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Investigation of the Effect of COVID-19 on Kidney Functions

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Abstract: COVID-19 disease, which first appeared in Wuhan, China and affected the whole world, often affects the kidneys as well as the lungs. Acute kidney injury (AKI) is frequently seen in severe patients and its pathophysiology has not yet been fully elucidated. In our study, 336 patients were included and divided into two groups as AKI negative (n:299) and AKI positive (n:37). There were 196 males and 103 females in the AKI negative group, and 31 male and 6 female patients in the AKI positive group. The mean age of the AKI negative group was 56.63±14.64 years and the mean age of the AKI positive group was 66.08±17.81 years, showing a statistically significant difference ($p<0.05$). Among the blood parameters, lymphocyte count, monocyte count, blood urea nitrogen, creatinine, sodium, potassium, albumin, CRP, ferritin, procalcitonin and pro-BNP showed statistically significant differences ($p<0.05$) between the groups. In conclusion, we think that advanced age and male gender are important in the development of AKI in COVID-19 patients, and that inflammatory parameters and clinical severity may guide differentiation from the AKI negative group.

Keywords: COVID-19, Renal function, Inflammation

COVID-19'un Böbrek Fonksiyonları Üzerindeki Etkisinin Araştırılması

Özet: 2019 yılında Çin'in Wuhan kentinde ortaya çıkan ve tüm dünyayı etkisi altına alan yeni tip koronavirüs (COVID-19), esas olarak solunum sistemini etkilemektedir. Böbrek tutulumunun patofizyolojisi kesin olarak bilinmemekle birlikte hastalarda akut böbrek hasarı (AKI) sıklıkla izlenmektedir. Çalışmamıza 336 COVID-19 pozitif hasta dâhil edilerek AKI negatif (n:299) ve AKI pozitif (n:37) olmak üzere iki gruba ayrıldı. AKI negatif grupta 196 erkek ve 103 kadın, AKI pozitif grupta 31 erkek ve 6 kadın hasta saptandı. AKI negatif grubun yaş ortalaması 56,63±14,64 yıl ve AKI pozitif grubun yaş ortalaması 66,08±17,81 yıl olup istatistiksel olarak anlamlı bir farklılık tespit edildi ($p<0,05$). Kan parametrelerinden lenfosit sayısı, monosit sayısı, kan üre azotu, kreatinin, sodyum, potasyum, albümin, CRP, ferritin, prokalsitonin ve pro-BNP gruplar arasında istatistiksel olarak anlamlı farklılıklar gösterdi ($p<0,05$). Sonuç olarak, COVID-19 hastalarında AKI gelişiminde ileri yaş ve erkek cinsiyetin önemli olduğunu, inflamatuar parametrelerin ve klinik şiddetinin AKI gelişiminin takibinde yararlı olabileceği kanaatini taşımaktayız.

Anahtar Kelimeler: COVID-19, Böbrek fonksiyonu, İnflamasyon

INTRODUTION

The coronavirus disease-2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, which was first detected in Wuhan, spread rapidly and affected the whole World (1). The respiratory system is often affected in people who develop the disease in response to

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SARS-CoV-2. However, the virus can also affect other organs in the body. The virus can directly damage these organs by binding to Angiotensin-Converting Enzyme 2 (ACE2) receptors in vascular endothelial cells, lungs, heart, brain, kidneys, intestine, liver, and other tissues. In addition, systemic effects caused by the virus can cause dysfunction in organs (2).

The virus can localize in the kidneys, especially in glomerular cells, tubular epithelium and podocytes. Acute kidney injury (AKI) can often be seen in patients with severe clinical symptoms (3). In our study, we wanted to investigate the effect of COVID-19 on kidney functions and its relationship with inflammatory parameters.

MATERIALS and METHODS

Our study was approved by the local ethics committee of our faculty (80576354-050-99/205) after it was approved by the Republic of Turkey Ministry of Health COVID-19 Scientific Research Evaluation Commission. Our study was conducted in accordance with the Declaration of Helsinki and a written informed consent form was signed by each participant.

A total of 336 participants were included in this study. The only criterion for the participants was the diagnosis of SARS-CoV-2 positive by Real-Time PCR technique. After the diagnosis of SARS-CoV-2 was made, both lung Computed Tomography (CT) scanning was performed and laboratory results were evaluated.

Blood samples were taken immediately after the diagnosis of SARS-CoV-2. Blood samples (approximately 6-7 ml) taken from the participants were taken into blood tubes and centrifuged at 4100 rpm for 15 minutes. Serum samples were separated and stored at -80 ^{o}C until the study day. Biochemical parameters with COBAS c 501 autoanalyzer, hematological parameters were measured with Pentra (xxx) automatic complete blood count device.

AKI was defined according to the Kidney Disease Improvement Global Outcomes (KDIGO) criteria: a change in serum creatinine of 0.3 mg/dL over 48 hours or a 50% increase in baseline creatinine. Serum creatinine was considered baseline creatinine within 7-365 days prior to admission. Serum creatinine values were recorded for all patients during their hospitalization and hospital stay. The definition of AKI was made by comparing creatinine values at or during hospitalization with baseline serum creatinine values.

Data were analyzed using SPSS 20.0 statistical software (IBM, USA). For descriptive statistics, number (n), percentage (%), mean and standard deviation (SD) values were used. Independent sample t-test or Mann-Whitney U test was used to compare numerical variables.

RESULTS

In our study, 336 patients were included and divided into two groups as AKI negative and AKI positive. There were 196 male and 103 female patients in the AKI negative group, and 31 males and 6 females in the AKI positive group. Gender distribution between the groups showed a statistically significant difference ($p<0.05$). The mean age of the AKI negative group was 56.63 ± 14.64 years and the mean age of the AKI positive group was 66.08 ± 17.81 years, showed a statistically significant difference ($p< 0.05$). Among the blood parameters, the lymphocyte count, monocyte count, blood urea nitrogen, creatinine, sodium, potassium, albumin, CRP, ferritin, procalcitonin and pro-BNP showed statistically significant differences between the groups (Table 1).

Table 1. Values of laboratory parameters between the groups.

	Acute kidney injury negative group	Acute kidney injury positive group	P value
Gender	196 male (65.6%) 103 female (34. 4%)	31 male (83.8%) 6 female (16.2%)	0,01
Mean age (Years)	56.63±14.64	66.08±17.81	0.006
White blood cell count (10^3/mm)	7140±6769	5532±1576	0.140
Neuthrophil count (10^3/mm)	4.94±2.97	4.22±1.38	0.597
Lymphocyte count (10^3/mm)	1.41±4.65	8.2±0.44	0.000
Monocyte count (10^3/mm)	0.53±0.43	0.38±0.19	0.000
Blood urea nitrogen (mg/dL)	15.45±8.92	38.91±12.66	0.000
Creatinine (mg/dL)	0.98±0.42	1.84±0.61	0.000
Sodium (mmol/L)	137.68±4.09	135.59±3.27	0.003
Chloride (mmol/L)	98.05±4.32	98.49±4.35	0.351
Potassium (mmol/L)	4.33±0.57	4.99±0.72	0.000
Platelet count (10^3/mm)	216±87	195±55	0.400
Total protein (g/dL)	7.16±0.63	7.14±0.40	0.162
Albumin (g/dL)	3.94±0.55	3.67±0.41	0.000
C-reactive protein (mg/L)	70.27±68.18	130.97±98.38	0.001
Procalsitonin (ng/ml)	0.32±0.93	0.15±0.13	0.160
Ferritin (ng/ml)	597.30±831.22	1489.37±1132.76	0.000
Pro-BNP (pg/ml)	608.40±1795.42	2386.91±4408.24	0.005

When the vital values of the patients participating in our study were compared according to the groups, sPO2, diastolic blood pressure, respiratory rate and body temperature were statistically significantly different between the groups (Table 2).

Table 2. Comparison of vital parameters between groups.

	Acute kidney injury negative group	Acute kidney injury positive group	P value
CT negative/positive	163/138	7/30	0.000
sPO2	94.08±4.67	91.67±3.27	0.000
Systolic blood pressure	129.53±17.76	123.45±18.91	0.089
Diastolic blood pressure	77.70±11.29	72.43±12.33	0.033
Pulse rate	96.10±14.17	95.76±11.77	0.903
Respiratory rate	20.18±4.66	26.76±6.26	0.000
Body temperature	37.39±0.93	37.88±0.87	0.001

DISCUSSION

COVID-19 can be followed in different clinics, from asymptomatic infection or self-limiting flu-like illness to very serious clinics such as sepsis, acute hypoxic respiratory failure (AHRF), acute respiratory distress syndrome (ARDS), coagulopathy (5). It is thought that the SARS-CoV-2 virus exerts its effects in the body through the angiotensin converting enzyme 2 (ACE2) receptor by interacting with the renin angiotensin aldosterone system (RAAS). ACE2 receptors are located in the respiratory tract, as well as in the heart, intestines and kidneys (6,7).

In a systematic review and meta-analysis involving 20 cohorts of 13.137 patients diagnosed with COVID-19, the prevalence of AKI was 17%, compared with 11% in our study (8). In the study of Arıkan

et al. (2021), with 578 patients, male gender was found to be more common in all AKI groups and age was associated with the severity of AKI (9). In our study, the male gender was more dominant and the mean age of the AKI positive group was higher. Similar to our data, in another study carried out on 99 patients to define the factors related to the development of AKI in Mexico, advanced age was found to be associated with the development of AKI and it was reported that the development of AKI was higher in patients with severe clinical symptoms (10). In our study, the development of AKI was higher in pulmonary CT positive individuals than in negative ones.

Hypoxia, ischemia and nephrotoxicity are known as the most accused factors in the development of AKI. The kidneys are particularly susceptible to ischemia and toxins resulting from vasoconstriction, endothelial damage, and triggering of inflammatory processes (11). A significant relationship between the development of AKI and respiratory failure in severe COVID-19 patients has been reported previously (12), and the vital findings in our study also support this view.

In the study of Casas-Aparicio et al. (2021), laboratory parameters in the group developing AKI were found to be high in CRP, procalcitonin, and low in lymphocyte levels, similar to our study. This situation was associated with the virus increasing the release of proinflammatory cytokines, increasing inflammatory parameters and decreasing lymphocytes through apoptosis, and it was stated that the retention of lymphocytes in the lung may be another reason (10).

CRP, an acute phase protein, is produced by the liver and many inflammatory cells. Acute inflammation is frequently used as a biomarker in clinical diagnosis. Similar to the study stating that AKI positive COVID-19 patients showed higher serum CRP levels than AKI negative patients and that serum CRP levels could be used as a risk factor for AKI in COVID-19 patients (13), in our study, CRP was found to be statistically significantly higher in the AKI positive group.

Similar to the thought that some cytokines released by lung injury in COVID-19 patients, especially IL-6, may cause an increase in alveolar capillary permeability and pulmonary hemorrhage, and even cause end organ dysfunction by causing damage to the vascular endothelium in the kidneys (14), inflammatory parameters were found to be higher in the AKI positive group. Endothelial damage, third space fluid loss and hypotension trigger renal hypoperfusion and may impair hemodynamics. Impaired hemodynamics may cause hyperkalemia in AKI-positive patients, as in our study, and briefly suggest that there may be many reasons for the development of AKI.

As a result, we think that advanced age and male gender are important in the development of AKI in COVID-19 patients, and that inflammatory parameters and clinical severity can guide the differentiation from the AKI-negative group, and that further studies may contribute to the elucidation of the development of AKI.

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