JOJ
Urology & Nephrology
ISSN: 2476-0552

Juniper Publishers
key to the Researchers

Research article
Volume 8 Issue 1 - June 2023
DOI: 10.19080/JOJUN.2023.08.555731

JOJ uro & nephron

COVID-19 among Hospitalized Chronic Hemodialysis Patients: Clinical Features and Predictors of Mortality

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Submission: June 05, 2023; **Published:** June 20, 2023

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Abstract

Objectives: Chronic hemodialysis patients have an increased susceptibility to COVID-19 infection, and worse outcomes compared to the general population. This study aims to describe the clinical course and outcomes of hemodialysis patients with COVID-19 infection, and to describe predictors of mortality.

Methods: This retrospective observational study included adult chronic hemodialysis patients hospitalized to a tertiary care center with COVID-19 infection between January 1, 2020 and December 31, 2022. Data about their clinical features at time of diagnosis, and rate of complications were collected.

Results: 49 hemodialysis patients were hospitalized with COVID-19. The mortality rate was 26.5%, 45% required ICU admission, 28% required mechanical ventilation, 12% developed VTE, and the average length of hospitalization was 17 ± 15 days. When comparing survivals with non-survivals, age, initial level of C-reactive protein, LDH, haemoglobin, and initial abnormal chest X-ray were predictors of mortality.

Conclusions: This study confirms the high mortality rate observed among hemodialysis patients with COVID-19, and it suggests some clinical variables as predictors of mortality. We discuss the possibility of a geographical pattern of excess complications of COVID-19 among dialysis patients in the western region of Saudi Arabia compared to other regions, and we call for a higher prioritization to the western region for all supportive and preventative measures, especially the holy cities of Makkah and Medina. We believe this prioritization will have a positive impact on controlling COVID-19 infection nationally and internationally, because of the yearly mass gathering of all Muslims from all over the world in these two cities.

Keywords: COVID-19; Coronavirus; SARS-CoV-2; Hemodialysis; Chronic dialysis; End-stage renal disease.

Abbreviations: ICU: intensive care unit; LDH, lactate dehydrogenase; VTE: venous thromboembolic events.

Introduction

Coronavirus disease 2019 (COVID-19) is an illness that is caused by a novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. Patients with end-stage renal disease (ESRD) who are on maintenance hemodialysis are at increased risk of acquiring COVID-19, and having worse outcomes compared to the general population [2–6]. This could be due to the high burden of comorbidities, altered immune system, and/or frequent visits to healthcare facilities with subsequent contact with patients and healthcare workers [6,7]. Despite having worse outcomes, their presenting clinical symptoms could be milder than those of the general population, and this might be explained by their weak immune system [8]. Several studies have been published to describe the clinical features of COVID-19 and risk factors for severe illness in chronic hemodialysis patients. These factors may differ from those observed in the general population. For example, D-dimer level is not a good predictor of mortality in hemodialysis patients with COVID-19 infection, however, it may be associated with outcomes when the general population develops COVID-19 [8]. Other predictors, like dialysis vintage, level of serum lactate dehydrogenase (LDH), lymphocytes count, and level of c-reactive proteins (CRP) have been associated with outcomes in hemodialysis patients [8]. Understanding of COVID-19 is still evolving, and not all the study results are generalizable, illustrated by the variation in the incidence and the mortality rates from country to country [9]. In fact, some data suggests that the rate of mortality from COVID-19 infection among dialysis patients is affected by geographical and temporal patterns observed within the same country [10]. Data about the clinical features and outcomes of hemodialysis patients with COVID-19 in Saudi Arabia are limited [11-13]. Identifying and understanding risk rates and factors are important when planning and implementing interventions, such as the COVID-19 vaccination. This study aims to describe the clinical course and the outcomes of hospitalized ESRD patients who tested positive for COVID-19 from January 1, 2020 till December 31, 2022. We also aim to describe risk factors that could affect mortality.

Materials and Methods

This retrospective study included patients older than 18 years who had ESRD and were on chronic hemodialysis before presentation. All included patients were admitted to a single tertiary care hospital in Makkah, Saudi Arabia, (King Abdullah Medical City (KAMC), Makkah) from January 1, 2020, until December 31, 2022, and tested positive for COVID-19 at the time of/or during admission. Multiple admissions for one patient during the same month were counted as one admission.

This study received the approval of the Institutional Review Board (IRB) of KAMC, with IRB number 22-992. Eligible patients were identified by an independent electronic retrospective chart review conducted by two different authors. The following data were collected: patient's age, gender, nationality, body mass index (BMI), duration on hemodialysis in years, history of diabetes (DM), Hypertension, ischemic heart disease (IHD), cerebrovascular accidents (CVA), history of chronic lung disease, Charlson Score (calculated), vaccination status, symptoms and vital signs at the time of testing (fever, cough, shortness of breath, gastrointestinal symptoms, fatigue, loss of smell or taste, respiratory rate, oxygen saturation, systolic blood pressure, and diastolic blood pressure), laboratory results at the time of COVID-19 testing (white cell counts (WBC), lymphocytes count, hemoglobin level, platelets, CRP, erythrocytes sedimentation rate (ESR), procalcitonin, LDH, Brain-natriuretic peptide (BNP), troponin, ferritin, and D- dimer), Chest X-ray (CXR) findings at the time of testing (normal CXR, unilateral infiltrate, bilateral infiltrate). Additionally, data on management strategies during hospitalization (requirement of continuous renal replacement therapy (CRRT), and use of antibiotics, antiviral, steroids, and biological agents), and complications and outcomes (venous thromboembolic (VTE) events, length of hospital stay, requirement of admission to the intensive care unit (ICU), requirement of mechanical ventilation, and death) were collected. COVID-19 was confirmed positive by detecting SARS-CoV-2 RNA using reverse transcription-polymerase chain reaction (RT-PCR) on a nasopharyngeal sample taken by a trained nurse. All samples were sent to a regional lab for testing.

Discrete variables were reported using counts and percentages, while continuous variables were reported using means and standard deviations. Comparative analysis was conducted between both mortality outcomes (non- survivals vs. survivals) using the T-test for continuous variables, and Fisher's exact test for categorical variables. The significant p-value is less than 0.05.

Results

During the study period, forty-nine chronic hemodialysis patients were hospitalized, and all were diagnosed with COVID-19 infection during their hospitalization. Their main demographic, clinical characteristics, and main lines of management are summarized in Table 1. The average age of included patients was 57 ± 11.6 years, their average years on dialysis was 4.16 ± 2.7 years, and most of them (92%) were tested for COVID-19 because of suspicious symptoms, while the remaining (8%) were tested either pre-procedural or because of history of contact with a suspected patient. Most patients (92%) received no vaccination prior before their current infection or hospitalization. Of note, 22 of the total positive cases (45%) were in the year 2020, and 11 cases (22%) in 2021, the remaining 16 (33%) cases were in 2022. Out of the 49 patients, 13 patients died leading to a mortality rate of 26.5%, 22 patients (45%) required ICU admission, 14 patients (28%) required mechanical ventilation, and 6 patients (12%) developed venous thromboembolic disease. The average length of hospitalization was 17 ± 15 days. Of note, 70% of the mortalities occurred in the years 2021 and 2022.

When comparing survivals with non-survivals (Table 2), non-survivals were older (63.5 ± 9 vs. 54.7± 11.7, p = 0.017), had a higher initial CRP level (170 ± 113 vs. 72 ± 68 mg/dl, p = 0.008), a lower initial hemoglobin level (85 ± 38 vs. 103 ± 49, p = 0.02), a higher initial LDH level (8.7 ± 3.84 vs. 6.1 ± 2.45, p = 0.02), and more likely to have had an abnormal chest X-ray at the time of COVID-19 testing. Additionally, non-survivals were more likely to have had a longer dialysis vintage (5.6 ± 3.5 vs. 3.7 ± 2.5, p = 0.07), and a higher initial troponin level (0.54 ± 3.7 vs. 0.07 ± 0.09, p = 0.09), but the difference was not statistically significant (Table 2). When looking at different lines of management, non-survivals were more likely to have required CRRT (92.3% vs.16.6%, p = 0.0001), to have received steroids (92.3% vs. 33.3%, p = 0.0003), to have received antibiotics (100% vs. 80.5%, p= 0.05), to have required ICU admission (92.3% vs. 27.7%, p = 0.001), and to have required mechanical ventilation (100% vs. 2.7%, p = 0.0001). There was no difference between non- survivals and survivals concerning receiving antiviral therapy (46% vs. 47% respectively, p = 1.0), or tocilizumab (23% vs. 16.6% respectively, p = 0.68) of note; there was no difference between non-survivals and survivals concerning the VTE events (15% vs.11%, respectively, p = 0.6).

Discussion

The Center for Disease Control and Prevention (CDC) has adopted the recommendations of the Advisory Committee on Immunization Practices (ACIP) for the allocation of the COVID-19 vaccine [14]. These recommendations suggest giving certain

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groups of people a priority for receiving the COVID-19 vaccine according to certain risk factors and classifying people into two groups (Group 1 and Group 2) [14]. Group 1 is further classified into Group 1a (which includes healthcare personnel and long-term care facility residents), Group 1b (which includes frontline essential workers, persons aged ≥ 75 years), Group 1c (which includes persons aged 65–74 years, persons aged 16-64 years with high-risk medical conditions, and essential workers not recommended for vaccination in group 1b). Group 2 includes all people over the age of 16 who have not been recommended for vaccination in Group 1. The highest priority is given to group 1a and the priority then goes in descending order. Hemodialysis patients currently fall into group 1c because of their high-risk medical condition. However, the International Society of Nephrology has urgently called for a higher prioritization of dialysis patients worldwide and moving them up to group 1a [15]. This "Call to Action" is justified by the following: [15]. The fact is that patients receiving in-center hemodialysis are required to go to their dialysis centers three times a week, during which they may come in close contact with other patients as well as health care providers. This makes them no different from residents of long-term care facilities, which are currently classified as group 1a.

The great impact of vaccinating hemodialysis patients on protecting other patients, dialysis staff, and patients' families. This is especially true with the easy accessibility to dialysis patients and hence the delivery of vaccination, which could be given during their hemodialysis sessions.

To minimize the indirect effect of the COVID-19 pandemic on hemodialysis patients which comes from patients fear and anxiety of contracting the infection during hemodialysis, leading to their decision (or sometimes the dialysis unit decision during the surge of infection) of reducing their dialysis sessions from 3 to 2 with subsequent potential impact on their clinical condition and the health care system.

Above all, dialysis patients are at a higher risk of acquiring COVID-19 compared to the general population [2-6,15], and once infected, they are 30% to 130% more likely to die than hospitalized patients with COVID-19 but no chronic kidney disease with case fatality rates varying from 16% to 32% [15]. These increased risks are higher than the risk of the other groups (i.e., patients with other comorbidities like diabetes, obesity, etc.) currently classified as 1c [15].

A systematic scoping review of the COVID-19 data on chronic HD patients indicates the poor prognosis among hospitalized patients, with up to 70.5% requiring ICU admission with their mortality rate reaching up to 100% [16]. Are these rates and results generalizable? The answer is likely no, supported by the variation in the reported mortality rate of COVID-19 among hemodialysis patients from country to country [17]. Even within the same country, the mortality rate may differ, as exampled by the geographic and temporal patterns of excess mortality observed among HD patients dialyzing in different facilities in the United States when comparing their observed and predicted monthly number of deaths [10]. Understanding this variation is important when implementing different preventative strategies, like vaccination, as well as when managing and prioritizing the allocation of resources. Therefore, each country (and maybe each region within a country) may need to study their patients' risks as well as various factors affecting their outcomes, especially with the evolving knowledge about COVID-19 and its episodes of outbreaks. Data about COVID-19 among chronic HD patients in Saudi Arabia are limited [11-13]. Table 3 summarizes the currently available data about the outcomes of COVID-19 among chronic dialysis patients in Saudi Arabia. Although all studies were single centers and included a small number of patients, each study attempted to address the mortality rate and predictors of outcomes of COVID-19 among dialysis patients (mostly hemodialysis) within a different region in Saudi Arabia. Tawhari et al. looked at ESRD patients who developed COVID-19 in the central and found an overall mortality rate of 18% [11]. However, the mortality rate was higher (up to 23%) among patients who were symptomatic at the time of admission, and predictors of mortality were the need for inotropes, age, and CRP level on admission [11]. Of note, in this study all patients were admitted as part of the center routine practice with ESRD patients who tested positive for COVID-19 regardless of the severity of symptoms. In another study from the southwest region of Saudi Arabia, Hakami et al. reported a mortality rate of 19.8% among chronic HD patients with COVID-19 and found that age, heart disease, lymphocytopenia, neutrophilia, D-Dimer, ferritin, blood urea nitrogen, and aspartate transaminase level were the predictors of mortality [12]. Alkhunaizi et al looked at ESRD patients who developed COVID-19 in the eastern region and found an overall mortality rate of 17%, which increased to 30% among those who developed pneumonia [13]. In this study, half of the patients had mild symptoms, and the remaining half developed pneumonia. Age, diabetes and coronary artery disease were predictors of the development of pneumonia [13]. In our current study, an overall mortality rate of 26.5% (27.6% among symptomatic patients) was observed. We found that age, CRP level, anemia, LDH level, and abnormal initial chest X-ray were predictors for mortality. When having a general look at these four studies, there are no geographical or temporal patterns of excess mortality among chronic HD patients in Saudi Arabia. However, there is a tendency toward a higher rate of all complications observed in our current study. Nevertheless, it is hard to make a solid conclusion if we take into consideration the small sample size of all four studies, differences in the characteristics of the included patients (e.g. severity of symptoms), and the potential effect of some difference in the timeliness between our study and other conducted studies which may have coincided with different waves of COVID-19 and/or different COVID-19 variants. However, there is a possibility that this higher rate of complications from COVID-19 among HD patients in the western region compared to other regions is a true difference. This possibility is because the complications rate

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among HD patients may mirror that of the general population. In the general population, data looking at the overall mortality rate caused by COVID-19 in Saudi Arabia by region found that the highest rate is in the western region, specifically Makkah city [20]. Another data which looked at the incidence of the prevalence of COVID-19 in Saudi Arabia found that it varies by region or areas, reflected by a higher seroprevalence rate of COVID-19 observed in Makkah city compared to some other cities [21]. This could be explained by the fact that the city of Makkah and Medina cities are travel destinations for millions of pilgrims across the world, and international travel has been shown to have a major role in the spreading of COVID-19 [22]. Even before the era of COVID-19, it was known that the epidemiology of respiratory viruses in Saudi Arabia is likely affected by the mass gathering during the Islamic rituals (Hajj and Umrah) in the holy sites of Makkah and Medina [23]. In fact, a few cases of COVID-19 occurred in Umrah pilgrims before international travel was banned, and the first patient who died of COVID-19 in Pakistan was a returned Umrah pilgrim. Saudi Arabia suspended the Umrah on March 03, 2020, and on June 22, 2020, the Saudi government announced the complete ban of international visitors for the 2020 annual Hajj pilgrimage to Makkah, and Hajj was restricted to a limited number of residents who had no chronic diseases and were younger than 65 years. Even after the end of the global health emergency of COVID-19, Makkah and Medina cities will continue to require more efficient preventative measures and support compared to other cities, as they will continue to be a travel destination for millions of pilgrims across the world. These measures will have a national and international impact on controlling COVID-19 pandemic. Our current study is limited by the fact that it was retrospective, had a small sample size, and some patients had missing laboratory data during the peak of the pandemic when no more laboratory reagents were available. Additionally, the limited number of patients who had received the vaccine or some other lines of management (e.g. antiviral or tocilizumab) makes it difficult to study their effects on outcomes.

Table 1: Demographics and clinical characteristics of the study population. (hospitalized chronic hemodialysis patients with positive COVID-19 testing).

Gender [number (%)]:		**Nationality [number (%)]:**	
Male	23 (47%)	Saudi	38 (77.5%)
Female	26 (53%)	Non-Saudi	11 (22.5%)
Age [number (%)]:		**Dialysis Vintage** [number (%)]:	
18-39 years	4 (8.2%)	≤ 5 years	31 (63%)
40-59 years	24 (49%)	> 5 years	9 (18.5%)
60-79 years	21 (42.8%)	unknown	9 (18.5%)
Body Mass Index [number (%)]		Previous Vaccination [number (%)]:	
< 30 Kg/m2	37 (75.5%)	yes	4 (8.2%)
> 30 Kg/m2	12 (24.5%)	No	45 (91.2%)
Co-morbidities [number (%)]:		Charlson Score [number No (%)]	
Diabetes	32 (65%)	Mild (1-2)	3 (6%)
Hypertension	43 (88%)	Moderate (3-4)	9 (18.5%)
Ischemic heart Disease	22 (45%)	Severe ≥ 5	37 (75.5%)
Cerebrovascular Disease	5 (10%)		
Chronic lung Disease	7 (14%)		
Presenting Symptoms [number (%)]:		**Laboratory Results at Time of Diagnosis (mean ± SD)**	
Asymptomatic:	4 (8.2%)	C-reactive protein (mg/L)	110 ± 90.0
Symptomatic:	45 (91.8%)	Erythrocytes sedimentation rate (mm/hour)	81 ± 32.2
Fever:	30 (61%)	Procalcitonin (mcg/L)	19 ± 43.0
Cough:	23 (47%)	White blood cells (X 109/L)	9.0 ± 5.8
Shortness of breath	24 (49%)	Lymphocytes count (X 109/L)	1.7 ± 3.6
GI symptoms	17 (35%)	Hemoglobin (gm/L)	74.0 ± 46.0
Fatigue	16 (33%)	Platelets (X 109/L)	202 ± 83
Loss of smell/taste	0	Lactate dehydrogenase (µkat/L)	6.9 ± 3.1
Presenting Vital Signs (mean ± SD)		Brain natriuretic peptide (ng/L)	(2559 ± 3341)
Respiratory rate (breath /minute)	20 ± 3	Troponin (µg/L)	0.23 ± 0.54

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Oxygen saturation (%)	93 ± 7	Ferritin (μg/L)	2135 ± 1960
Systolic blood pressure (mmHg)	133 ± 31	D-Dimer (nmol/L)	25.7 ± 29
Diastolic blood pressure (mmHg)	73 ± 15		
Initial Chest X-ray [number (%)]		**Management** [number (%)]	
Normal	18 (37%)	Requirement of CRRT	18 (37%)
Unilateral infiltrates	12 (24.5%)	Use of antiviral therapy	23 (47%)
Bilateral infiltrates	19 (38.5)	Dexamethasone A	24 (49%)
		Antibiotics	42 (86%)
		Tocilizumab	10 (20%)

CRRT: Continous Renal Replacement therapy, SD: standard deviation.

Table 2: Demographic, clinical, laboratory, and radiological charatcterestics according to survival status (univariate analysis)

	Patients by Survival Status		
Variable	**Non- survivals (number = 13)**	**Survivals (number = 36)**	**p - value**
Age in years [mean ± SD]	63.5 ± 9	54.7 ± 11.7	0.017
Male gender [number (%)]	7 (54%)	16 (44%)	0.74
Body mass index (Kg/m²) [mean ± SD]	28.6 ± 11	26 ± 6	0.39
Saudi nationality [number (%)]	10 (77%)	28 (78%)	1
Dialysis vintage in years [mean ± SD)	5.6 ± 3.5	3.7 ± 2.5	0.07
Comorbidities: Diabetes[number(%)] Charlson score [mean ± SD]	10 (77%) 6.6 ± 3.5	22 (61%) 5.3 ± 3.2	0.4 0.16
Presenting clinical features:			
No symptoms [number (%)]	2 (15%)	2 (5.5%)	0.2
Fever [number (%)]	7 (53.8%)	23 (64%)	0.5
Cough [number (%)]	5 (38.5%)	18 (50%)	0.5
Shortness of breath [number (%)]	6 (46%)	18 (50%)	1
Gastrointestinal symptoms [number (%)]	5 (38.5%)	12 (33.3%)	0.7
Fatigue [number (%)]	2 (15%)	14 (39%)	0.1
Respiratory rate (breath/minute) [mean ± SD]	20 ± 2.4	20 ± 3.4	0.8
O2 saturation (%) [mean ± SD]	93.5 ± 6	93 ± 7.3	0.8
Systolic blood pressure (mmHg) [mean ± SD]	134 ± 27	132 ± 32	0.88
Diastolic blood pressure (mmHg) [mean ± SD]	71 ± 12	74 ± 16	0.6
laboratory parameters			
C-reactive protein (mg/L) [mean ± SD]	170 ± 113	72 ± 68	0.01
Erythrocytes sedimentation rate (mm/hour) [mean ± SD]	78.6 ± 39	82 ± 28.6	0.75
Procalcitonin (mcg/L) [mean ± SD]	30.9 ± 70.5	8.1 ± 8.4	0.36
White blood cells (X 109/L) [mean ± SD]	10.8 ± 7.2	1.8 ± 1.5	1
Lymphocytes count (X 109/L) [mean ± SD]	1.3 ± 1.6	1.1 ± 1.0	1
Haemoglobin (gm/L) [mean ± SD]	85 ± 38	103 ± 49	0.02
Platelets (X 109/L) [mean ± SD]	170 ± 66.2	213 ± 86.5	0.11
Lactate dehydrogenase (μkat/L) [mean ± SD]	8.7 ± 3.84	6.1 ± 2.45	0.02

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Brain natriuretic peptide (ng/L) [mean ± SD]	729 ± 871	3076 ± 3674	0.11
Troponin (µg/L) [mean ± SD]	0.54 ± 3.7	0.07 ± 0.09	0.09
Ferritin (µg/L) [mean ± SD]	2894 ± 2434	1846 ± 1775	0.22
D-Dimer (nmol/L) [mean ± SD]	47.6 ± 43.26	19.1 ± 21.9	0.09
Chest X- ray at time of COVID-19 testing:			
Normal Chest X- ray	1 (7.7%)	17 (47.2%)	0.017
Unilateral infiltrates	5 (38.5%)	7 (19.5%)	0.2
Bilateral infiltrates	7 (53.8%)	12 (33.3%)	0.3

Table 3: Summary of studies conducted in Saudi Arabia on outcomes of COVID-19 among chronic dialysis patients (mostly hemodialysis).

Study, published year	Hakami et al, 2021	Tawhari et al, 2022	Alkhunaizi et al, 2022	Dahlan et al, current study
Region in Saudi Arabia	Southwest	Central	Eastern	Western
City in Saudi Arabia	Jazan	Riyadh	Dhahran	Makkah
Study period	From May 2020 until December 2020	From March 2020 until March 2021	From June 2020 until October 2021	From Janauary 1 2020 until December 2022
Number of patients	101	104 (3 were PD)	30 (one was on PD)	49
Age (in years)	Mean: 55 ± 18.8	Mean: 62.6 ± 17.4	Median: 63 (55-75)	Mean: 57 ± 11.6
Outcomes				
Mortality rate	19.80%	18% *	17 %**	26.5
ICU admission	17%	19%	17%	45%
Mechanical ventilation	17%	14%	17%	28%
VTE events	not reported	0%	3%	12%
Length of hospitalization (days)	Median: 7-9 days #	not reported	Mean:13 ± 2.4 days	Mean: 17 ± 15 days
Predictors of outcomes	Predictors of mortality: age, heart disease, lymphocytopenia, neutrophilia, D-Dimer, ferritin, BUN, AST	predictors of mortality: requirement of inotropes, age, CRP level at time of admission	Predictors of developing pneumonia: age, diabetes, and coronary artery disease.	Predictors of mortality: age, CRP, anaemia, lactate dehydrogenase, dialysis vintage, troponin level, abnormal initial chest X-ray)

#: Median duration from admission to recovery: 7 days, median duration from admission to death: 9 days
*: The mortality rate was 23% among patients who were symptomatic at time of diagnosis.
**: The mortality rate was 30% among patients who developed pneumonia
AST: aspartate transaminase, BUN: blood urea nitrogen, CRP: C-reactive protein, ICU: intensive care unit, PD: peritoneal dialysis, VTE: venous thromboembolism,
Note: all studies looked at hospitalized patients, except Alkhunaizi et al study (90% of patients were hospitalized).

Conclusion

Our study agrees with other national and international studies which showed a high rate of mortality from COVID- 19 infection among chronic hemodialysis patients compared to the rate observed in the general population. Age, initial hemoglobin, LDH, CRP levels, and abnormal CXR on presentation are found to be predictors of mortality in this study. There is a tendency or a possibility of a geographical pattern of excess rate of complications from COVID- 19 among chronic dialysis patients in Makkah city compared to other cities in Saudi Arabia. Although this finding needs to be supported by a stronger level of evidence and large sample size, this possibility falls in with the available data about a higher rate of COVID-19 mortality in the western region (specifically Makkah) observed in the general population when compared to other regions. Mass gathering, during the Islamic rituals (Hajj and Umrah) in Makkah and Madina cities of the western region, takes place every year. The International Society of Nephrology is calling for a higher prioritization of chronic dialysis patients worldwide to receive COVID-19 vaccination, and we call for a local prioritization for those who live in the western region of Saudi Arabia, especially Makkah and Medina cities. Not only to

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give them priorities for vaccination but for all other supportive and preventative measures, as these preventative measures will likely have national and international beneficial effects.

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How to cite this article: Dahlan Randah A, Faqihi, Ahmed Y, Alsulami Hajar A, Alkatheeri Ali M. COVID-19 among Hospitalized Chronic Hemodialysis Patients: Clinical Features and Predictors of Mortality. JOJ Urology & Nephrology, 2023; 8(1): 555731. DOI: 10.19080/JOJUN.2023.08.555731

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