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Original Article

Mortality Rates and Predictors in Hospitalized COVID-19 Patients Receiving Hemodialysis for Different Conditions

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Abstract

Background: To determine the mortality rates and predictors in patients hospitalized and treated for COVID-19 infection, who are also receiving hemodialysis (HD).

Method: This retrospective study included 104 patients who received HD and were hospitalized due to COVID-19 between March 2020 and 2021. Hospitalized patients who received HD were categorized into three groups: maintenance HD (MHD) patients, those receiving HD due to acute kidney injury (AKI) or chronic kidney disease (CKD), and those receiving HD due to AKI without CKD.

Results: Sixty-four (62%) of the patients were male. The mean age of the patients was 68±13 years. 37 were receiving MHD, 41 were receiving HD due to AKI on CKD, and 26 received HD due to AKI without CKD. 12(32%) of MHD patients and 29(71%) of patients receiving HD due to AKI on CKD died (p=0.002). Of the patients receiving HD due to AKI without CKD, 26(100%) died. Patients receiving HD due to AKI without CKD had the highest mortality rate compared to both MHD and AKI in CKD groups (p<0.001). Factors predicting mortality included lymphopenia, HD due to AKI on CKD, a more than two-fold increase in AST, the requirement of mechanical ventilation, and elevated d-dimer levels.

Conclusions: We showed high mortality in all patients receiving HD for different clinical conditions. These findings highlight the necessity of close monitoring and early intervention in COVID-19 patients who received HD.

Keywords: Hemodialysis, Chronic Kidney Disease, Mortality, Acute Kidney Injury, COVID-19

INTRODUCTION

Patients with chronic kidney disease (CKD) are at increased risk of Coronavirus Disease 2019 (COVID-19) infection and its complications due to neutrophil and monocyte dysfunction, impaired T-cell activation, and a diminished humoral response (1). Additionally, multiple factors—such as reduced clearance of inflammatory mediators, oxidative stress, frequent infections, metabolic acidosis, and technical aspects related to dialysis—contribute to a state of chronic inflammation in patients receiving maintenance hemodialysis (MHD). These factors further increase susceptibility to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection (2). Moreover, patients undergoing hemodialysis (HD) have a higher risk of COVID-19 transmission because they receive treatment in crowded and enclosed dialysis units three times per week (3). Therefore, the risk of COVID-19 infection and its complications is significantly elevated in patients with CKD. In addition, COVID-19 infection may present atypically in this patient population (4).

Patients undergoing MHD may require hospitalization due to COVID-19. Furthermore, patients with or without CKD who are hospitalized for COVID-19 may develop acute kidney injury (AKI). In such cases, renal replacement therapy (RRT) may be necessary. Previous studies have reported that 37% of patients hospitalized

with COVID-19 develop AKI, and 14% of these patients require RRT (5).

COVID-19 infection may lead to kidney injury ranging from subclinical AKI to AKI necessitating RRT (5,6). The primary mechanism is multi-organ dysfunction; however, electron microscopic examinations have demonstrated the presence of SARS-CoV-2 in renal tubules, suggesting that direct viral cytopathic effects may also contribute to AKI (7). It has been reported that COVID-19 patients who develop AKI have a significantly higher risk of in-hospital mortality (8). Additionally, a study conducted in Turkey found that mortality rates were higher among patients with CKD, AKI, and those undergoing HD who contracted COVID-19 compared to the general population (9).

This study aimed to determine the mortality rates and predictors in patients hospitalized due to COVID-19 who were receiving HD for different clinical indications.

METHODS

Study Protocol and Patients

This retrospective study was conducted at the Hemodialysis Unit of the Nephrology Clinic at Dışkapı Educational and Training Hospital. A total of 104 patients aged ≥18 years who were hospitalized for COVID-19 and received HD between March 2020 and March 2021 were included in the study. Patients were classified as having COVID-19 infection if they tested positive for COVID-19 by real-time polymerase chain reaction (RT-PCR) and had clinical findings consistent with the disease. Patients with thoracic computed tomography (CT) findings suggestive of COVID-19 but a negative RT-PCR test result were not included. Patients under 18 years of age, those who were transferred to another center during hospitalization, and those with insufficient follow-up data were excluded from the study. Additionally, patients referred from another hospital were excluded. The evaluated parameters were recorded retrospectively, and patients with missing data were not included in the analysis. The flowchart illustrating the selection of the study population is presented in **Figure 1.**

The following parameters were recorded during the first HD session following hospitalization: age, sex, COVID-19 severity, comorbidities, smoking history, and the use of renin-angiotensin-aldosterone system (RAAS) blockers. In addition, laboratory findings were documented, including serum creatinine, hemoglobin, leukocyte count, lymphocyte count, platelet count, D-dimer, C-reactive protein (CRP), albumin, aspartate aminotransferase (AST), ferritin, and lactate dehydrogenase (LDH). Radiological lung evaluations, COVID-19 treatments, intensive care unit (ICU) admissions, mechanical ventilation (MV) requirements, and mortality status were also recorded. Pulmonary findings associated with COVID-19 were assessed based on thoracic CT reports. Mild disease was defined as the presence of mild clinical symptoms without CT-confirmed lung involvement. Moderate disease was defined as CT-confirmed lung involvement accompanied by fever, cough, and dyspnea. Severe disease was diagnosed in patients presenting with at least one of the following criteria: respiratory rate ≥30 breaths per minute, oxygen saturation ≤93%, or an arterial partial pressure of oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) ratio ≤300 mmHg. Additionally, patients exhibiting more than 50% progression in lung involvement within 24–48 hours on radiological imaging were classified as having severe disease. Critical illness was defined by the presence of shock, multiple organ failure, ICU admission, or respiratory failure requiring MV (12).

STATISTICAL ANALYSIS

Statistical analyses were performed using SPSS version 20.0 (IBM Corp., Armonk, NY, USA). The normality of data distribution was assessed using the Shapiro-Wilk test, histograms, and Q-Q plots. Parametric data are presented as mean ± standard deviation, while non-parametric data are presented as median (minimum–

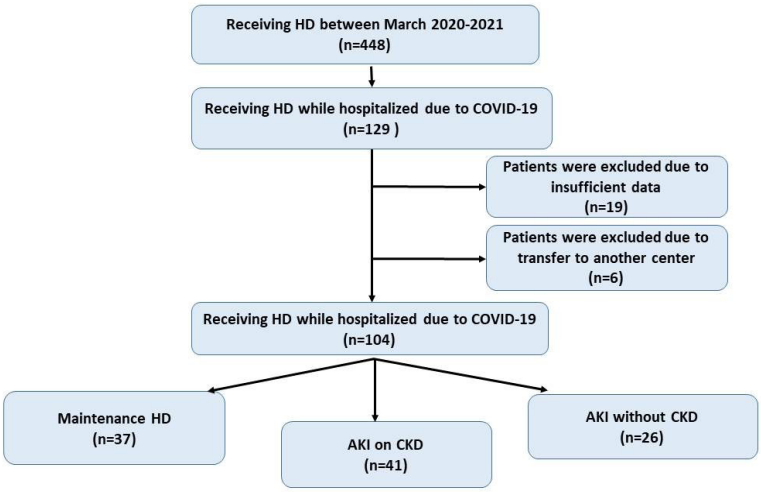

Figure 1. Flow chart illustrating the study population selection

Table 1. Demographic, clinical, and laboratory characteristics of patients

	All Patients (n=104)	Maintenance HD (n=37)	HD due to AKI on CKD (n=41)	HD due to AKI without CKD (n=26)	p-value
Gender, female, n (%)	40 (39)	18 (49)	17 (42)	5 (19)	0.054*
Age, mean ± SD	68 ± 13	61±14	71±11	71±13	0.001&
Comorbidities, n (%)					
HT	80 (77)	28 (76)	33 (81)	19 (73)	0.762*
DM	62 (60)	21 (57)	29 (71)	12 (46)	0.110*
CAD	40 (39)	15 (41)	18 (44)	7 (27)	0.555*
COPD	25 (24)	8 (22)	9 (22)	8 (31)	0.812*
Smoking, n (%)	44 (42)	10 (27)	15 (37)	19 (73)	0.001*
RAAS Blocker Use, n (%)	39 (38)	6 (16)	18 (44)	15 (58)	0.016*
Severe-Critical COVID-19, n (%)	64 (62)	13 (35)	29 (71)	22 (85)	<0.001*
Thorax CT Findings, n (%)					
Unilateral, single focus	13 (13)	9 (24)	3 (7)	1 (4)	0.025*
Unilateral, multiple foci	24 (23)	10 (27)	8 (20)	6 (23)	0.734*
Bilateral diffuse involvement	68 (65)	18 (49)	31 (76)	19 (73)	0.028*
Treatment, n (%)					
Favipiravir	99 (95)	34 (92)	39 (95)	26 (100)	0.334*
Glucocorticoid	72 (69)	16 (43)	33 (81)	23 (89)	<0.001*
Tocilizumab	31 (30)	6 (16)	13 (32)	12 (46)	0.036*
Convalescent Plasma	22 (21)	6 (16)	8 (20)	8 (31)	0.359*
Laboratory Findings (at HD initiation)					
Hemoglobin (g/dL), mean ± SD	9,8 ± 1,9	9,7 ± 1,7	9,9 ± 1,8	9,9 ± 2,2	0.938&
Leukocyte (mm^3), median (min-max)	9900(1200-54400)	6500 (2100-38000)	11400 (1400-49600)	19200 (1200-54400)	<0.001!
Lymphocyte (mm^3), median (min-max)	600 (200-5800)	700 (200-2500)	500 (200-1700)	600 (200-5800)	0.056!
Platelet (10^3/ mm^3), median (min-max)	170 (36-556)	181 (69-404)	157 (36-515)	165 (39-556)	0.958!
Creatinine (mg/dL), mean ± SD	5,7 ± 2,4	7,0 ± 2,6	5,3 ± 2,1	4,6 ± 1,5	<0.001&
AST (U/L), median (min-max)	32 (2-8110)	21 (8-504)	32 (2-2820)	114 (17-8110)	<0.001!
LDH (U/L), median (min-max)	468 (98-4687)	273 (98-1066)	562 (134-4464)	710 (237-4687)	<0.001!
Albumin (g/dL), mean ± SD	2,8 ± 0,5	3,1 ± 0,4	2,6 ± 0,4	2,5 ± 0,4	<0.001&
CRP (mg/L), median (min-max)	127 (1-529)	103 (1,4-439)	110 (8,1-529)	167 (1-437)	0.030!
Ferritin (µg/L), median (min-max)	1286 (70-59618)	1615 (263-12623)	1216 (70-51367)	1939 (176-59618)	0.186!
D-Dimer (mg/L), median (min-max)	3,0 (0,2-20,5)	2,3 (0,2-20,5)	3,4 (0,7-20,5)	3,8 (0,6-20,0)	0.020!
Evaluation of Laboratory Findings Based on Reference Ranges, n (%)					
Leukopenia, (<4000/mm^3)	4 (4)	2 (5)	2 (5)	0	0.306*
Lymphopenia, (<1500/mm^3)	70 (67)	21 (57)	30 (73)	19 (73)	0.142*
Thrombocytopenia, (<150x10/mm^3)	43 (41)	13 (35)	18 (44)	12 (46)	0.516*
CRP increase (>ten-fold)	85 (82)	28 (76)	33 (81)	24 (92)	0.195*
LDH increase (>two-fold)	54 (52)	3 (8)	29 (71)	22 (85)	<0.001*
AST increase (>two-fold)	27 (26)	2 (5)	10 (24)	15 (58)	0.045*
Clinical Outcomes					
Length of Hospital Stay, days, median (min-max)	9 (2-45)	8 (3-45)	8 (2-28)	12 (2-25)	0.355!
ICU admission, n (%)	64 (62)	13 (35)	27 (66)	24 (92)	<0.001*
Mechanical ventilation, n (%)	61 (59)	9 (24)	27 (66)	25 (96)	<0.001*
Mortality, n (%)	67 (64)	12 (32)	29 (71)	26 (100)	<0.001*

AKI, acute kidney injury; CKD, chronic kidney disease; HD, hemodialysis; ICU, intensive care unit; SD, standard deviation; CT, computed tomography; HT, hypertension; DM, diabetes mellitus; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; RAAS, renin angiotensin aldosterone system; CRP, C-reactive protein; AST, aspartate transaminase; LDH, lactate dehydrogenase. *Chi-square or Fisher's exact test. & One-way ANOVA test. ! Kruskal Wallis test

maximum). Categorical variables are presented as frequency (percentage). The Kruskal-Wallis test was used to compare non-parametric data among more than two groups, and the Mann-Whitney U test was used for pairwise comparisons. Parametric data between two independent groups were compared using Student's t-test, and data from more than two groups were compared using analysis of variance (ANOVA).

Table 2. The comparison results between surviving and deceased patients

Characteristic	Surviving Patients (n=37)	Deceased Patients (n=67)	p-value
Gender, female (n (%)	18 (49)	22 (33)	0,113*
Age, years, mean ± SD	61 ± 13	71 ± 12	<0,001&
Comorbidities, n (%)			
HT	31 (84)	49 (73)	0,217*
DM	24 (65)	38 (57)	0,417*
CAD	14 (38)	26 (39)	0,923*
COPD	8 (22)	17 (25)	0,668*
Smoking, n (%)	13 (35)	31 (46)	0,271*
RAAS blocker use, n (%)	9 (24)	30 (45)	0,039*
Mild-to-moderate COVID-19, n (%)	34 (92)	6 (9.0)	<0,001*
Laboratory findings at hemodialysis admission			
Hemoglobin (g/dL), mean ± SD	9,7 ± 1,6	9,9 ± 2,0	0,688&
Leukocyte (10^3/μL), median (min-max)	5,7 (2,1-25,4)	15,1 (1,2-54,4)	<0,001!
Lymphocyte (10^3/μL), median (min-max)	0,7 (0,3-2,5)	0,5 (0,2-5,8)	0,048!
Platelet (10^3/μL), median (min-max)	203 (78-515)	153 (36-556)	0,053!
AST (U/L), median (min-max)	22 (6-63)	62 (2-8110)	<0,001!
LDH (U/L), median (min-max)	269 (98-815)	593 (182-4687)	<0,001!
Albumin (g/dL), mean ± SD	3,1 ± 0,4	2,6 ± 0,5	<0,001&
CRP (mg/L), median (min-max)	78 (1-529)	161 (1-439)	<0,001!
Ferritin (μg/L), median (min-max)	836 (70-8372)	1672 (95-59618)	0,010!
D-Dimer (mg/L), median (min-max)	2,2 (0,2-20,5)	4,3 (0,6-20,5)	<0,001!
Evaluation of laboratory findings based on reference ranges, n (%)			
Leukopenia, (<4000/mm^3)	2 (5)	2 (3)	0,615*
Lymphopenia, (<1500/mm^3)	21 (57)	49 (73)	0,088*
Thrombocytopenia, (<150x10/mm3)	10 (27)	33 (49)	0,028*
CRP increase (≥ten-fold)	25 (68)	60 (90)	0,005*
LDH increase (≥two-fold)	4 (11)	50 (75)	<0,001*
AST increase (≥two-fold)	0	27 (40)	<0,001*
Clinical Outcomes			
Mechanical ventilation, n (%)	1 (3)	60 (90)	<0,001*
ICU admission, n (%)	6 (16)	58 (87)	<0,001*
Hospitalization duration (days), median (min-max)	8 (5-35)	9 (2-45)	0,624*

SD, standard deviation; HD, hemodialysis; DM, diabetes mellitus; HT, hypertension; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; RAAS, renin angiotensin aldosterone system; AST, aspartate transaminase; LDH, lactate dehydrogenase; CRP, C-reactive protein; CT, computed tomography. *Chi-square or Fisher's exact test. & Student's t test. ! Mann-Whitney U test

Categorical data were compared using either Fisher's exact test or Pearson's chi-squared test, as appropriate. Factors predicting mortality were evaluated using Cox regression analysis (Backward Likelihood Ratio method). Variables included in the mortality prediction model were age, lymphopenia, D-dimer level, HD due to AKI on CKD, a more than two-fold increase in AST, the requirement for MV, a more than two-fold increase in LDH, and albumin level. A p-value <0.05 was considered statistically significant.

Table 3. Predictors of mortality in patients hospitalized with COVID-19 and receiving HD

Variable	HR	95%CI for HR		p-value
		Lower	Upper	
Age	1.009	0.985	1.034	0.461
Lymphopenia	1.001	1.001	1.002	0.001
D-Dimer	1.066	1.014	1.121	0.012
HD due to AKI on CKD	1.816	1.058	3.116	0.030
AST increase (>two-fold)	2.005	1.123	3.580	0.019
Requirement of mechanical ventilation	4.433	1.703	11.544	0.002
LDH increase (>two-fold)	0.847	0.383	1.876	0.683
Albumin	0.998	0.613	1.626	0.993

RESULTS

A total of 104 patients were included in the study. Sixty-four patients (62%) were male. The mean age was 68±13 years. Among these patients, 37 were receiving MHD, 41 were HD due to AKI on CKD, and 26 were receiving HD due to AKI without CKD. The demographic, clinical, and laboratory parameters of the patients, as well as the comparison results among the three groups, are presented in **Table 1.**

Twenty-four MHD patients were receiving HD through an arteriovenous fistula. The median duration of HD in the MHD group was 8 years (range: 0–17 years).

Follow-up data demonstrated that the median duration of hospitalization was 9 days (range: 2–45 days). During follow-up, 64 patients (62%) required admission to the ICU, 61 patients (59%) required MV, and 67 patients (64%) died. The comparison results between surviving and deceased patients are presented in **Table 2.** Independent factors associated with mortality are shown in **Table 3.**

While 12 patients (32%) in the MHD group died, 29

patients (71%) in the AKI on CKD group died (p=0.002). All patients (n=26; 100%) receiving HD due to AKI without CKD died. The mortality rate was highest among patients receiving HD due to AKI without CKD when compared to both the MHD and AKI on CKD groups (p<0.001).

DISCUSSION

In our study, mortality was found to be high among patients receiving HD across three different clinical conditions. Furthermore, patients receiving HD due to acute kidney injury (AKI) without CKD had the highest mortality rates. In addition, the study identified several predictors of mortality in patients undergoing HD, including elevated AST, lymphopenia, increased D-dimer levels, HD due to AKI on CKD, and the requirement for MV.

In the general population, COVID-19-related mortality rates have been reported to range from 1.4% to 8% (13). In chronically immunosuppressed uremic patients, increased proinflammatory cytokine levels and decreased clearance of these cytokines contribute to higher mortality rates (14,15). In our study, the overall mortality rate was 64%. Specifically, mortality was 32% in patients receiving MHD, 71% in patients receiving HD due to AKI on CKD, and 100% in patients receiving HD due to AKI without CKD.

Previous studies involving MHD patients have reported similar mortality rates, with 24% in Italy, 31% in Spain, and 32% in New York (16–18). The mortality rates among MHD patients in our study were consistent with these findings. Similarly, a study conducted in Turkey demonstrated that 74% of patients with CKD who developed stage 3 AKI died, which aligns with our results (19). A large-scale study involving 5,449 patients found that 97% of the 285 patients with AKI requiring RRT also developed respiratory failure requiring MV (5). During the study period, 119 patients with AKI requiring RRT remained hospitalized, while 157 of the 166 patients (95%) died (5). The high mortality rates observed in our study among patients with AKI requiring RRT are consistent with the existing literature.

Additionally, AKI is directly associated with increased rates of ICU admission, MV requirement, and mortality, which may explain the high mortality rates observed in our cohort of patients with AKI (8). Mechanical ventilation has also been shown to be an independent predictor of AKI development and mortality in patients with AKI (20). Another study demonstrated that the need for MV is a significant risk factor for mortality in patients receiving HD due to AKI (21). Therefore, patients requiring both RRT and MV should be closely monitored, as they are at significantly increased risk of mortality.

The cytokine storm that occurs during COVID-19 infection can lead to fever and elevated ferritin levels, along with secondary hemophagocytic lymphohistiocytosis. It can also result in elevated AST and LDH levels due to hepatic involvement (22,23). A study conducted in the general population demonstrated an association between COVID-19-related mortality and lymphopenia (24). Similarly, lymphopenia was identified as a predictor of mortality in another study involving patients undergoing HD, consistent with findings in the general population (25. In addition, a separate study reported that a more than two-fold elevation in AST levels during hospitalization was associated with increased mortality in patients receiving MHD (26). It has also been shown that disease severity increases in COVID-19 patients who develop AKI as serum D-dimer levels rise (27). Another study investigating patients undergoing HD found that D-dimer levels were significantly higher in those who died from COVID-19 compared to those who survived (28). The same study also reported that the requirement for MV was a strong predictor of mortality in HD patients (28).

In our study, the predictors of mortality included lymphopenia, a more than two-fold increase in AST levels, elevated D-dimer levels, and the need for MV during follow-up. Although the mortality predictors identified in our study are consistent with previous reports in the literature, further comprehensive studies are needed to validate these findings.

Limitations of the Study

The limitations of our study include its retrospective design and relatively small sample size. Additionally, the absence of a control group and the single-center nature of the study further limit the generalizability of the findings. The fact that this was a single-center and retrospective analysis prevented the evaluation of potential variations in clinical practices among different HD centers. Another important limitation is that the study included only pre-vaccination data. COVID-19 vaccination has been shown to induce antibody responses and provide protection against infection in HD patients (29). Therefore, our findings may not be directly comparable to current patient outcomes in the post-vaccination era. Future multicenter, prospective studies that include vaccinated populations are necessary to validate and expand upon these results.

CONCLUSION

Our study demonstrated high mortality rates among patients receiving MHD, HD due to AKI on CKD, and HD due to AKI without CKD. In addition, we found that laboratory parameters such as elevated AST, lymphopenia, and increased D-dimer levels were independent predictors of mortality in patients undergoing HD. These findings highlight the critical

need for close monitoring and early intervention in COVID-19 patients requiring HD, particularly those with AKI. Future pandemic preparedness strategies should prioritize early identification and management of these high-risk populations. Moreover, prospective multicenter studies are needed to evaluate the impact of vaccination and post-COVID-19 complications in patients receiving HD.

DECLARATIONS

Ethics committee approval: This study was carried out according to the ethical rules and principles of the Declaration of Helsinki. Patient data was retrospectively accessed and anonymized before analysis. Approval for the study protocol was obtained from the Ethics Committee of Dışkapı Education and Training Hospital (approval date: 21 March 2022; approval number: 133/13).

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