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Yasaman Sadat Keshmiri

Shahid Beheshti University of Medical Sciences

Sina Khosravi Mirzaie

Shahid Beheshti University of Medical Sciences

Shahnaz Sali (✉ dr.shsali@gmail.com)

Shahid Beheshti University of Medical Sciences

Davood Yadegarynia

Shahid Beheshti University of Medical Sciences

Sara Abolghasemi

Shahid Beheshti University of Medical Sciences

Shabnam Tehrani

Shahid Beheshti University of Medical Sciences

Amir Zamani

Shahid Beheshti University of Medical Sciences

Mohamad Mehdi Derisi

Shahid Beheshti University of Medical Sciences

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1. Yasaman Sadat Keshmiri

Affiliation: Student Research Committee, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

E-mail: Yk1376@gmail.com

2. Sina Khosravi Mirzaie

Affiliation: Student Research Committee, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

E-mail: Sinakhosravi1997@gmail.com

3. Shahnaz Sali

Affiliation: Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

E-mail: dr.shsali@gmail.com

4. Davood Yadegarynia

Affiliation: Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

E-mail: d.yadegarynia@gmail.com

5. Sara Abolghasemi

Affiliation: Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

E-mail: a59sara@yahoo.com

6. Shabnam Tehrani

Affiliation: Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

E-mail: shabnam89@yahoo.com

7. Amir Zamani

Affiliation: Student Research Committee, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

E-mail: Zamani.amir44@gmail.com

8. Mohamad Mehdi Derisi

Affiliation: Student Research Committee, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

E-mail: Derisi.mohamad@yahoo.com

***Corresponding Author**

Shahnaz Sali

Affiliation: Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

E-mail: dr.shsali@gmail.com

Phone number: +98 912 306 77 84

ORCID:

Fax: +98 21 2254 6026

Address: Labbafinezhad hospital, 9th Boostan St, Tehran, Tehran Province, Iran

Introduction

Today's world is facing a huge 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 as well as COPD can affect the severity of the disease in different people and the mortality rate (5 - 7). 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, which eventually leads to increased blood coagulation and microangiopathy (10). Studies have shown that ICU hospitalization rates, as well as 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.

Material and methods

Study design

This study, which is 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 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 computed tomography scan (CT-scan) compatible to COVID-19 pattern confirmed by experts [14]. 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 time period, out of 78 patients who were eligible for the study. Patients are divided into 4 subgroups (fig 1):

- 1) patients who were not on dialysis
- 2) patients on maintenance dialysis
- 3) patients who underwent dialysis following COVID-19 and
- 4) patients with a history of a kidney transplant.

Figure 1: Consort diagram

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 quick COVID-19 Severity Index (qCSI) was used to assess the severity of COVID-19 in patients. The qCSI ultimately requires only 3 variables, all of which are accessible at the bedside [26].

Statistical Analysis

The collected data were summarized as descriptive profiles by using mean, median, standard deviation, and variance. The percentage, mean, median, standard deviation of patients 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 Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois, USA) version 26.0.

Result

Based on the results in 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, 7 (8.97%) underwent dialysis following COVID-19 and 20 (8.97%) patients had a history of a kidney transplant. Hypertension (72.5%), diabetes (63.8%) and Cardiovascular disease (38.2%) were the most common among patients, respectively. Among all participants, 40 (52.6%) patients died. The most common symptom was dyspnea (56.6%), followed by dry cough (38.7%). Quick COVID_19 severity index (qCSI) results show 35.7% of patients were in the low intermediate group which means they have had a 30% chance of critical illness. 28.2 % of patients were in the high intermediate category, which means they have had a 44% risk of critical illness.

Table 1. Clinical and demographic features of patients based on renal therapy

Variables	Total	T(M)	Non dialysis CKD (n=23)	T(M)	CKD on maintenance dialysis(n=28)	T(M)	Dialysis in covid patients(n=7)	T(M)	KT (N=20)	T(M)	p-value
Age (mean ± SD)	64.4± 15.03	76	65.90± 12.39	23(1)	64.27± 14.82	28(1)	62.00± 22.62	7(0)	57.00± 13.29	20(0)	0.069
Sex		77		23(0)		27(1)		7(0)		20(0)	
Male (%)	24(31.2%)		6(26.1%)		5(18.5%)		3(42.5%)		10(50%)		0.111
Female (%)	53(68.8%)		17(73.9%)		22(81.5%)		4(57.1%)		10(50%)		
Initial symptoms											
Fever	22(30.1%)	5	8(34.8%)	23(0)	9(37.5%)	4	1(14.3%)	0	4(21.1%)	1	0.529
Chills	10(13.2%)	2	2(8.7%)	•	2(7.4%)	1	1(14.3%)	•	25(26.3%)	1	0.270
Dry cough	29(38.7%)	3	9(39.1%)	•	11(42.3%)	2	3(42.9%)	•	30(31.6%)	1	0.882
Dyspnea	43(56.6%)	2	15(65.2%)	•	15(55.6%)	1	3(42.9%)	•	10(52.6%)	1	0.701
GI symptoms	19(25%)	2	6(26.1%)	•	7(25.0%)	1	2(28.6%)	•	4(20%)	1	1.000
Comorbidities											
Diabetes	44(63.8%)	4	15(75%)	3	15(60.0%)	3	3(50.0%)	1	11(61.1%)	2	0.407
Hypertension	50(72.5%)		14(70.0%)	3	19(76.0%)	3	4(66.7%)	1	13(65%)	2	0.743
Cardiovascular diseases	26(38.2%)		8(40.0%)	3	11(44.0%)	3	0(0%)	1	7(41.2%)	3	0.178
Quick COVID severity Index*											0.482
Low-risk group			0	2	0	1	0	2	0	2	
Low-intermediate risk group	20(35.7%)		5(29.4%)		7(33.3%)		3(75%)		5(31.3%)		
High-intermediate risk group	14(25%)		2(11.8%)		7(33.3%)		0(0%)		5(31.3%)		
High-risk group	22(28.2%)		10(58.8%)		7(33.3%)		1(25%)		6(37.5%)		
Death	40(52.6%)		18(78.3%)		20(71.4%)		0(0%)		2(10.5%)		<0.001
ICU care	34(44.7%)		14(60.86%)		16(57.14%)		2(33.33%)		2(10.52%)		<0.001

DM: Diabetes mellitus; HTN: Hypertension; CD: Cardiac disease

Comparison of blood, inflammatory, biochemical and clinical indices between the four groups in patients shows that LDH (P=0.022), AST (P=0.038) and ALT (P= 0.004) indices were significantly different between groups of patients.

Table 2. Laboratory data in admission and discharge of COVID-19 patients

variable	Non dialysis CKD (n=23)		CKD on maintenance dialysis(n=28)		Dialysis in covid patients(n=7)		KT (N=20)		p-value
CBC on admission: median (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)	•	•/∆∇∇
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)	•	•/∇∇∇
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)	•	•/∇∇∇
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)	•	•/∆∇∇
Neut:	80.0(72.75-92.75)	∧	85.0(79.0-87.0)	∧	77.0(75.0-82.0)	∇	80.0(75.75-89.0)	•	•/∆∇∇
Lymph:	14.5(5.0-22.25)	∧	14.0(10.0-17.0)	∧	18.0(13.0-19.50)	∇	16.0(7.50-20.0)	•	•/∇∇∇
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)	∧	•/∇∇∇
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)	∇	•/∇∇∇
Biochemical									
Alb	3.0(2.75-3.4)	∧	2.8(2.5-3.35)	∇	3.4(3.15-3.57)	∇	3.2(3-3.9)	∆	•/∇∇∇
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(353.25-584.5)	∆	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)	2	37(36.8-37)	2	36.5(36.15-36.67)	1	37.1(36.65-37.45)	3	0.033
RR	19(17-26)	6	18(16.5-24)	7	18(17.25-22.5)	3	18(17.25-21)	4	0.731
PR	85(80-92)	0	82(80-93.5)	2	82(70-90)	0	86(86-99.9)	0	0.859
Systolic BP (Mean ± SD)	121.95±_26.36	2	126.2±_34.48	4	133.66±_20.94	1	123.73±_27.82	1	0.272
Diastolic BP (Mean ±SD)	72.57±_16.16	2	74.39±_15.47	5	76.33±_10.32	1	78.15±_17.98	1	0.427
O2 Sat	87.5(85.25-94.25)	3	90 (82-94.5)	3	95(93.75-97)	1	90(84.25-93.75)	0	0.073

Ad: Admission; Dis: Discharge; Alb=albumin, Trop=troponin; LDH=lactate dehydrogenase; Cr=creatinine; ICU=intensive care unit;

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. 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.

Table 3. Radiologic findings and vital signs

	Non dialysis CKD (n=23)	Missin g value	CKD on maintenance dialysis(n=28)	Missin g value	Dialysis in COVID-19 patients(n=7)	Missin g value	KT (N=20)	T(M)	p-value
Radiologic findings		12		13		2		6	
Unilateral GGO	6(54.5%)		3(20%)		1(20%)		1(7.1%)		0.050*
Bilateral GGO	5(45.5%)		5(33.3%)		3(60%)		9(64.3%)		0.383
Pleural effusion	5(45.5%)		5(33.3%)		4(80%)		5(35.7%)		0.337
Collapse	1(9.1%)		0(0%)		0(0%)		1(7.1%)		0.621
Consolidation	0(0%)		1(6.7%)		0(0%)		1(7.1%)		1.000
Emboli	0(0%)		1(6.7%)		0(0%)		0(0%)		1.000
Band	1(9.1%)		5(33.3%)		0(0%)		3(21.4%)		0.378
Drugs		0		2		0		0	
Hydroxychloroquine	20(87%)		20(76.9%)		7(100)		19(95%)		0.283
Kaletra	12(52.2%)		17(65.4%)		3(42.9%)		5(25%)		0.054
INF	2(8.7%)		0(0%)		0(0%)		0(0%)		0.332
Anibiotics	22(95.7%)		26(100)		7(100)		20(100)		0.658

Ggo=ground glass opacity, GCS=Glasgow coma scale

Discussion

COVID-19 can cause a variety of symptoms in patients. And 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 dyspnea. Also, dyspnea was the most common symptom in all patients on dialysis too, 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 on dialysis COVID-19 patients [16]; however, in this study, the prevalence of gastrointestinal symptoms was only 25%. 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 present study, 89.7% of patients had a history of underlying diseases. 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].

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]. It cannot be said that there is a strong correlation between albumin levels and patient outcome [24]. It is worth mentioning that 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 outcome of patients [25].

Taking the patients' CT-Scan into consideration, align 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 useful 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 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 important factors that can cause poor prognosis in COVID-19 patients. For this reason, it can be said that, it is important to evaluate clinical manifestations, radiologic findings, laboratory data, and outcome of COVID-19 patients with CKD, to establish a perspective for physicians to manage patients.

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Authors' contribution

Y.S.K., S.K.M. contributed to the acquisition of data, drafting the article, and interpretation of data. S.S. contributed to the conception and design and interpretation of data. S.T and D.Y contributed to the initiation of the research and interpretation of data. A.Z. and M.M.D. 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.

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Availability of data and materials

Data supporting the results reported in the article can be found by academic researches 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.

Competing interests

The authors declare that they have no competing interests.

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Figures

Figure 1

Consort diagram

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