

Clinical Characteristics and Early Outcome of COVID-19 Infection in Hemodialysis Patients: A Retrospective Cohort Study.

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Abstract

Objectives: A new strain of Coronavirus was identified in late 2019, resulting in an acute respiratory illness, Coronavirus Disease 19 (COVID-19), with variable outcomes, including mortality risk. As hemodialysis patients are a vulnerable group, we aimed this study to report the clinical characteristics and results of this infection in this particular group of patients, along with their predictive risk factors.

Methods: This single-center retrospective cohort study was conducted at King Abdul-Aziz Medical City, Jeddah, Saudi Arabia. We aimed to investigate the clinical presentations and outcomes of COVID-19 infection among hemodialysis patients.

Results: Among the 91 patients, 32 (35%; 95% confidence interval [CI] 25-45 %) developed pneumonia, 23 (25%; 95% CI 16-34%) had hypoxia, 13 (14%; 95% CI 7-22%) were admitted to the intensive care unit, and 8 (9%; 95% CI 3-15%) died. The period analysis suggested a lower rate of pneumonia with more recent COVID-19 infections (beyond January 2022). The most common presenting symptom was fever in 42 patients (46%). Pneumonia developed in 35% of patients, while 25% formed hypoxia.

Conclusion: In our study, the related mortality rate was 9%, compared to 8% in non-dialysis patients reported from the same institution. The reported mortality rate in our cohort is low compared to other studies conducted nationally and internationally; the lower mortality rate in our study could be attributed to a milder disease at the time of presentation, the protocol we implemented, and the availability of resources for management.

Keywords: COVID-19, COVID-19 pneumonia, COVID-19 related mortality, SARS COV-2 infection, Hemodialysis

Introduction

In late 2019, a new strain of Coronavirus was identified as the cause of severe acute respiratory syndrome (SARS COV-2 infection) in Wuhan, the capital of Hubei province in China. It rapidly spread, resulting in an epidemic throughout China and a global pandemic. The WHO named the disease as COVID-19 in February 2020 [1]. Since the first reports of COVID-19, the infection has continued to spread, infecting more than 190 million people worldwide [8].

In Saudi Arabia, more than 840,000 cases of COVID-19 were reported up to date; the rate of patients was decreasing, reaching the lowest level in January 2023, with reported mortality of more than 9500 cases, based on data from the WHO website.

The clinical spectrum of the disease was widely ranging from asymptomatic cases to severe acute respiratory distress syndrome (ARDS), sometimes causing fatal diseases. Most of the patients have

mild or even no symptoms [2]. The common comorbidities associated with the disease severity include age, hypertension, diabetes, obesity, and chronic kidney disease [3-4].

End-stage renal disease (ESRD) patients are considered from the high-risk group for severe SARS-CoV-2 infection. A large prospective study conducted over 5 months in Canada, involving 12,501 dialysis patients, showed the infection rate is five times higher than the general population over the same period [5]. Also, other studies done in the US and France showed that around 60% of infected dialysis patients required hospital admission with a mortality rate exceeding 20 % [6-7], [9].

According to the Saudi Center for Organ Transplantation (SCOT), data published in 2020 revealed 28,769 chronic dialysis patients in

Saudi Arabia. Most (19,715) are treated by hemodialysis through 274 dialysis centers, and the remaining 1,781 by peritoneal dialysis [10]. The course of SARS-CoV-2 infection among hemodialysis patients' needs to be better documented in Saudi Arabia. This retrospective cohort study aims to review the SARS-CoV-2 infection among dialysis patients in our context, Saudi Arabia, and how it can contribute to infection control measures.

Materials and Methods

This was a single-center retrospective cohort study conducted at King Abdul-Aziz Medical City, Jeddah, Saudi Arabia, to investigate the clinical presentations and outcomes of COVID-19 infection among hemodialysis patients. The study included all hemodialysis patients who tested positive for COVID-19 between February 2020 and September 2022. Patients were identified through the hospital's electronic medical records system. This study was approved by the institutional review board of King Abdullah International Research Center (KAIMRC), Saudi Arabia (IRB number: NRJ21J/138/05). Informed consent was waived due to the retrospective nature of the study.

The medical records of all eligible patients were reviewed to extract the following information: demographic data (age, gender), duration on hemodialysis, comorbidities (diabetes mellitus, hypertension, ischemic heart disease, malignancy, prior kidney transplantation, chronic obstructive pulmonary disease, bronchial asthma), vaccination status (unvaccinated, one-dose, two-doses, or three-doses vaccination), period (before February 2022 vs. February 2022 and beyond), clinical presentation, development of pneumonia, radiological presentation, inflammatory markers (white blood cell count, C-reactive protein, procalcitonin, and ferritin), and clinical outcomes (hypoxia, intensive care unit admission, and mortality).

Descriptive statistics (counts and percentages for categorical data, mean or median for continuous data) were used to summarize the

patient characteristics and outcomes. The factors associated with the development of COVID-19 pneumonia were explored by comparing patients who tested positive for COVID-19 and developed pneumonia with those who tested positive but did not develop pneumonia, using demographic (age, gender), hemodialysis vintage, comorbidities (diabetes mellitus, ischemic heart disease), prior vaccination status, and period as potential predictors. The chi-square or Fisher's exact test was used for categorical variables, and the t-test or Mann-Whitney U test was used for continuous variables, as appropriate. A p-value less than 0.05 was considered statistically significant.

Results

Study population:

A total of 91 hemodialysis patients developed COVID-19 infection, with a mean age of 59 years (standard deviation [SD] 17) and a female predominance (52%). The mean duration on hemodialysis was 5.1 years (SD 4.8), and the most common comorbidities were diabetes mellitus (63%), hypertension (88%), and ischemic heart disease (40%). Only one patient had chronic obstructive pulmonary disease, and one had bronchial asthma. Most patients (81%) were infected before February 2022; 41% received at least two doses of COVID-19 vaccine, while 37% were unvaccinated. Table 1: Presents the characteristics and clinical presentations.

Clinical presentation and treatment:

The most common presenting symptom was fever in 42 patients (46%). Pneumonia developed in 35% of patients, while 25% formed hypoxia. Table 1 presents the patients' characteristics and clinical presentation. Combination antibiotics (doxycycline or Azithromycin combined with cephalosporin) were the standard of care for all COVID-infected patients who developed pneumonia, and IV dexamethasone was used for all patients who developed hypoxia. Only one patient received a biological agent.

Table 1: Characteristics and clinical presentation

Variable	Frequency %
Baseline characteristics	
Age, mean (SD)	59 (17)
Gender, female	47 (52%)
Dialysis Vintage, years, mean (SD)	5.1 (4.8)
DM	57 (63%)
HTN	80 (88%)
IHD	36 (40%)
History of malignancy	2 (2%)
Prior kidney transplantation	3 (3%)
COPD	1 (1%)
Bronchial asthma	1 (1%)
Vaccination status	
Unvaccinated	32 (37%)

Post-first-dose	19 (22%)
Post-second-dose	34 (39%)
Post-third-dose	2 (2%)
Prior Two-Dose Vaccination	36 (41%)
Time period: Before Feb 2022	74 (81%)
Clinical Presentation	
Fever	42 (46%)
SOB	23 (25%)
Cough	40 (44%)
Diarrhea	8 (9%)
Hypoxia n=86	23 (25%)
Pneumonia on CXR	32 (35%)
CXR pneumonic infiltration	
None	51 (51%)
Unilateral	12 (14%)
Bilateral	20 (24%)
WBC, mean (SD)	5.9 (3)
Leukopenia <4 86	22 (26%)
Neutrophils, mean (SD)	3.6 (2.3)
Lymphocytes, mean (SD)	1.2 (0.7)
Lymphopenia <1.5 81	61 (75%)
Ferritin, mean (SD)	1238 (1154)
CRP	34 (11-75)
Ferritin	849 (396-1678)
Procalcitonin	0.7 (0.3-1.9)

Clinical outcomes

Among the 91 patients, 32 (35%; 95% confidence interval [CI] 25-45%) developed pneumonia, 23 (25%; 95% CI 16-34%) had hypoxia, 13 (14%; 95% CI 7-22%) were admitted to the intensive care unit, and 8 (9%; 95% CI 3-15%) died. There was a trend toward more pneumonia among patients with diabetes mellitus or ischemic heart disease. Prior two-dose vaccination was not associated with the incidence of pneumonia, its severity (hypoxia, ICU admission), or

mortality. None of the two patients who received three doses of the COVID-19 vaccine developed pneumonia or other related clinical outcomes (hypoxia, ICU admission, or mortality). The period analysis suggested a lower rate of pneumonia with more recent COVID-19 infections (beyond January 2022). **Table 2** presents the characteristics of COVID-19-infected patients who developed pneumonia.

Table 2: Characteristics of COVID-19 infected patients who developed pneumonia.

	Total	Pneumonia	No pneumonia	p value
	91	32	59	
Age, years	59 (17)	60 (16)	59 (18)	0.650
Gender, female	47 (52 %)	15 (47 %)	32 (54 %)	0.502
DM	57 (63 %)	22 (69 %)	35 (59 %)	0.375
IHD	36 (40 %)	16 (50 %)	20 (34 %)	0.134
Dialysis Vintage, years	5.1 (4.8)	5.1 (4.9)	5.1 (4.8)	0.970
Time Period: January 2022 or before	74 (81 %)	30 (94 %)	44 (75 %)	0.027
Prior Two-Dose Vaccination	36 (41 %)	12 (41 %)	24 (41 %)	1
Unvaccinated	32 (37 %)	11 (38 %)	21 (36 %)	
Post one-dose	19 (22 %)	6 (21 %)	13 (22 %)	
Post two doses	34 (39 %)	12 (41 %)	22 (38 %)	
Post 3 doses	2 (2.3 %)	0	2 (3.4 %)	

WBC	5.9 (3)	6.3 (3.7)	5.7 (2.5)	0.433
Lymphocytes	1.2 (0.7)	1.1 (0.8)	1.3 (0.6)	0.188
CRP	34 (11-75)	84 (30-114)	16 (8-42)	< 0.001
Ferritin	849 (396-1678)	1750 (663-3006)	612 (396-1097)	0.001
Procalcitonin	0.7 (0.3-1.9)	1.2 (0.8-3.9)	0.4 (0.2-1)	< 0.001

Discussion

Patients with ESRD are considered a high-risk group for COVID-19 infection and related complications [11-13]. In our study, the COVID-19 corresponding mortality rate was 9%, compared to 8% in non-dialysis patients from the same institution [14]. The reported rate of COVID-19-related mortality in our cohort is low compared to other studies published from different areas in the Kingdom of Saudi Arabia, 17%, 18%, and 20% from studies conducted in Dhahran, Riyadh, and Jazan, respectively [11-13]. Compared to international figures, the mortality rate was between 20-50 % [16-19]. The lower mortality rate in our study could be attributed to a milder disease at the time of presentation, the local institution's protocol of admitting all patients with COVID-19 infection regardless of symptoms for isolation in 2020 to 2022, which could have contributed to earlier recognition and interventions of early signs of severe disease.

Other reported clinical outcomes in this study are Pneumonia 35%, Hypoxia 25%, and ICU admission 14%. We observed a lower rate of pneumonia with more recent COVID-19 infections beyond January 2022, which could be attributed to the presence of the less virulent pathogen, omicron, that we cannot confirm as testing for the genetic strain was not undertaken. Our study found no association between prior two-dose vaccination and the incidence of pneumonia, its severity (hypoxia, ICU admission), or mortality, but it likely reduces the overall incidence of COVID-19 infection. The lack of association with vaccination status in our cohort could be related to the rate and sustainability of vaccine sero-response across different types of vaccines. The efficacy of COVID-19 vaccination was documented with an overall seropositive rate of 88.7%, with 70% at maximum titer and with no significant difference in seropositivity between different types of vaccinations [24]. However, there was a difference in vaccine-induced zero response wane over time across vaccine types [25]. One limitation of our study was that we did not report the time of infection or time of vaccination, as well as the type of vaccine received.

Those who developed pneumonia were found to have very high inflammatory markers compared to no pneumonia, and all COVID-19-related mortality was in the pneumonia cohort. The association between high inflammatory markers and reduced survival in patients with COVID-19 infection was demonstrated earlier in several studies [22-23].

With regards to factors linked to outcomes of COVID-19 infection among hemodialysis patients, there was a trend towards more pneumonia in patients with DM and IHD, although not statistically significant in our cohort. However, a link has been observed in other

studies, particularly the presence of cardiovascular disease in hemodialysis patients [11,13,20] and severe inflammation as a predictor of poor outcomes in hemodialysis patients infected with COVID-19. Not only in hemodialysis patients, cardiovascular comorbidities, fever, and older age had been reported as prognostic indicators of poor outcomes of COVID-19 infection and the general population [20,26].

The most common presenting symptoms in our cohort were fever reported (46%), cough (44%), and shortness of breath (25%), which is similar to other reported studies [11-13, 16-17,20]. Pneumonic infiltration on chest X-ray was reported in 38%, either unilateral or bilateral, similar to the findings in the general population with COVID-19 infection and consistent with previous studies [15,17].

Regarding management, Combination antibiotics (doxycycline or Azithromycin combined with cephalosporin) were the institution's standard of care for all COVID-19-infected patients who developed pneumonia. Doxycycline was used in 32% and Azithromycin in only 4%. Ceftriaxone was the cephalosporin most commonly used (23%), followed by cefipime (8%) and ceftazidime (7%). Other antibiotics for more severe cases were prescribed, including meropenem in 11%, vancomycin in 23%, and Piperacillin/Tazobactam in 2%. Intravenous dexamethasone was used for all patients who developed hypoxia, and this has been shown to improve the outcome in patients with COVID-19 infection [21].

Conclusion

Although our study describes the presentation and outcomes of COVID-19 in one of the largest tertiary care centers in the Western region of Saudi Arabia, it has several limitations. First, it is retrospective observational and limited to a single center with a relatively small sample size. In addition, the lack of information on vaccine sero-response, including the lack of data on the timing of COVID-19 infection about the timing of vaccine booster doses, might have impacted the association between vaccination status and outcomes of COVID-19 infection.

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Conflict-of-interest statement: All authors have no conflict of interest to declare.

Ethical Approval: This study was approved by the institutional review board of King Abdullah International Research Center (KAIMRC), Saudi Arabia (IRB number: NRJ21J/138/05).

Author Contributions: LS: principle investigator, carried out literature search, prepared the proposal, wrote the abstract and discussion, and revised and aligned the whole manuscript; HM: conducted independent literature search, wrote the introduction and participated in discussion; RH: data collection and participated in writing the discussion; SS: data collection and participated in writing

the discussion; MQ: data collection and participated in writing the proposal and introduction; AM, conducted independent literature search, did the data management and analysis, and wrote the methodology section; all authors read and approved the final manuscript.

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