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Original article.

COVID-19 infection in Libyan chronic hemodialysis patients: Prevalence, risk factors, severity and predictors of mortality

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Abstract :

Background: Chronic kidney disease (CKD) is associated with the increased risk of both outpatient and inpatient pneumonia. This association is independent of comorbid diabetes, cardio-vascular disease (CVD), asthma, and chronic obstructive airway disease. Dialysis patients are considered at risk groups for SARS-CoV-2 infection; Short-term mortality in patients on chronic hemodialysis who were hospitalized with COVID-19 was high. Outcomes in those requiring intensive care unit (ICU) and mechanical ventilation management were poor .

Aim: This study mainly aimed to identify the prevalence, risk factors, severity and predictors of mortality in Libyan hemodialysis patients infected with COVID- 19 .

Methods: In this retrospective cohort study, data of CKD patients on maintenance hemodialysis diagnosed with COVID-19 infection from two large dialysis centers in Libya were collected and analyzed using SPSS version 22 for .demographic, clinical and laboratory profiles .

Results: The data of 810 patients from two hemodialysis centers in Libya showed infection rate was 10.2 %, and the overall mortality was 26.5% (39/83) 47% of patients needed admission to ICU for supportive mechanical ventilation (SPO2 ranged from 76-92%). The biochemical and laboratory data showed a decreased mean absolute lymphocyte counts. a high neutrophil-lymphocyte ratio (NLR), and a mild decrease in platelet counts. C-reactive protein (CRP), fibrinogen, ferritin, and D-dimer were also high at admission. (22/83, 26.5%) of total patients, and (17/39) 43.6% of ICU patients died in less than 28 days after COVID-19 diagnosis .

Conclusions: In CKD patients on maintenance hemodialysis diagnosed with COVID-19 infection; severity of disease at presentation, need for invasive supportive mechanical ventilation, older age, raised serum glutamic oxaloacetic transaminase, and lower level of albumin may have been valuable predictors of mortality and poor outcomes.

Keywords: COVID-19, hemodialysis, prevalence, outcome, Libya,

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Introduction:

COVID-19 infection is a severe acute respiratory syndrome caused by coronavirus 2 (SARS- CoV-2). It was first identified in December 2019 in Wuhan, China. Then after The World Health Organization declared, the outbreak is a Public Health Emergency of International Concern in January 2020 and a pandemic in March 2020. As far 21 February 2021, more than 111 million cases have been confirmed, with more than 2.46 million deaths attributed to COVID-19; it was identified in all age groups with a different spectrum of severity, as per population age group (less severe in very young patients), as well as patients' comorbid condition (more fatal in patients with chronic illness) .

Chronic kidney disease (CKD) is associated with an increased risk of both outpatient and inpatient pneumonia [1]. This association is independent of comorbid diabetes, cardiovascular disease (CVD), asthma, and chronic obstructive airway disease, (COPD). Dialysis patients are considered high-risk groups for SARS-CoV-2 infection due to many risk factors along with the proximity of patients during hemodialysis treatment. Short-term mortality in patients on chronic hemodialysis who were hospitalized with COVID-19 was high. Outcomes in those requiring intensive care unit (ICU) and mechanical ventilation management were poor [2]. Data from the ERA-EDTA registry showed that mortality risk in this group of patients was even 1.28 times higher than in matched dialysis patients [3]. Based on these data, there is consensus that COVID-19 has substantially affected mortality in patients receiving kidney replacement therapy given their burden of comorbidities and vulnerability to infectious diseases [5, 4].

In this study, we aim to determine the prevalence, risk factors, severity, and predictors of mortality in Libyan hemodialysis patients infected with COVID-19.

Abbreviations: COVID-19: coronavirus infectious disease 2019, CKD: chronic kidney disease, HD: hemodialysis, CVD: cardio-vascular disease, COPD: chronic obstructive pulmonary, ICU: Intensive care unit, RT-PCR: Real time-Polymerase chain reaction, CRP: C- reactive protein, SPO2: oxygen saturation, PCT: procalcitonin, TLC, Total leukocyte count; NLR, neutrophil-lymphocyte ratio; IL-6, interleukin-6; SGOT, serum glutamic oxaloacetic transaminase

Patients and methods:

We did a retrospective observational study on 810 HD patients infected with COVID-19 during the period from September 2020 until 31 December 2020, at two large hemodialysis centers in Libya (Azzawiyah kidney hospital in Zawia city and Alhawari nephrology center in Benghazi city). The data were extracted from the case sheets, screening documents, laboratory results, radiology reports, and treatment records. Demographic details, comorbidities, and various other parameters included oxygen saturation at presentation, hemodialysis sessions, intra or post-dialysis complications, ventilation treatment, course of the disease during hospitalization, length of hospital stay, and outcomes in terms of discharge from the hospital or death during hospitalization. All patients with inadequate data were excluded from the study

Patients' records were reviewed for clinical findings, laboratory and radiological investigations including: confirmed Positive results based on a reverse transcriptase-polymerase chain reaction (RT-PCR) test on samples obtained from the upper respiratory tract by nasopharyngeal or oropharyngeal swab, C-reactive protein (CRP), complete blood count (CBC), differential leucocyte count (DLC), D-DIMER, chest x-ray and computer chest scan (CT chest). The data were extracted from the case sheets, screening documents, laboratory results,

radiology reports, and treatment records. Demographic details, comorbidities, and various other parameters included oxygen saturation at presentation, hemodialysis sessions, intra or post-dialysis complications, ventilation treatment, course of the disease during hospitalization, length of hospital stay, and outcomes in terms of discharge from the hospital or death during hospitalization. All patients with inadequate data were excluded from the study. Patients' records were reviewed for clinical findings, laboratory and radiological investigations including: confirmed Positive results based on a reverse transcriptase-polymerase chain reaction (RT-PCR) test on samples obtained from the upper respiratory tract by nasopharyngeal or oropharyngeal swab, C-reactive protein (CRP), complete blood count (CBC), differential leucocyte count (DLC), D-DIMER, chest x-ray and computer chest scans (CT chest). The disease severity in the patients was categorized as mild, moderate, or severe. The mild disease was defined as a lack of respiratory symptoms and oxygen saturation $SpO2 \geq 96\%$. Moderate disease was defined as mild respiratory symptoms, radiological evidence of pneumonia, and $SpO2 < 96\%$. Severe disease was defined as $SpO2 \leq 93\%$ and the use of oxygen support or the initiation of steroid therapy. The critical disease was defined as a SpO2 remaining at or below 93% despite oxygen supplementation at 5 L/min or more via a facemask or death. To determine the risk factor for death in dialysis patients, various variables (age, sex, comorbid diseases, COPD, number of dialysis sessions, biochemical data, inflammation markers, clinical presentation symptoms, and status were recorded and analyzed. Infected patients were isolated for three weeks, and followed up according to disease progression. For database handling and analysis, we used Microsoft Excel® (Microsoft, USA) and IBM-SPSS statistics application version 22 (IBM Corporation, USA). Baseline characteristics expressed as mean ±SD, median (interquartile range), or percentage, as appropriate, p-value of < 0.05 considered statistically significant.

Results:

In this article, we describe the clinical course and outcome of hemodialysis patients infected with COVID-19 during the period from September 2020 until 31 December 2020 at two large dialysis centers in Libya,

Among 810 HD patients, 83 patients (83/810, 10.2%) tested positive for COVID-19 with RT-PCR. The median age of patients was 51 years (interquartile range (42.5, 74).

Original kidney diseases of patients are diabetes mellitus (45.6%), hypertension (25.5%), primary nephritis (16.9%) and others (12%). Overwhelming comorbidities are common in CKD patients, our data showed that some patients have more than one comorbid disease, and was expressed in forms of, hypertension 82%, diabetes 53%, anemia 80.4% and cardiovascular diseases (CVD) in 8% (table1).

The biochemical and laboratory data (table2) showed decreased mean absolute lymphocyte counts, and a high neutrophil-lymphocyte ratio (NLR), as the patients are HD patients, baseline, high blood urea and serum creatinine values were observed.

C-reactive protein (CRP), fibrinogen, ferritin, and D-dimer were high at admission. While the coagulation profile showed near-normal PT, APPT, and INR.

Clinical symptoms and outcome data analysis (figure 1. Table 3), showed that at presentation the patients were; fever (80%), dry cough (80.4%), flu-like symptoms (73%), anorexia (50%), and 42/83 (51.2 %) of patients were dyspneic at presentation.

47 % (39/83) of patients needed admission to ICU for supportive mechanical ventilation as their SPO2 ranged from 76-92% (table3) (22/83 26.5%) of total patients, and (17/39, 43.6%) of ICU patients died in less than 28 days after COVID-19 diagnosis.

The baseline radiological examinations were suggestive of COVID-19 infection as it showed

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bilateral infiltrates in chest X-ray, and CT-scan of the patients (67% and 86.7% respectively).

Detailed chest X-ray examinations showed pleural effusion in 24.4% of cases and consolidations in 39%. CT scan showed the usual ground-glass opacities in 83% of patients and was extensive and bilateral in 26.5% of patients.

Discussion:

Libya is not a heavily populated country, has limited public transport, and fewer people are traveling abroad. It was only until June 2020 to register the outbreak of COVID-19 among the general population (1.2%), and mortality due to COVID-19 complications was 2.3 % [6], while we found that in this cohort group the mortality rate was eight folds higher than in the general population as it counts 29.6 % (83/280 patients)..

In the general course of COVID-19, pneumonia can begin to worsen and reach critical severity about 7–10 days after clinical onset; mortality rates secondary to sepsis in dialysis patients are several hundred-fold higher than those observed in the general population, and approximately 15-fold higher in dialysis patients. Stratification for the race, gender, and DM, CKD remains highly associated with mortality secondary to sepsis [7], data on hemodialysis patients with COVID-19 pneumonia.is limited.

Biomarkers such as CRP, PCT, and D-Dimer are useful guides for predicting mortality; many studies concluded that LDH, PCT, D-dimer, CRP, and ferritin are effective biomarkers [8, 9].

Studies showed that; in the early stage of COVID-19; CRP levels were positively correlated with lung lesions and could reflect disease severity [9]; patients who died had a significantly higher D-dimer (>3,000) when compared with survivors [10].

Patients on hemodialysis and CKD tend to have different reactions and responses to infections and inflammations; they tend to have disorders of B- and T-cell function [11] and hence have an atypical presentation during infection. Lymphopenia is common in viral infection, and it might be a critical factor associated with disease severity and mortality [12], also; PCT has a higher level in CKD patients even in the absence of severe acute illness [13]. These limitations and the presence of co-morbid conditions in hemodialysis patients made the diagnosis of COVID-19 pneumonia depend on clinical epidemiology, radiographic findings, and RT-PCR.

In this study, we found that COVID-19 infection is associated with increased severity and mortality in CKD patients and HD patients; noticed more in patients with old age, diabetics, and anemic HD patients.

The obtained data revealed that most patients were middle-aged, with a median (IQR) age of 51 (IQR, 42.5, 63.5) years, and with one or more co-morbidities that had predisposed them to a higher risk of severe viral infection. More than 50% of the patients (55.3%) presented with moderate to severe disease. Most reported symptoms were cough (80.4%), fever (80.0%), and shortness of breath (51.2%), requiring treatment with oxygen support via a variety of oxygen delivery devices at admission; there was no significant difference between survivors and non-survivors in terms of symptomatology. A high baseline level of inflammatory marker CRP was observed in the majority of the patients most likely due to chronic inflammation seen mostly in CKD and HD patients; moreover, 80.7 % of the patients presenting with severe disease at admission, required invasive mechanical ventilation during ICU stay.

Non-survivors were significantly older ($p=0.016$), with a median age of 72 (IQR, 54, 74) years, have high TLC and lymphopenia, and were more likely to present with elevated values of neutrophil/lymphocyte ratio (NLR) more than those who survived ($p<0.045$) (table2).

Patient stratification into survival and non-survival has shown that; bilateral lung infiltrations, oxygen saturation (SPO2) at admission, and the need for mechanical

ventilation support at presentation have an impact on survival (table2)

Conclusions

Hemodialysis patients are at high risk of developing COVID-19; due to associated comorbidities and have exhibited a high rate of mortality. Comorbid diseases such as diabetes and COPD are risk factors for the severity of infection in these patients. The severity of the disease was significantly different from the general population ($p < 0.001$), especially in patients with low oxygen saturation (less than 95% at admission to ICU). Old age, bilateral lung lesions, high total leucocytic count, lymphopenia high Neutrophil-lymphocyte ratio, high SGOT, and low albumin levels, as well as the need for mechanical ventilation, are predictors of mortality in such patients.

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Table 1. Demographic Profile of studied patients

Variable	(n,%)
Total	(83) 10.2%
Age (y)	Range 50-72 (IQR42.5, 73.5)
Gender	
Male	58 (65.7)
Female	25 (34.2)
Primary kidney disease	
Diabetic	38 (45.6)
Hypertension	21 (25.5)
Primary nephritis	14 (16.9)
Others	10 (12)
Pre-COVID dialysis duration (y)	9.6±3.4
Comorbidity	
Hypertensive	32 (91.4)
Diabetic	67 (80.4)
Cardiovascular disease	7 (8)
Anemia	67 (80.4)

Table 2. Biochemical Profile Comparative to Outcomes

Variable (Normal Range)	Survivors (n = 61, 73.5%)	Non-survivors (n = 22)	P-Value
Hb (13 - 17 g/d)	8.7 (7.2, 10.3)	8.6 (7.7, 10.6)	0.369
TLC (4 - 10 × 103 /µL)	7.5 (5.1, 12.4)	15.4 (9.9, 22.1)	0.039*
Lymphocyte (11 - 30 × 102 /µL)	11.8 (7, 16.3)	3.4 (2.8, 7.6)	0.013 *
NLR (1 - 3)	7.1 (5.7, 12.1)	22.2(12.5, 29.9)	0.048 *
INR (1-3)	1.1 (1.0,1.2)	1.0 (0.8,1.4)	0.157
PT (10.2 - 13.2 (s))	12.8 (11.6, 14.2)	12 (10.8, 13.5)	0.146
APTT (25.4 - 38.4 (s))	33.2 (28.1, 36.53)	32.4 (28.5, 36.1)	0.937
Fibrinogen (180 - 350 mg/dL)	341 (285, 449)	396 (330, 499)	0.013
D-dimer (< 500 ng/mL)	390 (112, 809.1)	1488 (529, 2976)	0.146
CRP (0 - 0.5 mg/dL)	8.9 (3.5, 12.8)	11.3 (4, 21.2)	0.346
SGOT (< 34 U/L	25 (16.8, 52)	82.2 (59.9, 109.6)	0.001 *
Albumin (3.2 - 4.8 g/dL)	3.4 (3.1, 3.9)	3.0 (2.6, 3.4)	0.020 *

Table 3. Clinical Profile with Outcomes of studied patients

Variable	Total (n=83)	Survivors (n = 61, 73.5%)	Non-survivors (n = 22.26.5%)	P-Value
Age (y) median (range)	51 (42.5, 74)	47 (42, 55)	72 (54, 74)	0.016 *
Presenting symptoms				0.744
Shortness of breath	42 (51.2)	26 (42.6)	16 (72.7)	
Fever	76 (80.0)	57 (93.4)	19 (86.4)	
Dry Cough	67 (80.4)	48(78.7)	19 (86.4)	
Flu like	60 (73.0)	49 (80.3)	11 (50.0)	
Anorexia	42 (50.0)	29 (47.5)	13 (59.0)	
Severity of infection at admission				0.004 *
Mild	37 (44.6)	33 (54.2)	4 (18.2)	
Moderate	20 (24.1)	14 (22.9)	6 (27.3)	
Severe	26 (31.3)	14 (22.9)	12 (54.5)	
Chest radiograph				0.005 *
Bi-lateral infiltrates	72 (86.7)	50 82.0)	22 (100)	
Oxygen support at admission				0.020 *
Present	67 (80.7)	45 (73.8)	22 (100)	
Absent	16 (19.3)	16 (26.2)	0 (0)	

Figure 1: collective clinical symptoms in all patients