COVID-19 in patients with end stage kidney disease at a large community hospital in Eastern Saudi Arabia. *A prospective study*

Ahmed M. Alkhunaizi, MD, FACP, Hanaa Abd Elnabi, RN, Abdulrazack Amir, MD, Amber Anwar, MD.

ABSTRACT

Objectives: To report the outcome of patients with end stage kidney disease (ESKD) who were diagnosed with COVID-19 at a large community hospital in Eastern Saudi Arabia.

Methods: A single center, prospective observational study at Johns Hopkins Aramco Healthcare, Dhahran, Saudi Arabia. Patients with ESKD who were maintained on dialysis and developed COVID-19 between June 15, 2020 and October 31, 2021 were enrolled.

Results: In total, 30 patients with ESKD were diagnosed with severe acute respiratory syndrome coronavirus 2 infection. Twenty two (73%) patients developed the disease prior to COVID-19 vaccine rollout. The median age of the cohort was 63 (55-75) years. Most patients were diabetic (73%), hypertensive (97%) and had a median body mass index of 28 kg/m^2. Twenty seven (90%) patients required admission, 16 (52%) patients developed pneumonia, and 5 (17%) patients required mechanical ventilation. Patients who developed pneumonia were older, and the majority had diabetes mellitus and coronary artery disease. Five patients died with a total mortality of 17%.

Conclusion: Patients with ESKD who developed COVID-19 had a poor outcome with high mortality compared to the general population. Presence of diabetes mellitus, coronary artery disease and older age were associated with a higher risk of severe disease. There was a sharp decline in the number of positive cases following implementation of the vaccination program.

Keywords: COVID-19, SARS-CoV-2 infection, end stage kidney disease

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Coronavirus disease 2019 (COVID-19) secondary to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused devastating effects worldwide. Patients with chronic kidney disease (CKD) and especially those with end stage kidney disease (ESKD) requiring renal replacement therapy may be at a higher risk of poor outcomes. Reports from different countries have found variable results ranging from fewer symptoms and less requirement of intensive care in China to more severe illness with very high mortality in the United States and Europe.[1-4] In this study, we report the outcome of patients with ESKD who were diagnosed with COVID-19 at a large community hospital in Eastern Saudi Arabia.

Methods. A prospective observational single center study was conducted at Johns Hopkins Aramco Healthcare (JHAH), Dhahran, Saudi Arabia between June 15, 2020 and October 31, 2021. Adult patients aged ≥18 years with ESKD who were maintained on either hemodialysis or peritoneal dialysis and tested positive for SARS-CoV-2 infection by reverse transcription polymerase chain reaction (RT-PCR) were included. Patients were stratified according to age, gender, and presence of comorbidities including: diabetes mellitus (DM), hypertension (HTN), coronary artery disease (CAD), congestive heart failure, obesity, smoking history, presence of chronic obstructive pulmonary disease, sickle cell disease, and malignancy. Patients with CKD who required dialysis after the diagnosis of COVID-19 were excluded. Presenting symptoms were recorded including: fever, cough, shortness of breath, loss of smell sense, fluid overload, and development of pneumonia. In-hospital complications were recorded including development of pulmonary embolism, transfer to the intensive care unit (ICU), need for mechanical ventilation, and requirement of vasopressor support. Hematological and inflammatory markers were recorded including hemoglobin, neutrophil count, lymphocyte count, C reactive protein, serum ferritin, B-type natriuretic peptide, and D-Dimer.

The hospital course was followed until the time of discharge or death. Death was defined as mortality within 2 months from the time of diagnosis.

An informed consent was obtained from the patients or next of kin at the time of diagnosis. The study was approved by the Institutional Review Board at JHAH before the study began.

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Statistical analysis. Baseline and clinical demographics were reported as mean ± standard deviation or when appropriate median and interquartile ranges. Categorical variables were reported as numbers and proportions. Comparison of the mean values was performed using student t-test. Proportions were compared using Chi-square test. *P*-values <0.05 were considered significant. Microsoft Excel 2013 was used for the statistical calculations.

Results. The study concluded on October 31, 2021 due to the small number of patients who were enrolled over the preceding months. The monthly census of patients with ESKD during the study period averaged 195 (±3) patients. In total, 30 patients were diagnosed with SARS-CoV-2 infection by RT-PCR between June 15, 2020 and October 31, 2021. One patient became infected twice, 10 months apart. Twenty nine (97%) patients were maintained on hemodialysis and one (3%) was treated with peritoneal dialysis. Twenty two (73%) patients acquired the infection between June 15, 2020 and December 31, 2020 and 9 (27%) patients developed the infection between January 1, 2021 and end of the study period. The median age of the cohort was 63 (55-75) years. The demographics of the patients are shown in Table 1. Presenting symptoms and laboratory findings are listed in Table 1. Fever was present in 48% and cough in 52% of the patients. Approximately, 61% of the patients had shortness of breath and 55% had loss of smell sense. Twenty seven (90%) patients were admitted to the hospital and 3 (10%) were treated as outpatients. Sixteen (52%) patients were diagnosed with pneumonia by chest radiography or computed tomography. Seventeen (56%) patients received dexamethasone and 7 (23%) received Tocilizumab. Patients who developed pneumonia were older and the majority had DM and CAD as compared to those who did not have pneumonia, Table 2. Four patients died during hospitalization and one patient died 2 months after discharge. The overall mortality was 17% while mortality was 31% among those who developed pneumonia. The mean hospital stay was 13 (±2.4) days.

Patients' outcome and complications are listed in Table 3.

Discussion. The vaccination rollout program in Saudi Arabia started in December 2020. Most of the patients (73%) who developed SARS-CoV-2 infection acquired the infection before the COVID-19 vaccine rollout. The number of cases dramatically decreased after the wide and successful distribution of the vaccine and we did not encounter any positive cases of SARS-CoV-2 infection among our ESKD population after August 2021.

Half of our patients with ESKD who developed SARS-CoV-2 infection had mild symptoms while the other half developed pneumonia. Our cohort had severe comorbidities typically seen in the dialysis population

Table 1 - Patients' characteristics: upper panel; symptoms and laboratory findings: lower panel.

Characteristics	n (%)
Total number of patients (episodes)	30 (31)
Age, year, median (IQR)	63 (55-75)
Female	17 (56 %)
BMI (kg/m^2), median (IQR)	28 (23-31)
Comorbidities	
Diabetes mellitus	22 (73)
Hypertension	29 (97)
Coronary artery disease	14 (47)
Congestive heart failure	11 (37)
Smoking	1 (3)
Sickle cell disease	2 (6)
History of malignancy	6 (20)
COPD	3 (10)
Symptoms and laboratory findings	
Admission symptoms	
Fever	15 (48)
Cough	16 (52)
Shortness of breath	19 (61)
Loss of smell	17 (55)
Admission hematologic markers median (IQR)	
Hemoglobin g/dL	10.5 (8.5-11.5)
Neutrophil count 10^3 µl	5 (3.3-5.2)
% Neutrophil	69 (59-80)
Lymphocyte count 10^3 µl	1.1 (0.8-1.4)
% lymphocyte	18 (12-31)
Admission maximum inflammatory markers, median (IQR)	
CRP mg/L	3.1 (1.4-7.4)
Ferritin ng/ml	834 (594-1964)
BNP	973 (117-1386)
D-Dimer	2.0 (1.08-6.4)

IQR: interquartile range, BMI: body mass index, COPD: chronic obstructive pulmonary disease, CRP: C reactive protein, BNP: B-type natriuretic peptide, %: percentage

Table 2 - Characteristics of patients with and without pneumonia.

Characteristics	Pneumonia 16 (52)	No pneumonia 14 (48)	*P*-value
Median age, years	69.5	57	0.01065
DM (%)	94	47	<0.001
HTN (%)	94	93	NS
CAD (%)	56	33	0.042
CHF (%)	34	33	NS
BMI kg/m^2	29.4	26.5	NS

DM: diabetes mellitus, HTN: hypertension, CAD: coronary artery disease, CHF: congestive heart failure, BMI: body mass index

Table 3 - Clinical outcome of patients with end stage kidney disease and COVID-19.

Clinical outcome	n (%)
Pneumonia	16 (52)
ICU admission	5 (17)
Mechanical ventilation	5 (17)
Pulmonary embolism	1 (3)
Vasopressors	5 (17)
Length of stay, days (mean±SD)	13 ± 2.4
Mortality	5 (17)

SD: standard deviation, ICU: intensive care unit

including DM, HTN, obesity, CAD, and heart failure. In general, patients with CKD and specifically ESKD have a higher mortality rate compared with the general population, even after taking into consideration age, race, and presence of DM.[5] They have significant comorbid conditions in addition to advanced age which are considered risk factors for severe COVID-19 disease.[6,7] Based on the presence of such severe comorbidities, one could postulate that patients with ESKD who develop SARS-CoV-2 infection would have increased mortality compared to the general population. However, the data on the outcome of patients with ESKD who develop SARS-CoV-2 infection is not consistent and reports from different countries have revealed variable results ranging from mild disease in China to high mortality rates in Italy and Spain.[1,3,4] Registry reports in Europe have shown a high fatality rate of COVID-19 among patients with ESKD ranging between 20% and 30%.[8]

In a retrospective cohort study performed at Mount Sinai Healthcare system in New York City, Chan et al[9] have found that hospitalized patients with ESKD and COVID-19 had a mortality rate of 9% and were less likely to be admitted to ICU and require mechanical ventilation compared to a matched cohort without renal failure.

During the first wave of the pandemic the mortality rate of patients with ESKD admitted to New York City hospitals between March and April 2020 was 31.7%, higher than those without ESKD.[10]

In our cohort the mortality rate was 17%, much higher than the overall mortality of 1.6% that has been reported across the Kingdom of Saudi Arabia at the end of our study period, but lower than what has been observed in earlier reports from other countries in patients with ESKD.[2-4,10,11] This may be due to differences in ethnicities, baseline characteristics and available resources for treatment. Additionally, our study time frame which was at a later point after declaration of the pandemic may have influenced the outcome as more experience in handling the disease had been accumulated and new modalities of treatment had been adopted to combat COVID-19. In particular, most of our patients who were admitted received dexamethasone, a drug that has been shown to improve outcomes in patients with COVID-19.[12] Similarly, all of our patients with severe pneumonia received Tocilizumab, a monoclonal antibody targeting the interleukin 6 receptor, which may had a positive impact on the outcome of patients with severe COVID-19.[13]

The inflammatory markers associated with cytokine storm that is commonly observed in critical patients infected with SARS-CoV-2 infection were not particularly elevated in our cohort. The reason for this is not known.

Severe disease with COVID-19 has been attributed to direct viral damage in addition to the body's immune response responsible for the cytokine storm.[14] Alterations of variable aspects of the immune system in patients with uremia including the innate and adaptive immune response have been reported.[15] One may postulate that the diminished immune response in patients with ESKD could potentially protect against the cytokine storm observed with severe SARS-CoV-2 infection. In our cohort, the early administration of Tocilizumab may also have contributed to this phenomenon.

Study limitations. There are several limitations to our study including the small size of the cohort, lack of a control group, and the unique setup of our medical institution. Johns Hopkins Aramco Healthcare, Dhahran, Saudi Arabia has state of the art medical facilities that serve a certain population consisting of the employees of Saudi Aramco and their dependents. The available resources and the quality of medical care provided at JHAH facilities may not be reflective of reality in the general community setting. Therefore, the outcome of this study may not be generalizable to the wider community in the area. Additionally, the time frame of our study which took place after accumulating considerable experience in handling the complications of COVID-19 worldwide may have influenced the outcome of our cohort.

In conclusion, our study, albeit small in size, sheds light on the outcome of patients with ESKD and SARS-CoV-2 infection who developed COVID-19. The vaccine rollout has dramatically decreased the number of infected patients.

Understanding the course of illness and the outcome of COVID-19 in patients with ESKD is important as this information may help risk-stratify patients with ESKD who develop COVID-19 and provide guidance to the appropriate therapy these patients need upon diagnosis and admission to the hospital.

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From the Department of Medicine, Specialty Internal Medicine Division, Nephrology Unit (Alkhunaizi, Amir, Anwar), and from the Department of Nursing (Abd Elnabi), Johns Hopkins Aramco Healthcare, Dhahran, Kingdom of Saudi Arabia.

Address correspondence and reprints request to: Dr. Ahmed M. Alkhunaizi, Nephrology Unit, Specialty Internal Medicine Division, Johns Hopkins Aramco Healthcare, Dhahran, Kingdom of Saudi Arabia. E-mail: aalkhunaizi@gmail.com
ORCID ID: https://orcid.org/0000-0002-0580-9912

References

1. Xiong F, Tang H, Liu L, Tu C, Tian JB, Lei CT, et al. Clinical characteristics of and medical interventions for COVID-19 in hemodialysis patients in Wuhan, China. *J Am Soc Nephrol* 2020; 31: 1387-1397.
2. Valeri AM, Robbins-Juarez SY, Stevens JS, Ahn W, Rao MK, Radhakrishnan J, et al. Presentation and Outcomes of Patients with ESKD and COVID-19. *J Am Soc Nephrol* 2020; 31: 1409-1415.
3. Goicoechea M, Sánchez Cámara LA, Macías N, Muñoz de Morales A, Rojas Á G, Bascuñana A, et al. COVID-19: clinical course and outcomes of 36 hemodialysis patients in Spain. *Kidney Int* 2020; 98: 27-34.
4. La Milia V, Bacchini G, Bigi MC, Casartelli D, Cavalli A, Corti M, et al. COVID-19 outbreak in a large hemodialysis center in Lombardy, Italy. *Kidney Int Rep* 2020; 5: 1095-1099.
5. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu C-y. Chronic Kidney Disease and the Risks of Death, Cardiovascular Events, and Hospitalization. *N Engl J Med* 2004; 351: 1296-1305.
6. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature* 2020; 584: 430-436.
7. Hobbs ALV, Turner N, Omer I, Walker MK, Beaulieu RM, Sheikh M, et al. Risk factors for mortality and progression to severe COVID-19 disease in the Southeast United States (US): A Report from the SEUS Study Group. *Infect Control Hosp Epidemiol* 2021; 42: 1464-1472.
8. Hilbrands LB, Duivenvoorden R, Vart P, Franssen CFM, Hemmelder MH, Jager KJ, et al. COVID-19-related mortality in kidney transplant and dialysis patients: results of the ERACODA collaboration. *Nephrol Dial Transplant* 2020; 35: 1973-1983.
9. Chan L, Jaladanki SK, Somani S, Paranjpe I, Kumar A, Zhao S, et al. Outcomes of Patients on Maintenance Dialysis Hospitalized with COVID-19. *Clin J Am Soc Nephrol* 2021; 16: 452-455.
10. Ng JH, Hirsch JS, Wanchoo R, Sachdeva M, Sakhiya V, Hong S, et al. Outcomes of patients with end-stage kidney disease hospitalized with COVID-19. *Kidney Int* 2020; 98: 1530-1539.
11. Ministry of Health. Dashboard hcmgsMSAC-. [Updated 2022; Accessed 2022 Jan 5]. Available from: https://covid19.moh.gov.sa/
12. Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, Linsell L, et al. Dexamethasone in hospitalized patients with Covid-19. *N Engl J Med* 2021; 384: 693-704.
13. Salama C, Han J, Yau L, Reiss WG, Kramer B, Neidhart JD, et al. Tocilizumab in patients hospitalized with Covid-19 pneumonia. *N Engl J Med* 2021; 384: 20-30.
14. Tang Y, Liu J, Zhang D, Xu Z, Ji J, Wen C. Cytokine Storm in COVID-19: The current evidence and treatment strategies. *Front Immunol* 2020; 11: 1708.
15. Kato S, Chmielewski M, Honda H, Pecoits-Filho R, Matsuo S, Yuzawa Y, et al. Aspects of immune dysfunction in end-stage renal disease. *Clin J Am Soc Nephrol* 2008; 3: 1526-1533.