RESEARCH ARTICLE

Evaluation of COVID-19 Patients with Chronic Kidney Disease

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ABSTRACT

Objectives: The present study seeks to provide insight into managing patients with chronic kidney disease (CKD) infected with COVID-19.

Methods: Patients with COVID-19 with CKD were included in the study. The eligible patients were divided into four groups: 1) patients who were not on dialysis, 2) patients on maintenance dialysis, 3) patients who underwent dialysis following COVID-19, 4) patients with a history of a kidney transplant. After reviewing clinical charts, nursing records, laboratory findings, radiological reports, and other medical records of CKD patients with COVID-19 confirmed infection, clinical presentation, laboratory data, radiology findings, and results were extracted from documented medical records. The epidemiological, clinical, laboratory and outcome characteristics of the subgroups were evaluated and compared.

Results: Seventy-eight patients were included into the study. Hypertension (50 cases, 72.5%), diabetes (44 cases, 63.8%), and Cardiovascular disease (26 cases, 38.2%) were the most common risk factors in the studied patients. Among all participants, 40 (52.6%) patients died. The most common symptom was dyspnea (56.6%), followed by dry cough (38.7%). Comparison of blood, inflammatory, biochemical, and clinical indices among the patients' groups show that LDH (P=0.022), AST (P=0.038), and ALT (P= 0.004) indices were significantly different between groups of patients. According to the results in Table 3, Unilateral ground-glass opacity (GGO) in the radiological findings of the Non-dialysis CKD group was significantly (P=0.50) higher than the other groups.

Conclusion: It can be concluded that CKD is one of the critical factors that can cause poor prognosis in COVID-19 patients. J Microbiol Infect Dis 2021; 11(3):152-158.

Keywords: COVID19, chronic kidney disease, Dialysis, Transplant

INTRODUCTION

Today's world is facing a massive wave of COVID-19 virus disease. Thirty years after the virus was first discovered in the 1930s, evidence of its pathogenicity has been established in humans [1]. In December 2019, a viral outbreak of the same family was reported from Wuhan, China [2,3], and the spread of the disease has since infected more than 14 million people and killed more than 600,000 worldwide [4]. The presence of underlying diseases such as diabetes, hypertension, cardiovascular disorders, and COPD can affect the severity of the disease in different people and the mortality rate [5-7]. For example, chronic kidney disease (CKD) is a common disease that can lead to impaired renal function by reducing the glomerular filtration rate (GFR] [8]. Statistics show that in 2017, over 5 million patients worldwide were suffering from the disease [9]. Old age and the presence of underlying diseases in most patients with this

disease are among the factors that make CKD patients more susceptible to COVID-19.

In CKD, the glomerular filtration rate decreases due to a decrease in the number of nephrons. Adaptive responses are then generated by factors such as vasoactive hormones, growth factors, and cytokines [8]. The presence of cytokines causes a cytokine storm, activating the angiotensin II pathway, leading to increased blood coagulation and microangiopathy [10]. Studies have shown that ICU hospitalization rates and mortality in CKD patients are significantly higher due to symptoms such as cough, severe shortness of breath, and extreme fatigue [11,12]. Also, the results of laboratory tests of these patients have shown that ferritin and CRP in CKD patients are associated with a significant increase, which can be related to their severe inflammatory status [13].

Despite a large number of CKD patients, research in this area has been relatively largely neglected. In this study, we describe 78 patients in the Labafinejad Hospital in Tehran, Iran. Clinical manifestations, radiological findings, laboratory data, and results are reviewed to provide insights for physicians in managing patients with chronic kidney disease infected with COVID-19.

METHODS

Study design

This study, designed as a cross-sectional study from March 2, 2020, to May 9, 2020, has been approved by the Ethics Committee in Biomedical Research of Shahid Beheshti University of Medical Sciences with the code (IR.SBMU.REC.1399.018). Patients with the novel coronavirus (COVID-19) referred to Labbafinezhad Hospital in Tehran were included in the study if they met the inclusion criteria (cough, fever, fatigue, myalgia, chest pain, dyspnea, other upper respiratory symptoms, and gastrointestinal symptoms). Diagnosis of COVID-19 patients was based on the WHO interim guidance, a confirmed COVID-19 patient defined as an individual with a positive reverse transcriptase-polymerase chain reaction (RT-PCR) result or a patient with common COVID-19 symptoms and a tomography computed scan (CT-scan) compatible with COVID-19 pattern confirmed by experts [14]. In addition, the written informed consent form was obtained from all

patients by the Ethics Commission of the hospital.

A total of 91 patients presented within the specified period, and 78 patients were eligible for the study. Patients were divided into four subgroups (Figure 1): 1) patients who were not on dialysis, 2) patients on maintenance dialysis, 3) patients who underwent dialysis following COVID-19, 4) patients with a history of a kidney transplant.

After reviewing clinical charts, nursing records, laboratory findings, radiological reports, and other medical records of CKD patients with COVID-19 confirmed infection, clinical presentation, laboratory data, radiology findings, and results were extracted from documented medical records using data collection forms. Laboratory tests were performed again before discharge. The guick COVID-19 Severity Index (qCSI) was used to assess the severity of COVID-19 in patients. The qCSI ultimately requires only three variables, all of which are accessible at the bedside [26].

Statistical Analysis

The collected data were summarized as descriptive profiles using mean, median, standard deviation, and variance. Patients' percentages, mean, median, and standard deviation were calculated within different groups for specific variables. Independent t-test, paired t-test, and chi-square were used to compare the clinical features of patients with COVID-19. A p-value of less than 0.05 was considered to indicate statistical significance. All the statistical analyses were performed by the SPSS v.26.0 (Chicago, Illinois, USA).

RESULTS

Based on Table 1, of the 78 patients studied, 53 (68.8%) were female. The average age of patients was 64.04 years (32-96). Among the included patients, 23 (29.48%) were not on dialysis, 28 (35.89%) were on maintenance dialysis, seven (8.97%) underwent dialysis following COVID-19, and 20 (8.97%) patients had a history of kidney transplantation. Hypertension (50 cases, 72.5%), diabetes (44 cases, 63.8%), and Cardiovascular disease (26 cases, 38.2%) were the most common risk factors in the studied patients. Among all participants, 40 (52.6%) patients died. The most common symptom was dyspnea (56.6%), followed by dry cough (38.7%).

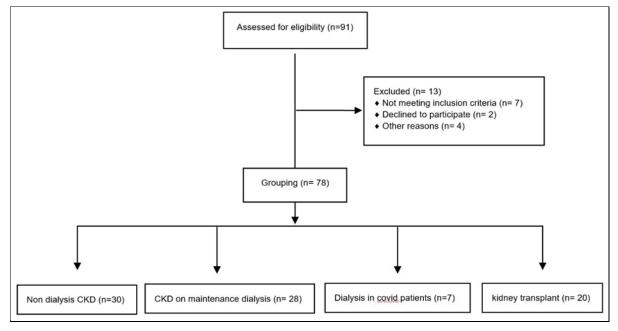


Figure 1. The CONSORT diagram.

Table 1. Clinical and	l demographic features	of patients based	I on renal therapy using ANOVA statistical method.

Variables	Total	Non-dialysis CKD (n=23)	CKD on maintenance dialysis (n=28)	Dialysis in Covid-19 patients (n=7)	KT (n=20)	p- value
Age (mean ± SD)	64.4 ± 15.0	65.9 ± 12.4	68.3 ± 14.82	62.00 ± 22.62	57.00 ± 13.29	0.069
Sex (M), n (%)	24 (31.2)	6 (26.1)	5 (18.5)	3 (42.5)	10 (50)	0.111
Female, n (%)	53 (68.8)	17 (73.9)	22 (81.5)	4 (57.1)	10 (50)	0.111
Initial symptoms,						
n (%)						
Fever	22 (30.1)	8 (34.8)	9 (37.5)	1 (14.3)	4 (21.1)	0.529
Chills	10 (13.2)	2 (8.7)	2 (7.4)	1 (14.3)	25 (26.3)	0.270
Dry cough	29 (38.7)	9 (39.1)	11 (42.3)	3 (42.9)	30 (31.6)	0.882
Dyspnea	43 (56.6)	15 (65.2)	15 (55.6)	3 (42.9)	10 (52.6)	0.701
GI symptoms	19 (25)	6 (26.1)	7 (25.0)	2 (28.6)	4 (20)	1.000
Comorbidities,						
n (%)						
Diabetes	44 (63.8)	15 (75)	15 (60.0)	3 (50.0)	11 (61.1)	0.407
Hypertension	50 (72.5)	14 (70.0)	19 (76.0)	4 (66.7)	13 (65)	0.743
CVD	26 (38.2)	8 (40.0)	11 (44.0)	0 (0.0)	7 (41.2)	0.178
Quick COVID severity Index*, n (%)						
Low-risk group	0	0	0	0	0	
Low-intermediate						
risk group	20 (35.7)	5 (29.4)	7 (33.3)	3 (75.0)	5 (31.3)	0.482
High-intermediate risk				()	· · ·	
group	14 (25)	2 (11.8)	7 (33.3)	0 (0.0)	5 (31.3)	
High-risk group	22 (28.2)	10 (58.8)	7 (33.3)	1 (25.0)	6 (37.5)	
Death, n (%)	40 (52.6)	18 (78.3)	20 (71.4)	0 (0)	2 (10.5)	<0.001
ICU care, n (%)	34 (44.7)	14 (60.86)	16 (57.14)	2 (33.3)	2 (10.52)	<0.001

DM: Diabetes Mellitus, HTN: Hypertension, CVD: Cardiovascular disease

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Variable	Non-dialysis CKD (n=23)	CKD on maintenance dialysis (n=28)	Dialysis in Covid-19 patients (n=7)	KT (n=20)	p- value
CBC at Ad-					
(IQR)					
RBC	3.8 (3.0-4.7)	4.13 (3.3-4.57)	3.9 (3.42-4.42)	3.8 (3.10-3.27)	0.572
Hct	33.20 (27.5-38.5)	36.05 (33.22-39.75)	33.10 (30.10-35.32)	35.65 (28.95-38.07)	0.229
Hb:	9.40 (8.50-12.50)	11.15 (9.65-12.87)	10.15 (9.25-10.75)	10.85 (8.92-12.65)	0.301
PLT	205.0 (127.0-253.0)	192.0 (116.0-289.0)	289 (217.0-411.5)	159.0 (124-221)	0.129
WBC	9.50 (6.90-12.90)	8.45 (6.55-11.95)	7.45 (6.20-9.62)	7.85 (4.85-10.10)	0.503
Neutrophil	80.0 (72.75-92-75)	85.0 (79.0-87.0)	77.0 (75.0-82.0)	80.0 (75.75-89.0)	0.546
Lymphocytes	14.5 (5.0-22.25)	14.0 (10.0-17.0)	18.0 (13.0-19.50)	16.0 (7.50-20.0)	0.664
Infection- related indices					
ESR	50.0 (16.50-83.50)	30.50 (20.25-72.25)	64.50 (51.0-78.0)	30.0 (26.0-57.0)	0.773
CRP	43.10 (33.0-55.25)	38.0 (21.0-47.0)	42.5 (5.87-60.0)	38.0 (14.25-53.42)	0.409
Biochemical	· · · · ·	()			
Albumin	3.0 (2.75-3.4)	2.8 (2.5-3.35)	3.4 (3.15-3.57)	3.2 (3-3.9)	0.116
Troponin	0.023 (0.005-0.80)	0.37 (0.007-0.258)	0.023 (0.001-0.428)	0.025 (0.012-0.75)	0.674
LDH	591 (433.0-1354.0)	625 (490-877)	329 (266.0-483.0)	447.5 (353.3-584.5)	0.022*
CPK	124 (67-451)	118.5 (44-352.25)	42 (41.5-134.5)	166 (70-351.5)	0.241
Urea	124.5 (56-212.5)	108.5 (63-176)	95 (50-119)	101 (83.25-149)	0.592
Cr	3.79 (2.39-8.10)	2.79 (1.93-5.45)	3.07 (1.98-5.31)	3.9 (2.79-6.48)	0.64
AST	40.5 (21.25-71.5)	28 (17-74)	13 (12-19)	26.5 (18.75-39.25)	0.038*
ALT	32 (19-74.5)	21 (11-75)	8 (3.25-9)	15.5 (11.5-35)	0.004*
Bil total	0.8 (0.55-1.65)	0.75 (0.47-1.1)	0.8 (0.5-1.1)	0.7 (0.5-2.3)	0.903
Bil direct	0.2 (0.2-0.4)	0.2 (0.2-3.25)	0.15 (0.1-0.2)	0.2 (0.15-1)	0.515
Vital signs					
Temperature	37 (36.5-37.5)	37 (36.8-37)	36.5 (36.15-36.67)	37.1 (36.65-37.45)	0.033
RR	19 (17-26)	18 (16.5-24)	18 (17.25-22.5)	18 (17.25-21)	0.731
PR	85 (80-92)	82 (80-93.5)	82 (70-90)	86 (86-99.9)	0.859
Systolic BP (Mean ± SD)	121.95 ± 26.36	126.2 ± 34.48	133.66 ± 20.94	123.73 ± 27.82	0.272
Diastolic BP	121.00 2 20.00	120.2 2 0 1.10	.00.00 2 20.04	.20.10 2 21.02	0.272
(Mean ±SD)	72.57 ± 16.16	74.39 ± 15.47	76.33 ± 10.32	78.15 ± 17.98	0.427
O2 Sat	87.5(85.25-94.25)	90 (82-94.5)	95 (93.75-97)	90 (84.25-93.75)	0.073

Table 2. Laboratory	/ data in admission and discharge	of COVID-19 patients using	a ANOVA statistical method.

Ad: Admission; RBC: Red Blood Cell Htc: Hematocrit, WBC: White Blood Cell PLT: Platelet Dis: Discharge; Bil :Bilirubin, Trop=troponin; LDH:lactate dehydrogenase; Cr:creatinine; ICU:intensive care unit.

Table 3. Radiologic findings and vital signs using ANOVA statistical method.

Variables	Non-dialysis CKD (n=23)	CKD on maintenance dialysis (n=28)	Dialysis in COVID- 19 patients(n=7)	KT (n=20)	p- value
Radiologic findings, n (%)					
Unilateral GGO	6 (54.5)	3 (20)	1 (20.0)	1 (7.1)	0.050*
Bilateral GGO	5 (45.5)	5 (33.3)	3 (60.0)	9 (64.3)	0.383
Pleural effusion	5 (45.5)	5 (33.3)	4 (80.0)	5 (35.7)	0.337
Collapse	1 (9.1)	0 (0.0)	0 (0.0)	1 (7.1)	0.621
Consolidation	0 (0)	1(6.7)	0 (0.0)	1 (7.1)	1.000
Emboli	0 (0)	1(6.7)	0 (0.0)	0 (0.0)	1.000
Band	1 (9.1)	5(33.3)	0 (0.0)	3 (21.4)	0.378
Drugs, n (%)					
Hydroxyqloroquine	20 (87)	20 (76.9)	7 (100.0)	19 (95.0)	0.283
Kaletra	12 (52.2)	17 (65.4)	3 (42.9)	5 (25.0)	0.054
INF	2 (8.7)	0 (0.0)	0 (0.0)	0 (0.0)	0.332
Anibiotics	22 (95.7)	26 (100.0)	7 (100.0)	20 (100.0)	0.658

GGO=ground glass opacity, GCS=Glasgow coma scale

Comparison of blood, inflammatory, biochemical, and clinical indices between the four groups in patients show that LDH (p=0.022), AST (p=0.038), and ALT (p= 0.004) indices were significantly different between groups of patients. Unilateral ground-glass opacity (GGO) in the radiological findings of the non-dialysis CKD group was significantly higher (P=0.50) than the other groups (Table 3). However, other radiological indices did not differ significantly between different groups. On the other hand, no significant difference was observed in the type of drug used by the groups.

DISCUSSION

COVID-19 can cause a variety of symptoms in patients. Furthermore, these clinical symptoms have different severity and nature depending on the history of underlying diseases, physiology, and severity of infection in each patient. The results indicate that in this study, the most common symptom in all patients was Also, dyspnea was the most dyspnea. common symptom in all patients on dialysis who were on maintenance dialysis or underwent dialysis following COVID-19. A previous study including five patients on hemodialysis with COVID-19 revealed that diarrhea and non-respiratory symptoms were the most common symptoms [15]. Another case report similarly reported that nausea and vomiting were the first symptoms of dialysis COVID-19 patients [16]; however, the prevalence of gastrointestinal symptoms was only 25% in this study. Also, in patients with a history of a kidney transplant, 52.6% had dyspnea, while the study of Akaline et al. declares that the initial symptom in these patients was fever [17]. However, given the nature and target tissue of the COVID-19 infectious agent, the prevalence of respiratory disorders can be predictable.

Contrary to the previous COVID-19 studies, in this study, there were more women (68.8%) than men (31.2%) [18-21]. However, looking at the mortality rate of patients, it can be seen that the number of deaths in women (52.8%) in the study was more than men (44%) which according to the changes in sex hormone levels among female patients with end-stage renal disease, these differences can be justified [22]. Based on the present study, 89.7% of patients had a history of underlying diseases. Furthermore, most patients with severe conditions had diabetes, hypertension, and coronary diseases, which is aligned with the data that have been reported [21, 23] so that, Comorbidities in patients with kidney disease are risk factors for poor outcomes in COVID-19 [5]. Quick COVID-19 severity index (qCSI) results show 35.7% of patients were in the low intermediate group, meaning they have had a 30% chance of critical illness.

On the other hand, 28.2 % of patients were in the high intermediate category, which means they have had a 44% risk of critical illness. This study declares that, even with the higher O2 saturation (mean=91.2) and normal respiratory rate (mean=16.71) in patients who underwent dialysis following COVID-19, the mortality rate was 80%. While in patients without dialysis who had the lowest O2 saturation (mean=86.73%) and the highest respiratory rate (mean=22.86), the mortality rate was only 45.5%.

In terms of laboratory data, the average level of creatinine in all patients was 4.37 mg/dl, and between subgroups, patients on maintenance dialysis had the highest average creatinine level (5.74 mg/dl), contrary to the study of Ajaimy et al., which the median of creatinine in COVID-19 patients with kidney disease was 2mg/dl [23]. Therefore, it cannot be said that there is a strong correlation between albumin levels and patient outcomes [24]. Furthermore, in our study, the mean LDH level in all patients was 667.058 U/L, while in previous studies, the mean LDH level in COVID-19 patients without kidney disease was 261 U/L and in patients with CKD was 264 U/L [13, 21]. On the other hand, in our study, the mean level of LDH in patients with a history of kidney transplantation at the time of admission was 815 U/L and at the time of discharge was 119.66 U/L, which is much higher than the amount reported in the same study (mean LDH level=336 U/L) [17]. Also, in line with other studies, the LDH level was higher in patients who died, and patients admitted to ICU, which shows the correlation between the high level of LDH and poor outcomes of patients [25].

Considering the patients' CT-Scan, aligning with other studies, bilateral ground-glass

opacity was the most radiological finding [21,23].

The implementation of the present study was accompanied by limitations that, for example, the evaluation of serum antibodies for COVID-19 (IgG and IgM) and hematologic tests have not been conducted to determine viremia have not been carried out, which might have some helpful information regarding patients' outcomes. Finally, our explanation may be restricted because of the small sample size.

Conclusion

According to the results, dyspnea was the most common symptom in patients in this study, while the levels of LDH, AST, and ALT had the most changes. Also, the most common finding on a shelf CT scan is a bilateral dimming of the ground glass. Also, the most common finding on chest CT-Scan is bilateral ground-glass opacity. On the other hand, due to the number of deaths and ICU admissions, it can be concluded that CKD is one of the essential factors that can cause poor prognosis in COVID-19 patients. For this reason, it can be said that it is crucial to evaluate clinical manifestations, radiologic findings, laboratory data, and outcomes of COVID-19 patients with CKD to establish a perspective for physicians to manage patients.

ACKNOWLEDGMENTS

The authors appreciate all the doctors, nurses, and health care workers' efforts involved in the diagnosis and management of our patients. We acknowledge the Medical Record Department of Labbafinezhad Hospital for coordinating data collection for CKD patients with COVID-19 infection. We thank Keivan Ranjbar and Dr. Reza Shahriarirad for revising the manuscript. We would also like to thank all patients involved in this study.

The article has been published in Research Square as PREPRINT. For sure it is not the certain edition and this do not has any contradiction with Copyright and Publisher's policy.

Declaration of Conflicting Interests: The authors declare that they have no conflict of interest.

Author contribution: YSK and SKM contributed to the acquisition of data, drafting the article, and interpretation of data. SS

contributed to the conception and design, and interpretation of data. ST and DY contributed to the initiation of the research and interpretation of data. AZ and MMD Contributed to the analysis and interpretation of data. S.A. contributed to drafting the article and revising it critically for important intellectual content. All authors have read and approved the final version of the manuscript.

Availability of data and materials: Data supporting the results reported in the article can be found by academic researchers by sending an email to the corresponding author at dr.shsali@gmail.com

Ethics approval and consent to participate: This research has been approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences with the approval code IR.SBMU.REC.1399.018. Written informed consent was obtained from all participants or their proxies.

Consent for publication: All participants or their proxies gave written consent for their personal or clinical details along with any identifying images to be published in this study.

Funding: Not applicable.

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