in patients with DM and CVD (7,9,19).

We analyzed the factors associated with the need for oxygen support and intensive care. Lymphopenia hyponatremia and high CRP were the most common abnormal laboratory parameters in our patients. In general population studies, severe COVID-19 disease and the need for intensive care have been associated with leukocytosis, lymphopenia, neutrophil elevation, trombocytopenia and increased CRP (9,11,12,14,19). In our study, a statistically significant relationship was found between lymphopenia and CRP between the need for intensive care and oxygen supply and the factors mentioned above. Lack of statistical significance with other laboratory parameters is probably the result of a small number of patients, which limits statistical analysis results.

In a meta-analysis, sodium and potassium levels were significantly lower in severe COVID-19 (3). Another study found that sodium, potassium, and chloride levels have high predictive power for COVID-19 to progress to severe disease (20). In a different study, lower basal sodium, chloride and higher mortality were associated with higher ICU and MV requirements and longer duration of hospitalization, and hyponatremia was frequent electrolyte disturbances (6,21). The most common electrolyte disorder in our study was hyponatremia and was related to the need for intensive care.

In one study, it has been shown that sodium levels are inversely related to cytokine storm and IL-6 levels. It can be thought that low sodium levels will be an indirect sign of increased IL-6 levels and may be associated with the severe disease phenotype (22). Studies have found that low calcium levels are associated with poor prognosis and longer duration of hospitalization in COVID-19 disease (6). In our study, too, hypocalcemia was associated with oxygen demand and long duration of hospitalization. Calcium deficiency may be due to insufficient intake or insufficient absorption as a result of nausea and diarrhea that develops due to gastrointestinal system involvement of COVID-19.

In addition, tissue and organ hypoxia caused by the disease during the course of COVID-19 may contribute to hypocalcemia by causing cell membrane damage and calcium entry into the cell (23). In addition, renal hypoxia, endothelitis, proximal tubule damage and angiotensin converting enzyme 2 up regulation in kidney tissue caused by coagulation disorders associated with COVID-19 may cause electrolyte abnormalities (24,25). In addition, inappropriate anti-diuretic hormone syndrome that may accompany viral pneumonias also contributes to electrolyte abnormalities (26).

Our study has some limitations. The low number of patients studied should be stated as a limitation. However, despite the small number of patients, clinicians interested in managing this patient group should be informed. In addition, diagnostic tests could not be performed to rule out other possible atypical pneumonia pathogens due to the high patient

**Table 1.** The features of the patients stratified by the oxygen support in the follow-up.

Parameters	Oxygen support (-)	Oxygen support (+)	Total	p value
	n: 81	n: 49	n: 130	
<b>Demographic features</b>				
Age	52.2±16.3 (54)	60.6 ±16.3 (64)	56.6±16.4 (56)	0.024
<b>Sex</b>				0.001
Female, n (%)	53 (65)	17(35)	70(54)	
Male, n (%)	28(35)	32(65)	60(46)	
DM, n (%)	25(31)	28(57)	53(41)	0.003
Hypertension, n (%)	32(40)	26(53)	58(45)	0.148
CHF, n (%)	4(5)	3(6)	7(5)	1.000
CVD, n (%)	9(11)	12(24)	21(16)	0.045
CKD, n (%)	8(10)	9(18)	17(13)	0.186
Astma, n (%)	7(9)	4(8)	11(9)	1.000
COLD, n (%)	2(3)	2(4)	4(3)	0.632
<b>Clinical characteristics</b>				
Dispne, n (%)	12(5)	18(37)	30(23)	0.005
Fever, n (%)	36(44)	24(49)	60(46)	0.631
Cough, n (%)	31(38)	26(53)	76(59)	0.368
Nausea, n (%)	3(4)	6(12)	9(7)	0.080
Vomiting, n (%)	2(2)	3(6)	5(4)	0.365
Diarrhoea, n (%)	4(5)	3(6)	7(5)	0.243
Myalgia, n (%)	11(14)	3(6)	14(11)	0.300
Weakness, n (%)	19(23)	15(31)	34(26)	0.413
Headache, n (%)	5(6)	1(2)	6(5)	1
Abdominal pain, n (%)	2(2)	5(10)	7(5)	0.103
Ageusia, n (%)	0	3(6)	3(4)	0.290
<b>Intensive care follow up, n(%)</b>	0	14(29)	14(11)	0.000
<b>Treatment regimens</b>				0.001
Hidroksiklorokin, n (%)	81(100)	49(100)	130(100)	
Favipiravir, n (%)	3(4)	27(55)	30(23)	
<b>Secondary infection, n (%)</b>	1(1)	13(27)	14(11)	0.000
<b>Discharge time</b>	5.3 ± 3.6	10.6 ± 6 (7.5)	7.35 ±5.3	0.000
<b>Mortality, n (%)</b>	0(0)	7(14)	7(5.4)	0.000
<b>Imaging features</b>				
Unilateral, single focus, n (%)	16(20)	1(2)	17(13)	
Unilateral, multiple focus, n (%)	5(6)	2(4)	7(5)	
Bilateral involvement, n (%)	57(20)	46(94)	103(79)	
Ground-glass opacities, n (%)	73(90)	48(98)	121(93)	0.152
Consolidation, n (%)	24(30)	17(35)	41(32)	0.564
<b>Laboratory findings</b>				
Hemoglobin, g/dl	12.9 ± 1.5 (13)	13 ± 1.9 (13.6)	12.9 ± 1.6 (13)	0.834
WBC, u/L	7206 ± 6477	7744 ± 3468	7220 ± 5522	0.969
Neutrophils, u/L	4518 ± 3735	5294 ± 3322	4810 ± 3591	0.234
Lymphocytes, u/L	1490 ± 837	1110 ± 475	1346 ± 743	0.004
Platelets, u/L	211444 ± 70364	194040 ± 56213	204884 ± 65711	0.144
CRP, mg/dl	25.5 ± 31.3	53.7 ± 57.7	36.2 ± 45.1	0.002
Na, mmol/L	137.1 ± 3	136.1 ± 3.5	136 ± 2.5	0.081
K, mmol/L	4.1 ± 0.4	4.1 ± 0.5	4.1 ± 0.4	0.930
Ca, mg/dl	4.8 ± 0.6	8.6 ± 0.5	8.7 ± 0.6	0.022
Albumin, g/dl, f	3.7 ± 0.5	3.5 ± 0.5	3.7 ± 0.5	0.094

CHF: Congestive heart failure, CVH: Coronary vascular diseases, COLD:Chronic obstructive lung disease, DM: Diabetes Mellitus, CKD: Chronic kidney disease, WBC: White blood cell CRP: C- reactive protein, Na: Sodium, K: Potassium, Ca: Calcium, f: 100 patient. Data are given as (mean±SD) (median)

load during the pandemic process. Another point is that the rRT-PCR test for SARS-CoV-2 was not positive in all study patients. However, all patients with negative rRT-PCR tests had typical lesions suggestive of COVID-19 disease on their CT. We evaluated a limited number of electrolyte effects on disease prognosis. We did not evaluate the etiology of electrolyte abnormalities due to the high patient load. Only hospitalized persons were included in the study. Therefore, the data are not representative of all COVID-19 patients.

As a result, low Na and low Ca levels in COVID-19 patients may be indicative of poor prognosis and long duration of hospitalization. Therefore, it has been concluded that the evaluation of the patients' electrolytes may be useful in the follow-up of COVID-19.

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