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Clinical Features of COVID-19 Hospitalized Patients with and without Chronic Kidney Disease: A Single-Center, Cross-Sectional Study

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ABSTRACT

Background and Objectives: The severity and mortality of coronavirus disease 19 (COVID-19) caused by severe acute respiratory syndrome coronavirus-2 are positively associated with underlying diseases such as hypertension, diabetes, and chronic kidney disease (CKD). In this regard, the current study aimed to evaluate the clinical characteristics, laboratory findings, and outcomes of coronavirus disease 2019 (COVID-19) hospitalized patients with and without CKD.

Methods: This cross-sectional matched study was conducted on hospitalized confirmed COVID-19 patients with and without CKD admitted to Baqiyatallah Hospital in Tehran, Iran, from February 26, 2020 to March 26, 2020. The patients were homogenized in terms of age, gender, body mass index, and underlying diseases such as hypertension and diabetes. Demographic data, clinical symptoms, and laboratory and radiological findings were collected from patients' medical records and compared between the patients based on their CKD status.

Results: Among the COVID-19 patients, 56 and 97 cases with and without CKD were investigated, respectively. In general, 111 (72.5%) patients with a mean age of 55 years were males. Patients with CKD had higher levels of blood urea nitrogen, creatinine, and red cell distribution width ($p<0.05$). No differences were found regarding chest computed tomography findings, ICU admission, and death among COVID-19 patients with and without CKD.

Conclusions: Overall, the findings support the use of red cell distribution width, blood urea nitrogen, and creatinine for monitoring the COVID-19 patients with CKD and assessing the risk of disease progression. Eventually, managing comorbidities including hypertension and diabetes will reduce COVID-19 severity in CKD patients.

Keywords: chronic kidney disease, clinical characteristics, COVID-19, hospitalized

INTRODUCTION

A wide variety of individuals worldwide have been affected by the coronavirus disease 19 (COVID-19) pandemic, which is due to severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The virus has led to 140,332,386 proved cases and over three million deaths by April 18, 2021 and the number is still increasing [1]. So far, there has been no approved antiviral agent against this infectious disease, and treatment methods are merely supportive and symptomatic [2-4]. COVID-19 can cause a range of diseases from mild to severe respiratory tract infections and multiple organ dysfunctions and may be asymptomatically transmitted between people in some cases [2,5]. According to numerous reports, the severity and mortality of this pandemic are positively related to underlying diseases. Hypertension, chronic kidney disease (CKD), and diabetes are the most prevalent underlying diseases in patients with COVID-19, and severe cases are more likely to occur among these individuals [6-8].

In this regard, high angiotensin-converting enzyme 2 expression was reported to be a cell entry route for the SARS-CoV-2 in the kidney [9]. Furthermore, SARS-CoV-2 was found in urine and kidney tissues in some COVID-19 patients, indicating that the kidney is a potential target for the virus. In a study on 701 COVID-19 patients, blood urea nitrogen (BUN) and serum creatinine increased in 13.1% and 14.4% of patients, respectively. Further, 33.7% of patients with increased baseline

Table 1. Baseline demographics and clinical features of COVID-19 hospitalized patients with and without CKD

Characteristics	Patients, No. (%)		p-value*
	With CKD (n=56)	Without CKD (n=97)	
Age, y			0.26
Mean±SD	56.79±11.93	54.35 ± 13.20	
Min-Max	35-84	22-88	
Gender			0.54
Male	39 (69.6)	72 (74.2)	
Female	17 (30.4)	25 (25.8)	
BMI, kg/m^2			0.56
Mean±SD	29.15±6.96	28.53±5.12	
Min-Max	20.96-66.60	17.93-44.59	
Comorbidities			
Hypertension	23 (41.1)	31 (32.0)	0.26
Diabetes	24 (42.9)	33 (34.0)	0.28
Heart disease	14 (25.0)	18 (18.6)	0.32
Lung disease	8 (14.3)	7 (7.2)	0.16
Liver disease	12 (21.4)	11 (11.3)	0.08
Symptoms at admission			
Fever (temperature≥37.3 °C)	33 (58.9)	59 (60.8)	0.82
Cough	38 (69.9)	63 (64.9)	0.71
Dyspnea	39 (69.6)	59 (60.8)	0.27
Chest Pain	12 (21.4)	26 (26.8)	0. 46
Weakness	29 (51.8)	57 (58.8)	0. 40
Myalgia	27 (48.2)	62 (63.9)	0. 06
Chill	30 (53.6)	55 (56.7)	0. 71
Rhinorrhea	9 (16.1)	10 (10.3)	0. 30
Sore Throat	6 (10.7)	17 (17.5)	0. 26
Diarrhea	10 (17.9)	22 (22.7)	0. 48
Vomiting	18 (32.1)	41 (42.3)	0. 21
Sputum production	20 (35.7)	26 (26.8)	0. 25

Note. Min-max: Minimum-maximum; SD: Standard deviation; COVID-19: Coronavirus disease 2019; CKD: Chronic kidney disease; BMI: Body mass index. *p<0.05 is statistically significant

serum creatinine died [10], highlighting the importance of COVID-19 in patients suffering from preexisting renal disorders. But, there are limited data regarding the clinical characteristics of CKD patients, who are infected with COVID-19, for better controlling the disease. Therefore, the current work aimed at evaluating and comparing the laboratory results, clinical characteristics, and consequences of COVID-19 patients with and without CKD hospitalized in different medical centers.

METHODS

Participants and Study Design

This cross-sectional study included 153 consecutive adult patients with proved COVID-19 admitted to Baqiyatallah Hospital, which is a selected hospital for the treatment of COVID-19 patients by the government, from 12 March to 10 April 2020. Among the patients, 56 COVID-19 adults with CKD and 97 controls without CKD were homogenized with regard to age, body mass index, gender, and underlying diseases such as diabetes and hypertension. COVID-19 was detected based on the interim guidance, which was issued by the World Health Organization. All COVID-19 patients were confirmed by the reverse transcription-polymerase chain reaction for SARS-CoV-2 RNA with nasopharyngeal specimens, and the follow-up was performed for the clinical outcomes until 18 April 2020. The present work was conducted under the approval of the Ethics Committee of the Baqiyatallah University of Medical Sciences, Iran (IR.BMSU.REC.1399.171). Based on the retrospective design of this study, written informed consent forms were obtained from all patients.

Data Collection and Statistical Analysis

The demographic data, chest computed tomography (CT) scans, laboratory findings, clinical symptoms, and outcome-related data of all patients were obtained from electronic medical records. The patients with missing data on the studied criteria and kidney transplant recipients were excluded from the study. Patients with CKD were identified based on the self-declaration form or medical documents confirmed by a nephrologist. Based on the Kidney Disease: Improving Global Outcomes, CKD was defined as the glomerular filtration rate (<60 mL/min/1.73 m^2) for a minimum of three months [11]. Eventually, patients' clinical outcomes were evaluated by experienced clinicians.

Categorical and continuous variables were expressed as the percentage (%) and mean ± standard deviation (SD), respectively. In addition, categorical and continuous variables were analyzed by the chi-square test/Fisher's exact test and independent t-test/Mann-Whitney U test, respectively. A *P*-value less than 0.05 represented a statistically significant difference. Finally, SPSS software (version 22.0, IBM) was used to analyze the obtained data.

RESULTS

In general, 153 patients (56 and 97 patients with and without CKD, respectively) suffering from confirmed COVID-19 were included in this cross-sectional study. **Table 1** represents the demographic and clinical characteristics of COVID-19 hospitalized patients with and without CKD. Based on the

Table 2. The radiographic and laboratory results among COVID-19 hospitalized patients with and without CKD

Characteristics (normal range)	Patients, Mean ± SD		p-value*
	With CKD (n=56)	Without CKD (n=97)	
Laboratory findings at admission			
Leucocyte count, $\times10^9$/L (3.5-9.5)	8.09 ± 8.49	6.42 ± 2.53	0.185
Neutrophil count, % (50-70)	69.13 ± 14.28	71.23 ± 12.43	0.406
Lymphocyte count, % (11-49)	22.80 ± 11.48	22.71 ± 11.16	0.966
RBC count, $\times10^{12}$/L (4.3-5.8)	4.83 ± 0.82	4.95 ± 0.53	0.383
Hemoglobin, g/dL (13.3-16.9)	13.55 ± 2.15	14.61 ± 1.48	**0.003**
Hematocrit, % (39-51)	40.17±5.37	42.38 ± 3.72	**0.014**
MCV, fL (80-98)	84.01 ± 7.90	86.11 ± 5.10	0.102
MCH, pg (27-35)	28.35 ± 3.67	29.68 ± 2.26	**0.026**
MCHC, g/dL (31-36)	33.64 ± 1.87	34.45 ± 1.19	**0.008**
Platelet count, $\times10^9$/L (125-350)	201.75 ± 79.56	182.47 ± 64.14	0.136
RDW-CV, % (11.5-15.5)	13.68 ± 1.67	13.06 ± 0.99	**0.013**
MPV, fL (6-13.5)	10.14 ± 1.17	10.15 ± 0.97	0.951
ESR, mm/h (0-20)	43.68 ± 24.61	41.43 ± 25.69	0.638
CRP, mg/L (0-10)	44.34 ± 22.58	45.69 ± 28.04	0.760
BS, mg/dL (70-126)	153.50 ± 84.34	149.07 ± 83.44	0.816
BUN, mg/dL (7-19)	19.38 ± 7.63	13.16 ± 4.57	**<0.001**
Creatinine, mg/dL (0.9-1.3)	1.58 ± 0.18	1.06 ± 0.28	**<0.001**
AST, U/L (<35)	39.76 ± 25.24	34.75 ± 15.04	0.316
ALT, U/L (<45)	40.94 ± 40.52	32.33 ± 16.97	0.247
ALP, U/L (up to 270)	217.84 ± 179.30	182.50 ± 78.61	0.299
LDH, U/L (207-414)	666.90 ± 207.27	654.32 ± 271.45	0.836
Sodium, mEq/L (136-145)	136.64 ± 4.24	131.10 ± 21.80	0.089
Potassium, mEq/L (3.5-5)	4.22 ± 0.49	5.98 ± 15.77	0.447
Chest CT findings, No.%			
Bilateral lung involvement	55 (98.2)	92 (94.8)	0.301
Ground-glass opacity	51 (91.1)	91 (93.8)	0.527
Consolidation shadow	5 (8.9)	5 (5.2)	0.363

Note. COVID-19: Coronavirus disease 2019; MCV: Mean corpuscular volume; CKD: Chronic kidney disease; RBC: Red blood cell; MCH: Mean corpuscular hemoglobin; RDW: Red cell distribution width, RDW-CV; MCHC: Mean corpuscular hemoglobin concentration; MPV: Mean platelet volume; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; BS: Blood sugar; BUN: Blood urea nitrogen, BUN; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; LDH: Lactate dehydrogenase; No.: Number; SD: Standard deviations; CT: Computed tomography. *p<0.05 is considered statistically significant. The values in bold represent a significant difference

results, no differences were found between the two groups in terms of age, gender, and underlying comorbidities (i.e., hypertension and diabetes) due to the matching design (p≥0.05). The mean (±SD) age of patients with and without CKD was 56.79 (±11.93) and 54.35 (±13.20) years, respectively, and most patients (72.5%) were males. Furthermore, no considerable differences were observed regarding clinical symptoms between the groups at the time of admission (p≥0.05).

Table 2 summarizes the comparison results of laboratory and radiographic findings between patients with and without CKD. The erythrocyte sedimentation rate (ESR, 43.68±24.61 mm/h), C-reactive protein (CRP, 44.34±22.58 mg/L), blood sugar (BS, 153.5±84.34 mg/dL), BUN (19.38±7.63 mg/dL), creatinine (1.58±0.18 mg/dL), aspartate aminotransferase (AST, 39.76±25.24 U/L), and lactate dehydrogenase (LDH, 666.9±207.27 U/L) were above the normal range in CKD patients. Based on laboratory findings, COVID-19 patients with CKD were at higher risk of inflammatory responses and myocardial and hepatic damages, leading to the unfavorable prognosis of COVID-19.

Regarding laboratory results on admission, CKD patients also demonstrated higher levels of BUN (19.38±7.63 vs. 13.16±4.57 mg/dL, p<0.001), creatinine (1.58±0.18 vs. 1.06±0.28 mg/dL, p<0.001), and red cell distribution width (RDW-CV, 13.68±1.67 vs. 13.06±0.99, p=0.013) compared to patients without CKD. Nonetheless, the values of hematological parameters (**Table 2**) were lower, including hemoglobin (13.55±2.15 vs. 14.61±1.48 g/dL, p=0.003), hematocrit (40.17±5.37% vs. 42.38±3.72%, p=0.014), mean corpuscular hemoglobin (MCH, 28.35±3.67 vs. 29.68±2.26 pg, p=0.026), and mean corpuscular hemoglobin concentration (MCHC, 33.64±1.87 vs. 34.45±1.19 g/dL, p=0.008).

On admission, chest CT abnormalities were detected in most patients. There was no significant difference between the CT or chest radiography results of COVID-19 patients with and without CKD (**Table 3**). Based on the results, bilateral lung involvement and ground-glass opacities were the most prevalent CT abnormalities. According to data in **Table 3**, no significant difference was found in mortality rates, ICU admission, and length of hospital stay between patients with and without CKD.

DISCUSSION

COVID-19 is a highly contagious and newly evolved disease related to the enhanced rates of hospitalization and mortality, especially in individuals with underlying diseases. Limited data exist on the clinical characteristics of COVID-19 hospitalized patients with CKD. The present paper sought to discuss and compare the clinical characteristics and differences between COVID-19 patients with and without CKD.

Based on the results, the proportions of male patients in the present work (72.5%) were higher compared to females, which is in line with the findings of previous studies [12,13].

Table 3. Clinical outcomes of COVID-19 hospitalized patients with and without CKD

Characteristics	Patients, No. (%)		p-value*
	With CKD (n=56)	Without CKD (n=97)	
Length of hospital stay, Mean±SD, days	6.25 ± 4.3	5.35 ± 3.7	0.194
Hospital discharge	33 (58.9)	62 (63.9)	0.540
ICU admission	7 (12.5)	11 (11.3)	0.830
Death	5 (8.9)	6 (6.2)	0.200

Note. COVID-19: Coronavirus disease 2019; CKD: Chronic kidney disease; ICU: Intensive care unit; No.: Number; SD: Standard deviations. *p<0.05 shows the statistical significance

They also suffered from more severe symptoms that were related to old age, nicotine dependence, and a higher number of comorbidities.

According to recent studies, CKD is among the most widespread comorbidities in COVID-19 patients [14]. In the current study, hypertension and diabetes between patients with and without CKD were matched for assessing the direct impact of CKD on the severity and death of COVID-19. No considerable differences were found in the clinical manifestation, radiological findings, and mortality rates between patients with and without CKD. These data revealed that the increased severity and mortality rate of the disease in COVID-19 patients with CKD, which was reported in other studies [15-17], may not be directly related to CKD per se. This means that other comorbidities, especially hypertension and diabetes, have great impacts on the undesirable outcomes of COVID-19 patients with CKD.

Laboratory findings in all admitted patients indicated higher CRP, LDH, and ESR rates than the normal range, revealing a severe status and multi-organ damage, which is consistent with the findings of earlier studies [18, 19]. Moreover, kidney damage indexes (i.e., the level of BUN and creatinine) were higher than the normal range and were also considerably higher in patients with CKD in comparison with patients without CKD. Conversely, the RDW-CV value significantly increased in patients with CKD compared to ones without CKD. This was reported as an important predictor for the severity of COVID-19 patients in previous studies [20-22]. However, other observed RBC indexes were significantly lower in CKD patients.

In the present study, although chest radiographic findings showed pulmonary involvement in all patients, there was no significant difference regarding the type of pulmonary manifestations between COVID-19 patients with and without CKD.

Additionally, no considerable differences were detected in the length of hospital stay, ICU admission, rate of hospital discharge, and mortality between the two groups during the follow-up. These results could highlight the importance of other comorbidities on the severity of COVID-19 infections in our study population.

This study has some limitations. The related data were only obtained from patients from a single center in Tehran. Accordingly, it would be more valuable to achieve more complete results by conducting larger studies in a multicenter manner. In addition, the data were acquired via electronic medical records, thus this study might not be unbiased regarding the missing data.

CONCLUSIONS

In general, RDW-CV, BUN, and creatinine were essential laboratory indexes for monitoring COVID-19 patients with CKD and evaluating the risk of disease progression in this study. It was found that disease severity and in-hospital mortality in COVID-19 patients with CKD are possibly correlated with other comorbidities, especially hypertension and diabetes rather than the ones caused by CKD per se. Therefore, the optimal management of these risk factors would be effective in preventing the development of critical circumstances and performing effective treatment measures.

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