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ORIGINAL ARTICLE

SARS-CoV-2 Related Morbidity and Mortality in Patients Undergoing Hemodialysis at The Kirkuk Hemodialysis Center

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) is a new emerging disease caused by SARS-CoV-2, first discovered in Wuhan, China, in December 2019. Infected patients of all age groups with associated medical diseases such as chronic kidney disease (CKD) stage five -end stage renal disease (ESRD) on hemodialysis are likely to have a higher risk of developing severe COVID-19 compared to patients without disease. The study aimed to address morbidity and mortality related to SARS-CoV2 infection in hemodialysis patients at the Kirkuk dialysis centre.

Methods: A prospective observational study that enrolled 385 COVID-19 patients with CKD-stage 5 (ESRD), who were on a regular hemodialysis program in the dialysis center in Kirkuk city for a period of 6 months.

Results: In hemodialysis patients, the incidence of SARS-CoV2 infection was 80 (20.75%), among these 80 patients, 43 (53.75%) required hospital admission due to the severity of the disease, 32 (40%) were admitted to the intensive care unit and received ventilation, 19 patients (23.75%) died from complications related to SARS-CoV-2.

Conclusion: There is a significant incidence of hospital admission and the need for ventilation among patients, as well as a notable mortality rate was observed in COVID-19 patients undergoing hemodialysis, with specific risk factors such as bronchial asthma, the presence of AV fistula, and type 2 diabetes mellitus contributing to a higher mortality percentage.

Key words: COVID-19; End Stage Renal Disease; Hemodialysis; Acute Kidney Injury; Morbidity.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by a new coronavirus that was first discovered in Wuhan, China, in December 2019. As this virus is a novel virus, data on it was deficient, and experts revealed new information every day regarding this virus. The spectrum of clinical presentation is variable, ranging from mild symptoms to severe disease. Old age and patients with underlying diseases are at high risk of developing severe disease [1, 2].

The risk of developing severe disease increases progressively as the patient ages compared to children who can present with different symptoms [3]. Furthermore, in addition to the old age, patients with medical diseases such as (cardiovascular disease, diabetes mellitus, or pulmonary disease, and chronic kidney diseases) are at greater risk of developing severe COVID-19 compared to patients without these diseases. Patients with stage five CKD (ESRD) on a regular hemodialysis program are prone to severe complications of COVID-19 infection with severe acute respiratory syndrome coronavirus2(SARS-CoV-2). The uremic syndrome induces immune suppression, and individuals in CKD stage five (ESRD) typically belong to an older age group with comorbidities, heightening the risk of a unfavorable COVID-19 outcome. Currently, data are inadequate on the results of COVID-19 in patients on a regular hemodialysis program [4–7].

These patients with renal replacement therapy (hemodialysis) are associated with a high risk of mortality, particularly those of the old age with variable associated chronic diseases such as hypertension, cardiovascular disease, and type 2 diabetes mellitus [8].

Those who are on renal replacement therapy (hemodialysis or kidney transplantation) are susceptible groups. Generally, the age-related cardiovascular and noncardiovascular mortality percentages in hemodialysis patients were already 8.8 and 8.1 times higher than in the general population, respectively. Furthermore, hemodialysis patients with CKD-5 (ESRD) were considered a vulnerable group for COVID-19 with an infection frequency of 16% [9].

It is common to expect that COVID-19 infection in CKD-5 (ESRD) is associated with hospitalization, admission to ICU, intubation and ventilation, and high mortality rates, due to the immune-incompetent state and associated comorbid diseases such as diabetes mellitus and cardiovascular diseases [10].

Several small studies from different countries, Italy (N=41, N=94), Spain (N = 36), and the USA (N = 59), reported a high mortality percentage in hemodialysis patients with proportions ranging from 29% to 41% [9].

The discovery of SARS-CoV-2 in the kidneys has led to the need for further research. In a postmortem series of 63 patients with confirmed COVID-19, SARS-CoV-2 RNA was observed in the renal tissue of 38 (60%) of infected patients. The detection of SARS-CoV-2 RNA in the kidneys has been associated with increased age and an increase in comorbid conditions. Furthermore, the detection of SARS-CoV-2 RNA in renal tissues was correlated with the reduced chance of survival of the patient, which was defined as the time interval between the diagnosis of COVID-19 and the death time. These data support a possible association between the extra respiratory course of the virus, the extent of the disease, and the high risk of early mortality within the first 21 days of infection [10]. The aim of this study is to explore the short-term results of SARS-CoV-2 among patients with (ESRD) stage 5 on regular hemodialysis.

MATERIALS AND METHODS

During the study period, 385 patients were enrolled in the hemodialysis center at Kirkuk General Hospital, located in Kirkuk city, Iraq. The primary objective of the study was to evaluate the impact of SARS-CoV-2 infection on morbidity and mortality among hemodialysis patients.

In this prospective observational study, we observed and followed all patients attending the dialysis centre. All of them had stage 5 chronic kidney disease on hemodialysis who received renal replacement therapy by regular hemodialysis (2 or 3 times a week for 3-4 hours) from the period 18 July 2020 to 1 February 2021. At the beginning of the study, all patients with ESRD who were on regular hemodialysis attended the dialysis centre for SARS-CoV-2 infection were screened by PCR technique.

During the period of the study, any patients who were on regular hemodialysis diagnosed with SARS-CoV-2 by PCR test from through using of nasal swab were questioned and followed both clinically and by PCR test performed with each hemodialysis session two or three times a week. All patients with SARS-CoV-2 received a hemodialysis session in an isolated ward area of the dialysis centre.

Those patients with severe COVID-19 infection categorized by clinical features (hypoxia, impaired level of consciousness hypotension), laboratory markers (lymphopenia high C-reactive protein, increased levels of D-dimer, and serum lactate dehydrogenase) and radiological features (more than

40% lung involvement by chest CT scan) were admitted to the hospital and some of them were admitted to the ICU according to WHO criteria of severity classification.

The time of observation for each patient was from the start of SARS-CoV-2 infection until the cure time, both by resolution of signs and symptoms and by negative PCR test results or death caused by complications from SARS-CoV -2 infection.

Patients with no history of chronic kidney disease who were diagnosed with SARS-CoV-2 infection complicated by acute kidney injury (AKI) were excluded from the study.

Regarding the statistical analysis, Mean, standard deviation, and median are used for the analysis of numerical variables. Logistic regression analysis is used to test the relationship of (continuous or categorical) independent parameters with one dichotomous dependent parameter. The probability (P) value was estimated, where the value of P less than 0.05 was considered as a significant difference, while the value of P greater than 0.05 was denoted as a nonsignificant result. A P value less than 0.01 is considered as highly significant result.

RESULTS

Thirty hundred eighty five patients enrolled in the current study, 80 (20.75%) patients were confirmed cases by nasal and pharyngeal swabs. As **Table 1** shows the results of SARS-CoV-2 infection on regular hemodialysis, their age ranged from 20 to 80 years, with a median age of 55 years. Sixty patients were male and 20 were females.

The percentage of associated hypertension was 37.5%, while the type 2 diabetes mellitus was 31.25%.

The duration of hemodialysis ranged from several months to up to 10 years. Dialysis access in 65 patients (81.25%) was an arm AV fistula and in 15 patients (18.75%) were internal jugular vein catheters.

as the most common symptoms were fever, cough, headache, diarrhoea, and vomiting, while the most common signs were high temperature, crackles, and wheezes on chest auscultation. **Table 2** shows the end result for all SARS-CoV-2 positive cases with a duration of illness ranging from 8 to 22 days with a median of 14 days. 43 cases (53.75%) required admission to the hospital due to the severity of the disease. Thirty-two hospitalized patients (40%) were admitted to the ICU (intensive care unit) and received invasive respiratory assistance.

Unfortunately, 19 patients, 13 males and 6 females, died from complications related to SARS-CoV-2 infection, while the number of deaths among patients with end-stage renal disease who were on regular hemodialysis with negative tests for SARS-CoV-2 infection during the study period was ten deaths from a total of 305 patients (Mortality percentage 3.9%).

Table 3 shows that the risk factors associated with increased mortality in patients on hemodialysis and SARS-CoV-2 infection with statistically significant results are the severity of COVID-19 disease (P value= 0.001), AV Fistula (0.005), bronchial asthma (P value = 0.001) and diabetes mellitus (p value 0.045).

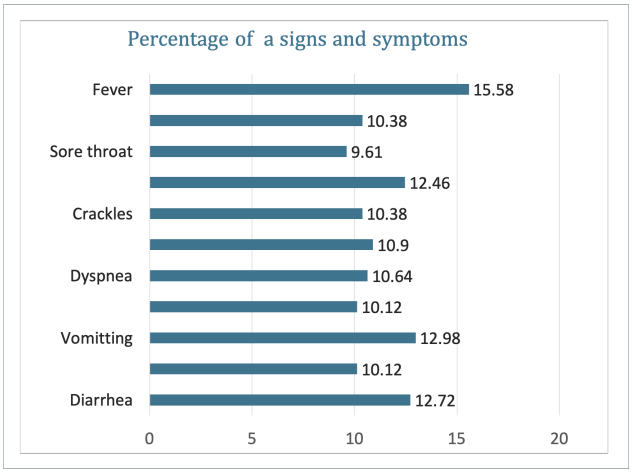

Figure 1. The percentage of the signs and symptoms were related to SARS-CoV2 infection.

Table 1. Comparison of different parameters between HS and CT techniques.

Variables (no.=80)	Category	No. (%)
Age Groups	(20-29)	10 (12.5%)
	(30-39)	28 (35%)
	(40-49)	15 (18.75%)
	(50-59)	13 (16.25%)
	(60-69)	8 (10%)
	(70-80)	6 (7.5%)
Age Sex	Male	60 (75%)
	Female	20 (25%)
BMI (Mean±SD)	Male patients	24.5±4.6
	Female patients	24.3±4.4
Comorbidities	Asthma	5 (6.25%)
	Type 2 diabetes mellitus	25 (31.25%)
	Hypertension	30 (37.5%)
	Others	20 (25%)
Dialysis Vintage	Larger than 15 months	43 (53.75%)
	Less than 15 months	37 (46.25%)
Dialysis Access	AV fistula	65 (81.25%)
	Dialysis catheter	15(18.75%)

Independent sample t-test, HS = Harmonic scalpel, CT= Conventional techniques

Table 2. SARS-CoV-2 according to sex and in patient sequelae

Variables	Male	Female	Total	Percentage
Duration of the illness days (Mean± SD)	15.9±9.5	17±8.1	N/A	N/A
Admission to hospital	28	15	43	53.75%
Admission to ICU	22	10	32	40%
No. of death	13	6	19	23.75%

ICU=Intensive care unit, N/A=Not applicable

Table 3. SARS-CoV-2 according to sex and in patient sequelae

Variables	CI RR (95%)		
	Lower	Upper	P Value
Age (year)	0.89	1.12	**0.093**
The severity of the COVID 19 disease	4.45	9.342	**0.001**
AV fistula	1.78	4.88	**0.005**
Asthma	0.88	2.34	**0.001**
Type 2 diabetes mellitus	0.897	1.456	**0.045**
Hypertension	0.19	0.64	0.55

AV fistula=Arteriovenous fistula, CI=Confidence interval, RR=Relative risk

DISCUSSION

Pandemic Covid-19 infection is an emerging virus that originated in China and spreads rapidly throughout the world, resulting in localized or systemic pneumonia [11]. Covid-19 is a multisystemic disease that affects the neurological system, the gastrointestinal tract, the respiratory system, and other bodily systems [12].

This study included 385 patients who attended at hemodialysis center with ESRD on regular hemodialysis during the study period, 80 patients (60 males, and 20 females) were diagnosed for SARS-CoV-2 infection with a percentage rate of approximately 20%, this percentage of infection was acceptable rate considering wide spread of infection worldwide and was comparable to John J. Sim. et al. in the Kaiser Permanente study of Southern California in the United States [13], probably due to strict policies of screening for dialysis of patients and case isolation, and also general lockdown in most regions around the world due to the pandemic during the study period.

The severity of SARS-CoV2 infection in the current study in terms of hospital admission and ICU admission with respiratory assistance was high 53.75% and 40%, respectively. A large European multinational retrospective study on European Renal Association Covid Database by L.B. Hilbrands et al. published in Nephro-Dial-Transplant journal 2020 also showed high percentage of severe COVID-19 cases admitted to hospital 70% of dialysis patients but the percentage of patients admitted to ICU with respiratory assistance in L.B. Hilbrands et al. study was 12% which was lower than our study (51%) which is disagrees with our findings, may be due to the number of patients with COVID-19 and on dialysis in that study that was higher than our study and included patients from seven countries in Europe [14].

The mortality rate of hemodialysis patients who also had SARS-CoV2 virus infection was high, 23.75% compared to the results of other studies like John J. Sim. et al in USA (23%) and L. B. Hilbrands et al European study (21.3%), but was higher than the mortality rate from SARS-CoV2 virus infection in general population which range from 3-4% mortality rate as stated by the Center for Disease Control and Prevention (CDC) and World Health Organization (WHO) for people with covid-19 diagnosed [13, 14].

Our study showed some risk factors that were associated with higher mortality rates in hemodialysis patients with SARS-CoV-2 infection (P value= 0.001), bronchial asthma (P value 0.001), presence of AV fistula (P. value= 0.005), diabetes mellitus (p value 0.045). In L. B.Hilbrands et al. study the most common risk factors associated with mortality was age and frailty, but in John J Sim. et al. study mentioned above, the factors associated with higher mortality were older age heart failure, ischemic heart disease, and diabetes mellitus [13, 14].

The reasons for the high mortality in patients with renal failure are not fully understood. Although the end stage of renal diseases associated with an immunosuppressive state, the patient on hemodialysis who is generally older and often has an associated comorbidity that increases the risk of the worst outcome in COVID-19. Furthermore, researchers have reported frequent renal failure and a greater incidence of acute kidney injury (AKI) with poor outcome in patients with COVID-19. Current data show that the prevalence of kidney damage upon admission and progression of AKI during hospital admission in patients with COVID-19 was high and this was associated with high hospital mortality. There are several theories. First, SARS-CoV-2 has the ability to induce endothelitis, an inflammation of the blood vessels in the kidneys, similar to how it

affects the lungs. According to another version, there may be direct damage to the kidneys as a result of an immune system reaction that leads to systemic inflammation and damage to body tissues [15–21].

This study has some limitations, as the small number of the study sample because this study was conducted in a single dialysis center, also the study period of approximately 6 months is short compared to the whole duration of the COVID-19 pandemic.

RECOMMENDATIONS

In the future pandemics, stricter health policies should be implemented by the health authorities and personnel of the medical service for patients on renal replacement therapy to protect those patients from communicable diseases. More studies are needed in the future for patients with CKD, kidney transplant patients infected by the SARS-CoV-2 virus, and also for patients with acute kidney injury (AKI) due to severe infection by the SARS-CoV-2 virus.

CONCLUSION

There is a significant incidence of hospital admission and the need for ventilation among patients, as well as a notable mortality rate was observed in COVID-19 patients undergoing hemodialysis, with specific risk factors such as bronchial asthma, the presence of AV fistula, and type 2 diabetes mellitus contributing to a higher mortality percentage.

ETHICAL DECLARATIONS

- **Acknowledgements**

  None.

- **Ethics Approval and Consent to Participate**

  Ethical approval with issue number (30) dated 29/3/2023 was granted from the ethics committee of the University of Kirkuk, College of Medicine.

- **Consent for Publication**

  Non.

- **Availability of Data and Material**

  The datasets are available from the corresponding author upon reasonable request.

- **Competing Interests**

  The authors declare that there is no conflict of interest.

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- **Authors' Contributions**

  All stated authors contributed significantly, directly, and intellectually to the work and consented it to be published.

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