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Clinical Characteristics of Hemodialysis Patients with COVID-19 Referred to Hemodialysis Centers Affiliated with the Shahrekord University of Medical Sciences Between 2020 and 2021

Nilofar Salehi [1], Seyed Mojtaba Sohrevardi [2, 3], Shahriyar Salehi Tali [4] and Golnaz Afzal [2, *]

[1] Faculty of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
[2] Clinical Pharmacy, Faculty of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
[3] Stroke Prevention and Atherosclerosis Research Centre, University of Western Ontario, Canada
[4] School of Nursing and Midwifery, Community-Oriented Nursing Midwifery Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran

[*] *Corresponding author*: Faculty of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Email: dr.golnaz.afzal@gmail.com

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Abstract

Background: The coronavirus pandemic (COVID-19) seriously threatens the health and life of people with underlying diseases, such as patients undergoing hemodialysis.
Objectives: This study aimed to determine the clinical characteristics of COVID-19 patients with chronic kidney disease undergoing hemodialysis referring to hemodialysis centers affiliated with the Shahrekord University of Medical Sciences between 2019 and 2021.
Methods: This was a retrospective descriptive-analytical study with a sample size of 144 hemodialysis patients with COVID-19. The data were collected by a demographic questionnaire, a checklist based on the presence of underlying diseases, the cause of the kidney failure, drugs received during hemodialysis, medications used for COVID, the result of COVID-19 treatment, and outpatient or inpatient treatment, and the checklist of laboratory indices extracted from the patient's medical records. Data were analyzed by SPSS version 20 and descriptive and analytical statistical tests.
Results: The average age was 57.2 ± 14.42 years, and 64.6% were men, 35.4% were women, 64.6% recovered, and 35.4% died, although 42.4% of patients were treated on an outpatient basis, and 57.6% needed hospitalization. Also, 93.7% of patients were vaccinated. The average duration of hemodialysis treatment was 6.44 years, and diabetes accounted for 31.1% of the causes of kidney failure, and these people had a higher chance of mortality. Positive c-reactive protein (CRP) results were found in 72.2% of patients, and 54.2% had a positive erythrocyte sedimentation rate (ESR). In addition, 22.2% of patients used mechanical ventilation, and 88.2% had positive PCR results. Iron, ferritin, albumin, and hemoglobin index were lower than normal in all patients. Patients with positive hepatitis B antigens were treated with sofosbuvir. In outpatient treatment, 65.6% used remdesivir, and 70.5% used dexamethasone. Regarding inpatient treatment, 75.9% used methylprednisolone, 56.6% used tocilizumab, and 54.2% used pirfenidone.
Conclusions: The rate of death and hospitalization in hemodialysis patients with COVID-19 was higher than that of normal people. Diabetes increases the chance of morbidity and mortality of COVID-19 in hemodialysis patients. The reduction of hemoglobin, iron, ferritin, and albumin weakened the therapeutic response of hemodialysis patients to COVID-19 and increased the chance of death. Although various drugs were used in the treatment of COVID-19 hemodialysis patients, the patients did not follow a single regimen.

Keywords: Chronic Kidney Disease, Hemodialysis, COVID-19

1. Background

COVID-19 is considered a serious threat to people's health and life, especially for patients who have underlying diseases, such as diabetes, kidney failure, tumors, heart and brain diseases, etc. (1). Among these conditions, hemodialysis patients are weaker and more prone to infection than ordinary people, their vulnerability and mortality are more severe (2). Compared to the general population, patients with chronic kidney disease under hemodialysis are susceptible to coronaviruses, especially people who are old and have underlying conditions, such as diabetes and high blood pressure (3). Also, in patients under hemodialysis, severe infection, and inflammation appear with milder symptoms, resulting from the weakening of the immunity (4).

Although many studies have been done on COVID-19 in various fields, such as treatment, clinical symptoms, diagnostic trends, systemic side effects, and even the presence of facilitating and aggravating factors, studies are very limited in Iran on COVID-19 patients under hemodialysis and their treatment process and results.

2. Objectives

This study aimed to investigate the clinical characteristics of patients with kidney failure undergoing hemodialysis with COVID-19 who were referred to hemodialysis centers affiliated with the Shahrekord University of Medical Sciences between 2019 and 2021.

3. Methods

3.1. Study Design and Sampling

This was a descriptive-analytical retrospective study approved by the Shahid Sadoughi University of Medical Sciences (IR.SSU.MEDICINE.REC.1400.205).

Sampling was based on the census so that the study population was all patients with chronic kidney disease under hemodialysis in Chaharmahal and Bakhtiari province who were infected with COVID-19 from the beginning pandemic of COVID-19 to the end of 2022.

3.2. Inclusion Criteria

(1) A patient with kidney failure undergoing hemodialysis in one of Shahrekord, Farsan, Borujen, and Lordegan hospitals in Chaharmahal and Bakhtiari province, who is suffering from COVID-19 and is undergoing medical treatment in an outpatient or inpatient basis.

(2) The medical information of the patients should be recorded and accessible.

(3) The patient's laboratory information should be recorded and accessible.

(4) All preventions, such as vaccination related to COVID-19, should be registered and accessible to the researcher.

3.3. Data Gathering

(1) Demographic questionnaire, including age, gender, duration of hemodialysis, cause of kidney failure, number of hemodialyses per week, underlying diseases, such as diabetes, high blood pressure, heart failure, and hepatitis B antigen positivity and negativity.

(2) Checklist of laboratory indices, including urea, creatinine, hemoglobin, hematocrit, ferritin, albumin levels, sodium, potassium, calcium, and phosphorus.

(3) Checklist of the inflammatory indices, including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cell count, and platelet count.

(4) Checklist of the treatment process, including outpatient, hospitalization, hospitalization in the intensive care unit (ICU), mechanical ventilation, O_2 saturation, receiving vaccines and the type of vaccine received, the use or non-use of drugs based on the diagnosis of specialist doctors and also the considerations of the Ministry of Health's COVID-19 headquarters.

3.4. Procedure

A letter was received from the Vice-Chancellor of Research at the Shahid Sadoughi University of Medical Sciences and presented to the Vice-Chancellor of Research at the Shahrekord University of Medical Sciences. Also, the necessary coordination was made with the Vice-Chancellor of Research of Treatment and the manager of Shahrekord hospitals. Then, the researcher entered the hemodialysis department of each hospital affiliated with the Shahrekord University of Medical Sciences. While introducing herself to the head of the department, the data related to the patients from the hemodialysis department, the COVID-19 department, and the medical records department were collected.

3.5. Statistical Analysis

Data were analyzed using SPSS version 20 software, and descriptive statistical tests, such as frequency, mean, and median and analytical statistics, such as independent *t*-test, Fisher's exact test, and chi-square test, were used.

4. Results

A total of 114 patients with chronic kidney disease were under hemodialysis. The average age of patients was 57.72 ± 14.42 years, 64.6% were men, 35.4% were women, the most important cause of chronic kidney disease was diabetes with 31.1%, and the most important underlying disease was heart failure with 27.1%. Also, 92.4% of patients were dialyzed three times a week, and the average duration of hemodialysis was 6.44 ± 3.5 years (Table 1).

The results showed that 63.4% recovered, 35.4% died, 42.4% received outpatient treatment, 57.6% were hospitalized, 84% received vaccines, 76.4% had oxygen saturation above 90%, 73.6% received oxygen by reservoir mask, and 82.2% had positive PCR (Table 2).

The results showed that hemoglobin, ferritin, and iron were lower than normal levels, serum glutamic-pyruvic transaminase (SGPT) and serum glutamic-oxaloacetic

Table 1. Demographic Characteristics of Hemodialysis Patients with COVID-19

Variables	Patients (N = 144) [a]
Age	57.72 ± 14.42
Sex	
Male	93 (64.6)
Female	51 (35.4)
Causes of renal failure	
Diabetes	45 (31.3)
Hypertension	36 (25)
Nephropathy	23 (16)
Infection	15 (10.4)
Reflex	14 (9.7)
Polycystic	11 (7.6)
Underlying diseases failure	
Diabetes	24 (16.7)
Heart failure	39 (27.1)
COPD	28 (19.4)
Hypertension	26 (18)
Diabetes and heart	14 (9.7)
None	13 (9)
Dialysis frequency	
Three times a week	133 (92.4)
Two times a week	11 (7.6)
Duration of hemodialysis, (y)	6.44 ± 3.5
Hepatitis antigen	
Positive	14 (9.7)
Negative	130 (90.3)

[a] Values are presented as No. (%) or mean ± SD.

transaminase (SGOT) were higher than normal levels, and 72.9% had positive CRP tests (Table 3).

The results showed that all patients with positive hepatitis B antigen were treated with sofosbuvir, and only one patient did not have hepatitis but received sofosbuvir. In outpatient, 65.6% received remdesivir, and 70.5% received dexamethasone, while in hospital treatment, 75.9% received methylprednisolone, 56.6% received tocilizumab, and 54.2% received pirfenidone (Table 4).

5. Discussion

The results showed that the average age of the patients was 57.72 ± 14.42 years, the average duration of hemodialysis treatment was 3.5 ± 6.44 years, and also 64.6% of the patients were male. Diabetes, with 31.3%, was the most important cause of kidney failure, and heart failure, with 27.1%, was the most important underlying disease.

Jia et al. reported that the average age of hemodialysis hospitalized COVID-19 patients was 57.72 ± 7.25, and the percentage of men in their study was 58.4% (5), which is in line with the results of this study.

Zhang et al. indicated that the average age of hemodialysis patients with COVID-19 was 62.3 years, 93.5% received dialysis three times a week, more than 50% had a history of dialysis for more than five years, and the most important underlying disease for kidney failure was diabetes (4). In the study by Aydin Bahat et al., the mortality rate in hemodialysis COVID-19 patients was between 14 and 51%, the hospital admission rate was 50%,

Table 2. Clinical Characteristics of Hemodialysis Patients with COVID-19 (N = 144)

Variables	Values [a]
Results treatment	
Positive (recovered)	93 (64.6)
Negative (died)	51 (35.4)
Clinical approach	
Outpatient	83 (57.6)
Inpatient	61 (42.4)
Vaccination	
Yes	121 (84)
No	23 (16)
O_2 saturation	
Upper 90%	110 (76.4)
Lower 90%	34 (23.6)
Oxygen use	
Nasal	6 (4.2)
Reservoir mask	106 (73.6)
Mechanical ventilation	32 (19.4)
PCR	
Positive	127 (82.2)
Negative	17 (11.8)

[a] Values are presented as No. (%).

Table 3. Laboratory and Inflammatory Indices of Hemodialysis Patients with COVID-19 (N = 144)

Variables	Normal Reference	Values [a]
Platelet count	145000 - 450000 (cu/mm)	123742 ± 27861
White blood cell	4000 - 10000 (cu/mm)	4752 ± 2152
FE	Male (60 - 160), female (80 - 180) mcg/dL	90.8 ± 12.16
Feretiene	10 - 122 (ng/dL)	86.85 ± 9.7
Calcium	8.5 - 10 (mg/dL)	9.08 ± 1.216
Potassium	3.5 - 5 (mEq/L)	4.88 ± 0.75
Phosphorous	3.5 - 5 (mg/dL)	7.8 ± 1.66
Albumin	3.5 - 5 (mg/dL)	4.08 ± 2.76
SGOT	< 38 (IU/L)	56.78 ± 13.11
SGPT	< 38 (IU/L)	54.31 ± 9.64
ESR	5 - 20 (mm/h)	28.29 ± 11.34
HCT	11 - 16 (g/dL)	10.4 ± 1.59
CRP		
Positive	-	105 (72.9)
Negative	-	39 (17.1)

[a] Values are presented as No. (%) or mean ± SD.

Table 4. Therapeutic Regimen in Hemodialysis Patients with COVID-19

Drug /Dosage	Inpatient (N = 83) [a]	Outpatient (N = 61) [a]
Remdesivir (100 mg)	41 (49.4)	40 (65.6)
Favipiravir (200 mg)	16 (19.3)	19 (31.1)
Azithromycin (500 mg)	66 (79.5)	36 (59)
Ivermectin (6 mg)	26 (31.3)	9 (14.8)
Sofosbuvir (400 mg)	5 (6)	7 (11.5)
Tocilizumab (400 mg/20mL)	47 (56.6)	17 (27.9)
Interferon alfa-2a	14 (16.9)	5 (8.2)
Interferon beta-1a	4 (4.2)	2 (3.3)
Dexamethasone (8mg)	31 (37.3)	43 (70.5)
Infliximab (100 mg)	14 (16.9)	16 (26.2)
Lopinavir/ritonavir (200/5 mg)	9 (10.8)	7 (11.5)
Prednisolone (5 mg)	30 (36.1)	10 (16.4)
Pirfenidone (200 mg)	45 (54.2)	17 (27.9)
Methylprednisolone (500 mg)	63 (75.9)	15 (24.6)

[a] Values are presented as No. (%).

the most common cause of kidney failure was diabetes, and the most common underlying diseases were diabetes and blood pressure (6). Asgharpour et al. conducted a study entitled "COVID-19 and kidney disease: Update on epidemiology, clinical manifestations, pathophysiology and management" (7), and their results and the results of the above studies confirmed our results.

According to the results, 35.4% died, 42.4% were treated as outpatients, 57.6% were admitted to the hospital, 84% received vaccines, 76.4% had oxygen saturation above 90%, 73.6% received oxygen through reservoir masks, 72.9% had positive CRP tests.

In the study by Stefan et al., the average age at death in hospitalized renal patients with COVID-19 was 63 years, and 38.4% died (8). Singh et al. reported that adults with chronic kidney disease, especially those on hemodialysis, were prone to more severe COVID-19 infection, and the mortality rate was higher in these patients (9). However, in our study, it was reported as 35.4%, and a high percentage of death was observed in hemodialysis patients suffering from COVID-19.

In the study by Preciado et al., more than 90% of the people with COVID-19 undergoing hemodialysis had an oxygen saturation of over 90%, while more than 84% of the dead people had an oxygen saturation of less than 90%. Also, 53.8% were hospitalized, and 46.2% received outpatient treatment (10). In the study by Indahningrum et al., 13.6% of COVID-19 patients with kidney disease were treated with mechanical ventilation, 10.4% were admitted to the ICU, and the hospital mortality of patients was %16 (11). Du et al. indicated that in addition to high blood pressure, a history of cerebrovascular accident, low oxygen pressure, pa02 < 80, and hospitalization in special wards were effective parameters in predicting the mortality rate of patients with COVID-19 (12). Therefore, the results indicated that severe lung damage combined with aggressive treatments, such as mechanical ventilation increased the chance of death in patients. Although this was also present in other patients, it was more significant in patients under hemodialysis. Although there are conflicting results regarding mortality in this study, the results of other studies confirm our other clinical characteristics.

According to the results, although most of the laboratory indicators were normal, the levels of hemoglobin, iron, and ferritin were low, so that 72.9% had positive CRP tests, ESR was higher than normal, and the SGPT levels were high.

Hong et al. indicated that all patients had high levels of CRP (13). Also, Li et al. showed that CRP was positive in most patients (14). Although there was no abnormal finding in the white blood cell count in the present study, in the study by Yuki et al., there was a significant relationship between age, gender, and the level of leukocyte count and

mortality of kidney patients with COVID-19., Also, 81.6% of the patients had a sedimentation rate higher than the normal level (15).

Rong et al. report that the CRP test, red blood cell sedimentation rate, white blood cell count, and neutrophil count have always been predictive markers of the severity of COVID-19 (12).

Sepe et al. indicated that in hemodialysis patients with COVID-19, the levels of inflammatory markers, such as CRP, ESR, procalcitonin, and dihydrogen lactate, were higher than the normal range (16). Therefore, the findings of other studies have shown that COVID-19 is associated with an increase in the inflammatory response of patients, which is in line with the results of our study.

Aiswarya et al. showed that in hemodialysis patients with COVID-19 under hemodialysis, the level of SGPT was higher than the normal level (17). Wang et al. indicated that SGPT was associated with an increase in hemodialysis rate in patients with COVID-19 (18). Therefore, the results of these studies supported our results.

The results showed that in outpatient treatment, remdesivir and dexamethasone, and in hospitalized patients, methylprednisolone, tocilizumab, and perfenidone were used for the treatment of COVID-19 in hemodialysis patients. Also, 65.65% of outpatients and 49.4% of hospitalized patients received remdesivir, and there was a statistically significant difference between outpatients and inpatients in terms of receiving remdesivir, and this drug was more commonly used in outpatients. Aiswarya et al. showed that more than 70% of the hemodialysis patients with COVID-19 received redeliver, and it was associated with improvements in arterial oxygen levels (17). It was in line with the results of the study.

The results of this study indicated that 70% of outpatients and 37.3% of inpatients used dexamethasone. Also, 54.1% of outpatients and 68.7% of inpatients under hemodialysis with COVID-19 used prednisolone. In addition, 24.6% of outpatients and 75.9% of inpatients used methylprednisolone, which is the drug of choice in the treatment of inpatients.

Pinzón et al. showed that treatment of severe COVID-19 pneumonia with high-dose methylprednisolone for three days followed by oral prednisolone for 14 days compared to 6 mg of dexamethasone for seven to ten days statistically reduced the need for transfusion. It reduced the patient's desire for special care and the indicators of CRP positivity (19). Another study reported that the use of dexamethasone in COVID-19 patients admitted to the ICU reduced mortality (20). Jeronimo CMP et al., in a clinical trial, indicated that the use of methylprednisolone in hospitalized COVID-19 patients had no effect on mortality (21). Although the results of studies have been conflicting, the results of this study indicated that corticosteroids are effective in the treatment of COVID-19 in hemodialysis patients.

The results showed that 27.9% of outpatients and 56.6% of inpatients used tocilizumab. There was a significant difference between the two groups, so that this drug was mostly used in hospitalized patients with inappropriate clinical conditions. However, in this study, it was not possible to comment on the result of the treatment and its efficacy.

Hasanin and Mostafa indicated that tocilizumab is able to prevent the progression of COVID-19 toward a critical level, especially when there are no symptoms of systemic inflammation (22). Although in this study, it is not possible to judge the effectiveness of the drug, tocilizumab was the first line in the treatment of hemodialysis patients.

The results showed that 27.9% of the hemodialysis patients with COVID-19 in outpatient treatment and 54.2% in inpatient treatment used pirfenidone (200 mg). There was a significant difference between outpatients and inpatients, which indicates that this drug is mostly used in inpatients and in inappropriate clinical conditions.

The results of Seri indicated that pirfenidone was a suitable drug for COVID-19 due to its anti-fibrosis effects (23). Bazdyrev et al. showed that pirfenidone, as an anti-fibrosis drug, was effective in rehabilitating patients with COVID-19 (24). Therefore, other studies have confirmed the use of pirfenidone in the treatment of COVID-19.

The results showed that 11.5% of the outpatients and 6.3% of the hospitalized people with positive hepatitis antigens received sofosbuvir.

Heo and Deeks indicated that sofosbuvir is a suitable and selective drug in the treatment of hepatitis C (25). Nourian and Khalili showed that sofosbuvir is the drug of choice in the treatment and prevention of COVID-19 and should be used before the virus invades the lungs (26). Abbass et al. indicated that the combined treatment of sofosbuvir with daclatasvir or ravidasvir was highly effective in the treatment of moderate to severe COVID-19 (27). Although in this study, it was used only for patients with hepatitis B-positive antigens.

5.1. Conclusions

The mortality rate of COVID-19 in patients under hemodialysis was higher than that of normal people, so that 35.4% of hemodialysis patients with COVID-19 died. The rate of hospitalization in these patients was much higher than in normal people, so that 57.6% of the patients were hospitalized. The mortality rate was 35.4% higher than in normal people, although the hospitalization rate

was 57.6%, much higher than in normal people. Old age, anemia, duration of hemodialysis treatment, low arterial oxygen saturation level, and diabetes were risk factors in COVID-19 patients. Most of the patients were treated with remdesivir and dexamethasone as outpatient treatment, and hospitalized patients were treated with tocilizumab, pirfenidone, and methylprednisolone; however, not all patients followed a single treatment regimen.

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Footnotes

Authors' Contribution: N. S. performed the study design and data collection. S. S. T. contributed to data collection and data analysis. S. M. S. performed administrative/technical/material support and critical revisions for important intellectual content. G. A. performed the study design and supervision.

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