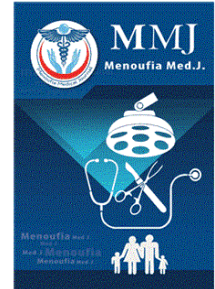




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ORIGINAL STUDY

Risk Factors and Outcomes of Covid 19 in Hemodialysis Patients

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Abstract

Objectives: To estimate the incidence of coronavirus disease 2019 (COVID-19) among the hemodialysis patients and the related risk factors of COVID-19 severity for critical outcomes, including intensive care unit (ICU) admission or death.

Background: Chronic kidney disease patients who receive maintenance dialysis are particularly vulnerable to COVID-19.

Methods: we evaluated the clinical outcomes of 70 patients on maintenance hemodialysis were divided according to the clinical severity of the confirmed COVID-19, into mild to moderate (group I), and sever (group II), including ICU admission, and death during 2020 till 2022 years. Demographic, clinical and laboratory data were collected.

Results: The clinical outcomes of hemodialysis COVID-19 patients with severe symptoms, including ICU admission 10 (100%) with mean duration of (10.43 ± 0.32) days and all patients unfortunately non-survived in comparison to 14 (23.3%) of patients with mild to moderate symptoms admitted to ICU ($P = 0.020$). The multivariate linear regression analysis showed that O₂ saturation followed by requiring ICU admission were the most independent risk factors of mortality among dialysis patients with COVID-19 OR, 8.974, 2.40, (CI:1.039–77.508) (CI:1.35–5.79), respectively ($P = 0.005$). We found also that old age ($P = 0.03$), hypertension as associated comorbidity ($P = 0.008$), elevated d-dimer ($P = 0.009$), and longer duration of hemodialysis (HD) ($P = 0.002$) were the most risk factors for mortality in COVID-19 dialysis patients.

Conclusion: Patients undergoing hemodialysis who have COVID-19 may have extended ICU stay and negative prognosis. There was a strong association between death related to COVID-19 infection in dialysis patients and the duration of dialysis, associated comorbidities, and severity of symptoms.

Keywords: Computed tomography, COVID-19 severity, Hemodialysis patients, Intensive care unit, Mortality rate

1. Introduction

The coronavirus disease 2019 (COVID-19) has rapidly spread in nearly three months after the discovery of its causative agent, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), leading to the ongoing pandemic [1].

While males and females of all ages have presented with COVID-19, the majority of severe cases and fatalities have occurred in a specific proportion of patients, including the elderly and those with chronic underlying conditions up to now [2]. The mortality rate in the general population ranges from 1.4% to 8%, and it increases significantly in patients requiring intensive care unit (ICU) admission [3].

Age and gender are well-established risk factors for severe COVID-19 outcomes: over 90% of the COVID-

19- related deaths in the United Kingdom (UK) have been in people over 60, and 60% in men [4]. Conditions, such as hypertension, cardiovascular disease, diabetes, advanced age, chronic obstructive pulmonary disease, obesity, and chronic kidney disease (CKD) are associated with greater risk of COVID-19 and more severe infection [5].

Hemodialysis patients are at a higher risk of worsened prognosis with COVID-19, as most of them are elderly and have multiple comorbidities, and some of them might be taking immunosuppressive drugs to treat an autoimmune disease or a failed kidney allograft [6].

Overall, end-stage renal disease (ESRD) has not been identified as a main prediction factor for poor outcomes in patients with COVID-19 in most previous studies [2]. The lack of the presence of

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kidney failure diseases among the prognostic factors of COVID-19 may be misinterpreted that these patients are not mainly at a higher risk for the poor outcomes of COVID-19. In other words, there is still insufficient evidence regarding the prognostic impact of ESRD on COVID-19 patients [7].

This study aims to estimate the incidence of COVID-19 among the hemodialysis patients and the related risk factors of COVID-19 severity for critical outcomes, including ICU admission or death.

2. Methods

This study was conducted at Police Hospitals, Kidney Dialysis Unit of Nephrology Department using a retrospective cohort analytic hospital-based study during 2020 till 2022 years. The study protocol was approved by the Ethical Committee of Faculty of Medicine, Menoufia University, and the patients received written informed consent about this study. The research was conducted on 70 hemodialysis patients, that were divided according to the clinical severity of the confirmed coronavirus disease 2019 (COVID-19), into 60 patients with mild to moderate (group I), and 10 patients with severe clinical presentation (group II). The diagnosis of COVID-19 infection was confirmed with a positive test of nasopharyngeal swabs specimen and/or a positive chest computed tomography (CT) scan. Patients on immunosuppressive therapy, viral infection other than COVID-19, malignancy and uncooperative patients were excluded from the study. The criteria of clinical severity of COVID-19 was evaluated [8] as the following, Mild illness included individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging, Moderate illness included individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation measured by pulse oximetry (SpO_2) \geq 94% on room air at sea level, severe illness as individuals who have $SpO_2 < 94\%$ on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) < 300 mmHg, a respiratory rate >30 breaths/min, or lung infiltrates $>50\%$ [8]. The data were collected from all patients, including full history (age, gender, comorbidities, HD duration, medications used in management of COVID-19), clinical presentation as (blood pressure, temperature, respiratory rate, dyspnea, cough, headache, vomiting, diarrhea, sore throat, and myalgia/arthralgia) and full routine laboratory investigations such as complete

blood count (CBC) by Sysmex xp 300 (Sysmex Company Germany), sodium potassium magnesium, phosphorus, calcium, iron, total iron binding capacity (TIBC), ferritin, urea, creatinine, and albumin by architect plus c 8000 (abbot company, Germany), (blood parameters, inflammatory markers, kidney function test, electrolytes, iron profile, intact parathyroid hormone (iPTH) and albumin). iPTH by Latinity (abbot company, USA). We also evaluated the clinical outcome, including intensive care unit (ICU) admission of individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction, duration of ICU admission and death. Dialysis Efficiency (Kt/V) calculated by the ratio of urea clearance (K) multiplied by dialysis time (t) to the volume of water in the body.

2.1. Statistical analysis

Statistical analysis of the data was performed by using IBM SPSS 22 software package under Windows 8.1® operating system. Qualitative data were described in the form of number and percentage.

Table 1. Demographic data of the hemodialysis COVID-19 patients.

Severity of The Disease	Group I (n = 60)	Group II (n = 10)	P value
Age/year	61.35 ± 4.67	66.42 ± 4.41	0.030*
Gender			
Female	18 (30%)	0 (0%)	0.097
Male	42 (70%)	10 (100%)	
Duration of hemodialysis (years)	3.52 ± 2.24	5.43 ± 2.24	0.023*
Time to reach pre-COVID state (days)	2.46 ± 1.45	2.52 ± 1.56	0.753
Cause of ESRD, n (%)			
Glomerulonephritis	7 (11.6%)	6 (60%)	
Autosomal dominant polycystic kidney disease	4 (6.7%)	4 (40%)	
Congenital diseases	3 (5%)	5 (50%)	
Diabetic nephropathy	14 (23.3%)	6 (60%)	
Interstitial Nephritis	4 (6.7%)	0 (0%)	
Pyelonephritis	1 (1.7%)	4 (40%)	0.025*
Vascular	6 (10%)	6 (60%)	
Comorbidities			
Hypertension	50 (83.4%)	7 (70%)	<0.001*
Diabetes	20 (33.3%)	9 (90%)	0.032*
Congestive heart failure	3 (5%)	10 (100%)	0.037*
Ischemic heart disease	7 (11.6%)	8 (80%)	0.426
Obesity	1 (1.7%)	4 (40%)	0.358
Lung diseases	1 (1.7%)	2 (20%)	0.732
Thalassemia	1 (1.7%)	1 (10%)	1

COVID-19, Coronavirus disease 2019; ESRD, End stage renal disease.

Both groups were compared using independent t test for data as mean ± SD, and using Chi-square test for data represented as N(%).

*Significant.

Table 2. Baseline data of patients according to clinical, laboratory and outcomes of HD COVID-19 patients.

Severity of The Disease	Group I (n = B60)	Group II (n = 10)	P value
Initial symptoms			
Temperature (° C)	38.46 ± 0.73	40.24 ± 0.24	0.748
O2 saturation	83.45 ± 3.45	75.46 ± 2.67	0.368
Respiratory rate (Cycle/min)	20.56 ± 2.65	16.54 ± 1.53	0.345
cough	50 (83.4%)	8 (80%)	0.846
Headache	35 (58.3%)	10 (100%)	0.047*
Dyspnea	26 (43.3%)	10 (100%)	0.037*
Sore throat	3 (5%)	6 (60%)	<0.001**
Vomiting	1 (1.7%)	5 (50%)	<0.001**
Diarrhea	1 (1.7%)	9 (90%)	<0.001**
Myalgia/Arthralgia	1 (1.7%)	9 (90%)	<0.001**
Laboratory data on admission			
HGB (gm/dl)	9.35 ± 0.42	9.17 ± 0.31	0.936
WBCs (10 ³ /cmm)	7.46 ± 2.78	8.32 ± 2.47	0.715
Lymphocytes (10 ³ /cmm)	0.85 ± 0.62	0.72 ± 0.47	0.883
PLTs (10 ³ /cmm)	252.13 ± 64.25	224.56 ± 63.24	0.069
D-dimer (mg/L)	3.23 ± 0.42	5.21 ± 0.34	0.035*
Ferritin (mic/L)	434.42 ± 33.24	552.44 ± 35.65	<0.001**
Iron (mcg/dL)	44.42 ± 5.36	46.85 ± 5.62	0.765
Total iron binding capacity (mcg/dL)	161.77 ± 24.68	169.55 ± 24.67	0.533
Urea (mg/dL)	136.43 ± 26.25	187.23 ± 25.21	<0.001**
Creatinine (mg/dL)	7.73 ± 1.75	8.75 ± 1.33	0.715
Serum Sodium (mEq/L).	135.57 ± 1.24	135.32 ± 1.14	0.952
Potassium (mmol/L)	4.44 ± 0.66	4.94 ± 0.66	0.742
Serum Magnesium (mg/dL)	2.44 ± 0.55	2.84 ± 0.54	0.635
Phosphorous (mg/dL)	4.24 ± 1.33	4.75 ± 1.77	0.736
Calcium (mg/dL)	8.64 ± 0.56	8.84 ± 0.53	0.574
iPTH ((pg/mL)	523.92 ± 35.44	593.75 ± 34.43	0.056
Albumin (g/dL)	3.41 ± 0.35	3.49 ± 0.37	0.843
KT/V	1.24 ± 0.73	1.84 ± 0.21	0.622
Clinical outcomes of COVID-19			
ICU admission	14 (23.3%)	10 (100%)	0.020*
Death	2 (3.3%)	10 (100%)	0.001*
Duration of ICU stay	7.33 ± 1.53	10.43 ± 0.32	0.033*

COVID-19, coronavirus disease 2019; Kt/V, Dialysis Efficiency; HD, Hemodialysis; HGB, hemoglobin; iPTH, Intact Parathyroid Hormone; ICU, intensive care unit; PLTs, platelets; WBCs, white blood cells.

Both groups were compared using independent t test for data as mean ± SD, and using Chi-square test for data represented as N (%).

*Significant.

Chi-Square test (X^2): was used for comparison of qualitative data. Student's t test was used for the comparison of quantitative data. Regression analysis: used to sort the markers according to their importance in discrimination between different studied groups of patients. The analysis of variance (ANOVA) test was used in comparing three or more means (parametric quantitative data) for statistical significance.

3. Results

According to the severity of the disease of hemodialysis (HD) coronavirus disease 2019 (COVID-19) patients, they were divided in mild to moderate group (42 males & 18 females) and sever presentation group (10 males) with no statistically significant difference between them. The mean age in group II

was higher (66.42 ± 4.41) than group I (61.35 ± 4.67) years with significant difference ($P < 0.05$). The most common causes of primary kidney disease in HD COVID-19 patients with severe symptoms were glomerulonephritis and diabetic nephropathy 6 (60%), the associated comorbidity was the congestive heart failure 10 (100%) ($P = 0.032$) and the mean duration of hemodialysis was (5.43 ± 2.24 y), ($P = 0.023$) while the most common cause of primary kidney disease in HD COVID-19 patients with mild to moderate symptoms was diabetic nephropathy 14 (23.3%), ($P = 0.025$), the associated comorbidity was the hypertension 50 (83.4%), ($P < 0.001$) and the mean duration of hemodialysis was (3.52 ± 2.24 y) with significant statistically difference between the two groups ($P = 0.023$) (Table 1),

The initial COVID-19 symptoms including headache ($P = 0.047$), dyspnea ($P = 0.037$), sore throat

($P < 0.001$), vomiting ($P < 0.001$), diarrhea ($P < 0.001$) and Myalgia/Arthralgia ($P < 0.001$) more presented at the severe group than the other group and, the associated collected laboratory data showed an elevation of the value of D-dimer ($P = 0.035$), ferritin ($P < 0.001$) and urea ($P < 0.001$) in group II than group I. The clinical outcomes of hemodialysis COVID-19 patients with severe symptoms, including intensive care unit (ICU) admission 10 (100%) with mean duration of (10.43 ± 0.32) days and all patients unfortunately non-survived in comparison to 14 (23.3%) of patients with mild to moderate symptoms admitted to ICU ($P = 0.02$) and only 2 (3.3%) of them non-survived ($P < 0.001$) (Table 2).

Table 3. Comparison of demographic, clinical, and laboratory data between survived and non-survived HD COVID-19 patients.

	Non-Survived N = 12 (17.1%)	Survived N = 58 (82.9%)	P value
Age/year	67.35 ± 2.14	63.23 ± 2.41	0.027*
Gender (male)	9 (75%)	43 (74.1%)	0.424
Duration of HD (years)	6.45 ± 2.56	3.78 ± 2.81	0.023*
Comorbidity (HTN)	10 (83.3%)	47 (81%)	0.643
Comorbidity (DM)	9 (75%)	20 (34.5%)	0.004*
Temperature (° C)	40.02 ± 0.82	37.74 ± 0.12	0.637
O2 saturation	90.5 ± 1.23	97.8 ± 1.53	0.035*
Systolic BP (mmHg)	135.3 ± 5.35	125.2 ± 5.42	0.025*
Diastolic BP (mmHg)	85.4 ± 3.42	80.1 ± 3.84	0.036*
ICU admission	10 (83.3%)	14 (24.1%)	<0.001**
Duration of ICU stay	9.07 ± 1.42	6.75 ± 0.32	0.003*
HGB (gm/dl)	9.15 ± 0.68	10.16 ± 0.42	0.957
WBCs (10 ³ /cmm)	8.23 ± 2.13	7.43 ± 2.21	0.753
Lymphocytes (10 ³ /cmm)	0.73 ± 0.23	0.84 ± 0.32	0.689
PLTs (10 ³ /cmm)	221.43 ± 65.23	264.55 ± 73.34	0.049*
D-dimer (mg/L)	5.24 ± 0.45	3.31 ± 0.54	0.045*
Ferritin (mic/L)	536.42 ± 43.32	451.43 ± 45.56	<0.001**
Iron (mcg/dL)	47.41 ± 5.26	42.85 ± 5.32	0.525
TIBC	169.76 ± 24.64	161.56 ± 24.25	0.536
Urea	189.43 ± 22.24	132.25 ± 23.22	<0.001**
Creatinine	8.34 ± 1.25	7.76 ± 1.14	0.965
Sodium	135.67 ± 1.53	135.46 ± 1.42	0.435
Potassium	4.49 ± 0.67	4.24 ± 0.24	0.726
Magnesium	2.94 ± 0.56	2.52 ± 0.14	0.433
Phosphorous	4.87 ± 1.45	4.15 ± 1.55	0.785
Calcium	8.86 ± 0.53	8.35 ± 0.25	0.272
iPTH	595.56 ± 33.56	523.75 ± 34.35	0.578
Albumin	3.49 ± 0.42	3.40 ± 0.63	0.346
Kt/V	2.25 ± 0.73	1.23 ± 0.53	0.047*

BP, blood pressure; COVID-19, coronavirus disease 2019; HD, Hemodialysis; HGB, hemoglobin; ICU, intensive care unit; iPTH, Intact Parathyroid Hormone; Kt/V, Dialysis Efficiency; PLTs, platelets; TIBC, total iron binding capacity; WBCs, white blood cells.

Both groups were compared using Mann–Whitney U test for data as mean ± SD, and using Chi-square test for data represented as N (%).

*Significant.

The nonsurvived COVID-19 dialysis patients with history of longer duration of hemodialysis associated with diabetes mellitus (DM) as comorbidity and low efficiency of dialysis urea clearance (K)/dialysis time (t) (Kt/V), (2.25 ± 0.73) ($P < 0.047$), 10 (83.3%) required longer duration of ICU admission with low O₂ saturation ($P = 0.035$) and higher systolic and diastolic blood pressure (BP) ($P = 0.25$, $P = 0.036$, respectively), there laboratory data showed higher urea, ferritin ($P < 0.001$ for each), D-dimer ($P = 0.045$) and less platelets values ($P = 0.049$) than survived patients (Table 3).

The multivariate linear regression analysis showed that O₂ saturation followed by requiring ICU admission were the most independent risk factors of mortality among dialysis patients with COVID-19 OR, 8.974, 2.40, (CI:1.039–77.508) (CI:1.35–5.79) respectively ($P = 0.005$). We found also that old age ($P = 0.03$), hypertension as associated comorbidity ($P = 0.008$), elevated d-dimer ($P = 0.009$), and longer

Table 4. Multivariate linear regression analysis of risk factors of mortality among dialysis patients with COVID-19.

	Univariate analysis	
	P value	OR (95%CI)
Age	0.030*	1.032 (1.005–1.058)
Gender (male)	0.863	1.04 (0.64–1.76)
Comorbidity (HTN)	0.008*	1.146 (1.076–1.563)
Comorbidity (DM)	0.463	0.765 (0.278–1.375)
Duration of HD (years)	0.002*	1.001 (1.000–1.000)
O ₂ saturation	0.046*	8.974 (1.039–77.508)
Systolic BP (mmHg)	0.036*	1.374 (0.775–2.465)
Diastolic BP (mmHg)	0.033*	1.335 (0.735–2.366)
Temperature (° C)	0.273	0.646 (0.296–1.1412)
ICU admission	0.005*	2.40 (1.35–5.79)
Duration of ICU	0.340	0.664 (0.277–1.854)
HGB (gm/dl)	0.444	0.642 (0.36–1.52)
WBCs (10 ³ /cmm)	0.439	1.356 (0.654–2.471)
Lymphocytes (10 ³ /cmm)	0.973	0.882 (0.675–1.402)
PLTs (10 ³ /cmm)	0.279	3.112 (0.389–24.3)
D-dimer (mg/L)	0.009*	1.283 (1.065–1.545)
Ferritin (mic/L)	0.257	0.503 (0.153–1.651)
Iron (mcg/dL)	0.733	21.081 (0.142–84.742)
TIBC	0.137	2.485 (0.750–8.109)
Urea	0.833	1.250 (0.158–9.895)
Creatinine	0.395	0.719 (0.337–1.536)
Sodium	0.595	1.517 (0.356–7.051)
Potassium	0.085	4.234 (0.820–21853)
Magnesium	0.312	0.887 (0.702–1.120)
Phosphorous	0.330	0.644 (0.207–1.724)
Calcium	0.119	0.341 (0.008–1.318)
PTH	0.067	0.371 (0.130–1.071)
Albumin	0.882	0.973 (0.675–1.402)
Kt/V	0.455	0.897 (0.674–1.094)

BP, blood pressure, CI, Confidence intervals, COVID-19, coronavirus disease 2019, HD, Hemodialysis, HGB, hemoglobin, ICU, intensive care unit, iPTH, Intact Parathyroid Hormone, Kt/V, Dialysis Efficiency, OR, Odd ratio, PLTs, platelets, TIBC, total iron binding capacity, WBCs, white blood cells.

duration of hemodialysis (HD) ($P = 0.002$) were the most risk factors for mortality in COVID-19 dialysis patients (Table 4).

4. Discussion

Coronavirus disease 2019 (COVID-19) infection emerged in Wuhan, China in December 2019 and has spread rapidly worldwide. The European Renal Association COVID-19 Database (ERACODA) Working Group previously reported a 28-day mortality of 25% in dialysis patients during the first pandemic wave. The incidence of COVID-19 infection among hemodialysis (HD) patients was 7.7% and the mortality rate was 22.4% [9]. This study aims to estimate the incidence of COVID-19 among the hemodialysis patients and the related risk factors of COVID-19 severity for critical outcomes, including ICU admission or death.

In the current study, 33.3% in mild to moderate covid 19 patients had diabetes as comorbidity, while in sever covid 19 group, 90% with a statistically significant difference in between. A significant elevation of d-dimer, ferritin, urea, with sever group than mild to moderate, but non-significant difference regarding to the other laboratory findings. Also, old age and comorbidity with hypertension are causes of death among dialysis patients with COVID-19. The causes of death among dialysis patients with COVID-19 was, old age, comorbidity, ICU admission, elevated d-dimer, increased duration of HD, O₂ saturation, systolic and diastolic blood pressure (BP). Oh *et al.* [10], found that lower socioeconomic status was associated with a higher risk of contracting COVID-19 in South Korea especially in the older population. Also, Hawkins *et al.* found that lower education levels, median income and poverty rate were strongly associated with higher rate COVID-19 cases [11]. Another explanation was that HD patients are more susceptible to COVID-19 infection because of greater age, coexistence of comorbidities, and immune-suppressed status [12,13]. Gu *et al.* [14], who stated that patients with diabetes were reported to have higher incidence of sever COVID-19. In a Chinese series by Tang *et al.* [15], the most common symptoms were fever, cough, and bilateral ground-glass or patchy opacity of the lungs. Hsu *et al.* [16], as they found that, older patients had higher mortality, particularly those over 80 years old. Ghonimi *et al.* [17], who stated that the main risk groups for mortality and developing complications during the COVID-19 pandemic are the elderly and people with chronic health conditions [4]. In the study done by Hsu *et al.* [16], found that in dialysis patients who developed COVID19, older age, hypertension, congestive heart failure, peripheral

vascular disease, and wheelchair use were associated with higher risk of death. In the study done by Salerno *et al.* [18], they found that older age, male sex, hispanic ethnicity, nursing home residence, and higher body mass index (BMI) were associated with higher postdiagnosis mortality.

5. Conclusions

Patients on maintenance hemodialysis suffering from severe COVID-19 infection have poor prognosis with high mortality (83.3%). Longer duration of hemodialysis in old age patients suffering from associated comorbidities, elevated d-dimer and lower O₂ saturation were the most independent risk factors for mortality in COVID-19 dialysis patients.

Conflicts of Interest

No conflict of interest.

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