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Outcomes of symptomatic coronavirus disease 19 in maintenance hemodialysis patient in India

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Abstract

Background: Maintenance hemodialysis (MHD) patients face disadvantages with higher risk of acquiring SARS-CoV-2 infection, atypical manifestations, and associated multiple comorbidities. We describe patients' outcomes with symptomatic COVID-19 on MHD in a large cohort of patients from India.

Methods: Data were collected prospectively from hemodialysis units in 11 public and private hospitals between March 15, 2020, and July 31, 2020. The survival determinants were analyzed using stepwise backward elimination cox-regression analysis.

Results: Of the 263 total patients (mean age 51.76 ± 13.63 years and males 173) on MHD with symptomatic COVID-19, 35 (13.3%) died. Those who died were older ($p = 0.01$), had higher frequency of diabetic kidney disease ($p = 0.001$), comorbidities ($p = 0.04$), and severe COVID-19 ($p = 0.001$). Mortality was higher among patients on twice-weekly MHD than thrice-weekly ($p = 0.001$) and dialysis through central venous catheter (CVC) as compared to arteriovenous fistula ($p = 0.001$). On multivariate analysis, CVC use (HR 2.53, 95% CI 1.26–5.07, $p = 0.009$), disease severity (HR = 3.54, 95% CI 1.52–8.26, $p = 0.003$), and noninvasive ventilatory support (HR 0.59, 95% CI 0.25–0.99, $p = 0.049$) had significant effect on mortality.

Conclusion: The adjusted mortality risk of COVID-19 in MHD patients is high in patients associated with severe COVID-19 and patients having CVC as vascular access.

1 | INTRODUCTION

Over 69 million people in 220 countries have been identified to have SARS-CoV2 infection around the world in the last 10 months since the first case was reported from Wuhan, China.[1,2] The high infectivity of the contagion and the public health actions taken to limit its spread and protect the vulnerable populations has adversely affected the care of people with preexisting conditions, including those with kidney disease.[3–5] COVID manifestations and fatalities vary and have shown enormous differences in different parts of the world and, in some cases, even within countries.[5–8] In part, they are determined by the surveillance, testing, quarantine, isolation, and hospitalization policies and differences in population characteristics.[9–12]

Patients on in-center maintenance hemodialysis (MHD) present unique management challenges because of their need to report to a healthcare facility several times every week.[6,13–15] Further, dialysis patients may be at increased risk of adverse outcomes if they contract the coronavirus disease (COVID-19) by virtue of having associated

comorbidities like diabetes mellitus, hypertension, and cardiovascular disease that independently increase the risk of severe COVID-19 and mortality.[13,16,17] Further, inherent immunocompromised state of these patients also affects the outcome.[17–19] The cytokine storm manifestation in patients on dialysis may be different from the general population.[20] A few studies have been published from developed nations about epidemiology and clinical presentation of dialysis patients with COVID-19.[6,14,15] These studies revealed that while dialysis centers represented high risk, most affected individuals had clinically mild COVID due to impaired cellular immune function[17–19] and poor cytokine response.[20] Severe COVID, however, poses a higher mortality risk because of the collateral impact of comorbidities.[6,7,14,15,21,22] During the pandemic, dialysis patients' management has presented unique challenges—with high dropout rates and death due to missing treatment.[23]

Further, there are several differences between the dialysis population in the developed world and those in emerging countries. For example, India's dialysis population is relatively younger than that of the western dialysis population,[12,24,25] and age has been consistently identified as a risk factor for death from COVID-19 in the United States.[3,12] There are no data, however, that has examined the impact of COVID-19 on the outcome of patients on MHD in developing countries. The present study was conducted to assess the outcomes of MHD patients and predictors of mortality with symptomatic COVID-19 disease.

2 | MATERIAL AND METHODS

2.1 | Study design and participants

In this prospective cohort study, data were collected from dialysis units in 11 public and private hospitals between March 15, 2020, and June 30, 2020, after obtaining approval by the institutional ethics committee.

2.1.1 | Screening and diagnosis of COVID

All centers started screening patients for fever, respiratory symptoms (cough and breathlessness), and new-onset digestive tract symptoms at a designated station before entering the dialysis room. Symptomatic patients were treated as COVID-19 "suspect" and dialyzed in isolation and underwent screening with reverse transcription polymerase chain reaction (RT-PCR) for SARS-CoV-2 infection in an approved laboratory.[22] Those with positive RT-PCR were diagnosed as confirmed COVID-19 cases. Cases were categorized as mild, moderate, and severe as per the Revised Guidelines on Clinical Management of COVID-19, Ministry of Health and Family Welfare, the Government of India.[26] The disease was classified as mild when symptoms were present without features of viral pneumonia on imaging (X-ray chest or high-resolution computed tomography [HRCT] scans), moderate if manifestation were present, while severe disease refers to the presence of hypoxia with respiratory rate >30 breaths/min, severe respiratory distress, SpO2 < 90% on room air including acute respiratory distress syndrome (ARDS).

All comorbidities like diabetes, hypertension, chronic obstructive airway diseases, cardiovascular diseases, and cancers were noted. All laboratory testings were performed according to the clinical care needs of the patient. Laboratory assessments consisted of a complete blood count, blood chemical analysis, coagulation testing, assessment of liver function, and measurement of electrolytes. The C-reactive protein (CRP), serum ferritin, D-dimer, and the interleukin-6 level was done as per the decision and availability of the test. The chest imaging criteria varied from center to center. An X-ray chest was performed in all cases, and HRCT was done as per the availability and decision of the treating physician.

All patients were admitted to a COVID facility and received antiviral, antibiotic therapy, glucocorticoid therapy, and respiratory support as required. MHD was continued as per the ongoing schedule of individual patients.

2.2 | Statistical analysis

Data were collected in an Excel sheet from all participating centers. Continuous variables were expressed as mean ± standard deviation (SD). Categorical variables were expressed in the form of percentages. Independent samples *t* test for parametric distribution was used to compare the mean values between the groups. A chi-square test was used to compare the categorical variables between the groups. Patients with mild–moderate categories and severe categories with and without ARDS were clubbed together for analysis purposes. We analyzed the differences in clinical manifestations between two categories (1) dead and alive and (2) disease severities of mild/moderate and severe COVID-19 patients. Time-dependent univariate Cox regression analysis was done to predict the survival of the patients. The significant factors were again tested on multivariate Cox regression with stepwise backward conditional elimination of nonsignificant factors to the model predicting the patients' survival. A two-sided *p* value of 0.05 was considered statistically significant. All analyses were performed using IBM.SPSS software version 20.0.

3 | RESULTS

3.1 | Baseline demography of patients by COVID severity and survival status

Out of a total of 1640 patients on MHD from all participating centers, COVID-19 infection was diagnosed in 263 patients, with a mean age of 51.76 ± 13.63 years and 173 males during the study period (Mar 25 to July 31, 2020). The basic demography and given therapy to the patients who died and survived is shown in Table 1. Of the 263 patients, 35 (13.3%) died. Those who died were older ($p = 0.01$), had higher frequency of diabetic kidney disease (DKD) ($p = 0.001$),

TABLE 1 Differences in baseline characteristics of COVID-19 patients based on survival outcome of the disease

Baseline characteristics	Total ($n = 263$)	Alive ($n = 228$)	Dead ($n = 35$)	p value[a]
Age (year), mean ± SD	51.76 ± 13.63	50.95 ± 13.45	57.00 ± 13.84	0.01
Sex, *n* (%)				0.15
Male (*n*, %)	173 (65.8)	146 (64.0)	27 (77.1)	
Female	90 (34.2)	82 (36.0)	8 (22.9)	
BMI (kg/m^2)	22.55 ± 5.39	22.46 ± 5.38	23.11 ± 5.48	0.81
Cause of ESRD, *n* (%)				0.001
DKD	142 (54.0)	114 (50.0)	28 (80.0)	
NDKD	121 (46.0)	114 (50.0)	07 (20.0)	
Comorbidities, *n* (%)	213 (81.0)	179 (78.5)	34 (97.1)	0.04
Previous dialysis access, *n* (%)				0.001
AVF	178 (67.7)	162 (71.1)	16 (45.7)	
CVC	85 (32.3)	66 (28.9)	19 (54.3)	
Dialysis frequency, *n* (%)				0.001
2 times/week	142 (54.0)	116 (50.9)	26 (74.3)	
3 times/week	121 (46.0)	112 (49.1)	09 (25.7)	
Dialysis yr, median (IQR)	2.0 (0.5–17.0)	2.0 (0.5–17.0)	2.0 (0.5–13.0)	0.96
*Hospitalization duration, mean ± SD	12.88 ± 7.56	13.95 ± 7.28	5.91 ± 5.30	0.001
Oxygen therapy				
No oxygen support (O_2 sat > 94%)	105 (39.9)	97 (92.38)	8 (7.61)	0.001
Only BiPAP	137 (52.1)	125 (91.24)	12 (8.75)	0.001
On ventilator	21 (8.0)	6 (28.57)	15 (71.42)	0.001
Pharmacotherapy				
Dexamethasone therapy	50 (19.0)	23 (46)	27 (54)	0.72
HCQ prophylaxis	112 (42.5)	104 (92.85)	8 (7.14)	0.001
HCQ therapy	57 (21.6)	47 (82.45)	10 (17.54)	0.001

Note: p values were calculated by the Cox regression test; p value[a] = p value calculated between dead and alive group; p value[b] = p value calculated between mild/moderate and severe/critical group; all significant values are in bold.

*Hospitalization duration is calculated by independent samples t test.

Abbreviations: AVF, arteriovenous fistula; BiPAP, bilevel positive airway pressure; BMI, body mass index; CVC, central venous catheter; DKD, diabetic kidney disease; percentages in brackets, IQR, interquartile range; HCQ, hydroxychloroquine; NDKD, nondiabetic kidney disease; *N*, number; SD, standard deviation.

had more comorbidities ($p = 0.04$), and severe COVID-19 ($p = 0.001$). Mortality was higher among patients on twice-weekly MHD compared to those on thrice-weekly dialysis ($p = 0.001$) and those getting dialysis through the central venous catheter as compared to those with an arteriovenous fistula ($p = 0.001$).

The basic demography of the patients according to the severity is shown in Table 2. Of 263 patients, 36 (13.6%) had severe/critical COVID-19. These patients were older ($p = 0.01$), had higher frequency of DKD ($p = 0.02$), and had higher comorbidities ($p = 0.03$). Compared to those with mild–moderate COVID, a higher proportion of patients with severe COVID-19 had CVC as vascular access ($p = 0.001$) and were on twice-weekly MHD as ($p = 0.001$). Of the 227 patients with mild/moderate COVID-19, only 17 (7.5%) died, while in severe, 18 (50%) out of 36 patients died. Of the 17 patients who died with mild/moderate COVID, the attributed causes of death were cardiovascular ($n = 8$), pneumonia with sepsis ($n = 6$), uremic complications in 2, and cancer in 1 patient. The cancer patient on MHD had metastatic cervical cancer. Two patients on MHD had cachexia with only mild COVID symptoms, and deaths were attributed to uremia. Among the eight patients with cardiovascular death, three had intracranial hemorrhages, one had cerebrovascular infarct in the fronto-parietal region, two had an acute myocardial infarction, and two had preexisting dilated cardiomyopathy and developed acute arrhythmia.

The attributed causes of death in severe COVID were severe ARDS in 11, cardiovascular death in 4, septic shock in 2, and sudden death in 1 patients. In addition to severe COVID, two patients had associated complications of bacterial sepsis and septic shock, and death attributed to sepsis. Of the four patients with cardiovascular death, two had intracranial hemorrhage, one had acute myocardial infarction during recovery, and one had cardiac arrhythmias. One patient developed sudden cardiac arrest during dialysis. The absolute risk of mortality among HD patients with severe COVID-19 was 12.3

TABLE 2 Baseline characteristics COVID-19 patients on the basis of the severity of the disease

Baseline characteristics	Mild/moderate ($n = 227$)	Severe/critical ($n = 36$)	p value[b]
Age (year), mean ± SD	51.11 ± 13.30	55.86 ± 15.10	0.01
Sex, *n* (%)			0.07
Male (*n*, %)	154 (67.8)	19 (52.8)	
Female	73 (32.2)	17 (47.2)	
BMI (kg/m^2)	22.53 ± 5.42	22.66 ± 5.23	0.57
Cause of ESRD, *n* (%)			0.02
DKD	118 (52.0)	24 (66.7)	
NDKD	109 (48.0)	12 (33.3)	
Comorbidities, *n* (%)	179 (78.9)	34 (94.4)	0.03
Previous dialysis access, *n* (%)			0.001
AVF	158 (69.6)	20 (55.6)	
CVC	69 (30.4)	16 (44.4)	
Dialysis frequency *n* (%)			0.001
2 times/week	114 (50.2)	28 (77.8)	
3 times/week	113 (49.8)	08 (22.2)	
Dialysis yr, median (IQR)	2.0 (0.5–17.0)	1.65 (0.5–13.0)	0.33
[*]Hospitalization duration, mean ± SD (days)	13.26 ± 7.22	10.50 ± 9.16	0.04

Note: p values were calculated by the Cox regression test; p value[a] = p value calculated between dead and alive group; p value[b] = p value calculated between mild/moderate and severe/critical group; all significant values are in bold.

[*]Hospitalization duration is calculated by independent samples t test.

Abbreviations: AVF, arteriovenous fistula; BMI, body mass index; CVC, central venous catheter; DKD, diabetic kidney disease; IQR, interquartile range; *N*, number; NDKD, nondiabetic kidney disease; SD, standard deviation.

times (95% CI 5.4–28.02) as compared to mild/moderate disease ($p = 0.001$).

3.1.1 | Comparison of clinical manifestations as per the severity of COVID-19 and mortality

The comparative clinical manifestations and the laboratory findings at diagnosis of patients with COVID-19 by mortality and severity are presented in Table 3. Most common clinical manifestation were fever 94.29%, cough 93.91%, and dyspnea 87.45%, in the study. The other common manifestations were nausea/vomiting, diarrhea, sore throat, expectoration, and chest pain. A significantly higher proportion of patients who died complained of chest pain. The baseline systolic blood pressure (SBP) and diastolic blood pressure (DBP) were lower, and the total leukocytes count, the liver enzymes (alanine transaminases and aspartate transaminases), and CRP levels were higher in those who died compared to those who survived COVID-19. The duration of hospital stay was shorter among patients who died.

3.2 | Cox regression analysis predicting mortality

On univariate Cox regression analysis (Table 4), factors associated with mortality included higher age, presence of comorbidities, DKD, dialysis frequency, vascular access type, the severity of COVID-19, and requirement of ventilatory support. However, on multivariate analysis adjusting the effect of independent variable significant on univariate analysis with dependent variables (death/alive), three different models were observed on Cox regression backward elimination analysis (Table 5). In model 1, only the severity of COVID-19 and central vascular catheter access was a significant mortality predictor. In model 2, on eliminating the DKD from the model, the severity of the disease and vascular access (CVC vs. AVF) remained significant predictors of mortality. In model 3, on removing dialysis frequency from the list, CVC (HR 2.53, 95% CI 1.26–5.07, $p = 0.009$) and severity of disease (HR = 3.54, 95% CI 1.52–8.26, $p = 0.003$) predicted higher mortality and noninvasive ventilatory support (HR 0.59, 95% CI 0.25–0.99, $p = 0.049$) as a significant predictor of decreased mortality.

3.3 | Treatment and outcomes of patients according to the requirement of oxygen therapy

The outcomes of patients according to the requirement of oxygen therapy through simple mask inhalation, invasive, and noninvasive ventilatory support are presented in Table 1. A total of 50 patients received dexamethasone therapy; of them, 23 survived, and 27 did not survive. Hydroxychloroquine (HCQ) prophylaxis was given in 112 patients; of them, eight (7.14%) patients died. HCQ as therapy had been used in 57 patients; of them, 10 (17.54%) patients died. Of

TABLE 3 Clinical characteristics of COVID-19 patients based on survival outcome

Clinical characteristics	Total ($n = 263$)	Alive ($n = 228$)	Dead ($n = 35$)	p value[a]	Mild/moderate ($n = 227$)	Severe/critical ($n = 36$)	p value[b]
Symptoms							
Fever	248 (94.29)	214 (93.85)	34 (97.14)	**0.44**	212 (93.39)	36 (100.0)	**0.11**
Cough	247 (93.91)	213 (93.42)	34 (97.14)	**0.39**	211 (92.95)	36 (100.0)	**0.10**
Dyspnea	230 (87.45)	196 (85.96)	34 (97.14)	**0.06**	194 (85.46)	36 (100.0)	**0.014**
Sore throat	46 (17.49)	35 (15.35)	11 (31.42)	0.02	36 (15.85)	10 (27.8)	0.08
Sputum	26 (9.88)	20 (8.77)	6 (17.1)	0.12	17 (7.48)	9 (25.0)	0.001
Hemoptysis	4 (1.5)	4 (1.75)	0 (0.0)	0.43	4 (1.76)	0 (0.0)	0.42
Nasal discharge	6 (2.3)	4 (1.75)	2 (5.7)	0.15	3 (1.32)	3 (8.3)	**0.009**
Nausea/vomiting	39 (14.8)	28 (12.28)	11(31.42)	**0.03**	25 (11.01)	14 (38.9)	**0.0001**
Headache	24 (9.1)	19 (8.3)	5 (14.28)	0.25	13 (5.7)	11 (30.6)	**<0.0001**
Body ache	39 (14.8)	32 (14.03)	7 (20.0)	0.36	27 (11.89)	12 (33.3)	0.0008
Abdominal pain	8 (3.04)	5 (2.19)	3 (8.57)	**0.04**	6 (2.6)	2 (5.6)	0.33
Chest pain	7 (2.66)	3 (1.3)	4 (11.42)	**0.0005**	2 (0.9)	5 (13.9)	**0.0001**
Diarrhea	15 (5.7)	11 (4.8)	4 (11.42)	0.12	12 (.3)	3 (8.3)	0.47
Systolic, BP mean ± SD	132.20 ± 34.72	142.32 ± 24.34	116.29 ± 13.30	**0.0001**	137.18 ± 31.29	100.81 ± 39.13	**0.0001**
Diastolic, BP mean ± SD	84.76 ± 23.08	92.29 ± 12.81	76.71 ± 12.43	**0.0001**	89.25 ± 18.56	56.42 ± 28.42	**0.0001**
Laboratory findings							
Hemoglobin (g/dl)	9.40 ± 1.81	9.45 ± 1.81	9.08 ± 1.77	0.26	9.46 ± 1.78	9.05 ± 1.95	0.21
TLCs, median (IQR)	7490.50 (1900–48,000)	7000.00 (1900–48,000)	8950.00 (3500–20,000)	**0.01**	7000.00 (1900–26,000)	7000.00 (2500–48,000)	**0.001**
Leucopenia	25 (9.9)	22 (10.1)	3 (8.8)	0.80	19 (8.8)	6 (16.7)	**0.01**
Platelet (10^9/L), median (IQR)	173.00 (2–5200)	173.00 (2–5200)	180.50 (15–4200)	**0.001**	179.50 (2–5200)	132.50 (15–440)	0.09
BUN (mg/dl)	116.91 ± 62.01	114.25 ± 60.91	132.30 ± 66.98	0.11	118.55 ± 59.56	108.04 ± 74.24	0.35
S. creatinine (mg/dl)	8.31 ± 3.39	8.22 ± 3.34	8.90 ± 3.73	0.027	8.37 ± 3.20	8.00 ± 4.42	0.54
SGOT, mean ± SD	32.30 ± 29.48	28.57 ± 26.06	56.63 ± 38.24	**0.0001**	30.56 ± 27.93	43.25 ± 36.43	**0.02**
SGPT, mean ± SD	32.37 ± 31.48	30.53 ± 32.44	44.34 ± 20.98	**0.002**	32.31 ± 32.85	32.75 ± 21.22	0.94
CRP, ($n = 31$), mean ± SD	54.49 ± 60.53	48.14 ± 57.05	146.50 ± 26.16	0.0001	32.18 ± 37.61	101.34 ± 73.95	**0.0001**
Radiologic findings							
CT scan image features, n (%) ($n = 74$)				0.55			0.63
Ground glass/patchy opacity	70 (94.6)	62 (93.9)	8 (100.0)		63 (94.0)	7 (100.0)	
Consolidation	4 (5.4)	4 (6.1)	0 (0.0)		4 (6.0)	0 (0.0)	

Note: p values were calculated by the Cox regression test; P value[a] = P value calculated between dead and alive group; p value[b] = p value calculated between mild/moderate and severe/critical group; All significant values are in bold. p value for *hospitalization duration is calculated by independent samples t test.

Abbreviations: BUN, blood urea nitrogen; CRP, C-reactive protein; IQR, interquartile range; N, number; SD, standard deviation; SGOT, serum glutamic-oxaloacetic transaminase; SGPT, serum glutamate pyruvate transaminase; TLC, total leucocyte count.

TABLE 4 Univariate Cox regression analysis predicting mortality of symptomatic COVID-19 patients

Characteristics	*B*	Expo-B	(95% CI)	*p* values
Age	0.03	1.03	(1.00–1.06)	0.01
Gender	−0.57	0.56	(0.25–1.24)	0.15
Body mass index	0.00	1.00	(0.94–1.07)	0.77
Diabetic vs. nondiabetic CKD	1.29	3.65	(1.59–8.38)	0.01
Comorbidities	−2.05	0.12	(0.01–0.94)	0.04
Dialysis frequency (3 times vs. 2 times)	−1.18	0.30	(0.13–0.67)	0.01
Vascular access (CVC vs. AVF)	1.22	3.40	(1.73–6.71)	0.01
Severity (severe vs. mild–moderate COVID-19)	2.04	7.75	(3.95–15.20)	0.001
Ventilatory support (noninvasive vs. mechanical)	−1.59	0.20	(0.11–0.36)	0.001

Abbreviations: AVF, arteriovenous fistula; BMI, body mass index; CVC, central venous catheter; DKD, diabetic kidney disease; mod, moderate; NDKD, nondiabetic kidney disease.

TABLE 5 Cox regression analysis showing hazard ratio of mortality with different models on stepwise backward elimination

					95.0% CI for the hazard ratio	
		B	*p* values	Hazard ratio	Lower	Upper
Model 1	Age	0.017	0.20	1.01	0.990	1.04
	Comorbidities	−1.38	0.18	0.25	0.033	1.91
	CVS vs. AVF	0.885	0.014	2.42	1.199	4.89
	Dialysis frequency (3 vs. 2 times/week)	−0.682	0.115	0.50	0.216	1.18
	Diabetes vs. no diabetes	0.547	0.235	1.72	0.701	4.26
	Severe vs. mild–mod COVID-19	1.07	0.015	2.93	1.229	7.008
	Noninvasive vs. invasive ventilation	−0.53	0.130	0.585	0.29	1.17
Model 2	Age	0.022	0.094	1.02	0.99	1.04
	Comorbidities	−1.624	0.112	0.197	0.027	1.46
	CVS vs. AVF	0.904	0.012	2.47	1.224	4.98
	Dialysis frequency (3 vs. 2 times)	−0.667	0.122	0.51	0.220	1.19
	Severe vs. mild–mod COVID-19	1.122	0.012	3.07	1.28	7.34
	Noninvasive vs. invasive ventilation	−0.592	0.089	0.55	0.28	1.09
Model 3	Age	0.020	0.109	1.02	0.99	1.04
	Comorbidities	−1.631	0.111	0.19	0.026	1.45
	CVC vs. AVF	0.928	0.009	2.53	1.26	5.07
	Severe vs. mild–mod COVID-19	1.266	0.003	3.54	1.521	8.264
	Noninvasive vs. invasive ventilation	−0.682	0.049	0.50	0.256	0.998

the 263 patients, 105 patients did not receive oxygen therapy, 137 received simple nasal cannula/high flow nasal cannula oxygen therapy/bilevel positive airway pressure (BiPAP) support, and 21 received mechanical ventilation. Of the 21 patients on mechanical ventilation, 15 (71.4%) died, while 12/137 (8.8%) who received BiPAP or high flow nasal cannula died, compared to only 8/105(7.6%) who did not require oxygen supplementation ($p = 0.001$).

4 | DISCUSSION

This paper presents the largest series of MHD patients with COVID-19 from a developing country. As described from other parts of the world, we confirmed the higher mortality among these patients, compared to the average national mortality (1.45%) among the COVID 19 infection in general population reported by the Ministry of Health and Family Welfare, Govt of India.[27] Patients who died were older, had severe COVID-19, and associated comorbidities. The multicentric study from Wuhan, China, the first epicenter of COVID, did not report any deaths among 130 MHD patients with COVID-19.[13] They showed that only 51.9% of their patients manifested fever, while 21.4% of infected patients were asymptomatic. In our study, only symptomatic patients were taken into study. A later survey from Wuhan reported a mortality of 5.65%.[14] In contrast, Madrid's study described the clinical course and outcomes of 36 RT-PCR for SARS-CoV-2 positive patients from two dialysis facilities caring for

282 patients and reported a mortality rate of 30.5% and 33% among those who required mechanical ventilation.[6]

The clinical characteristics of the COVID in MHD patients are not different from the COVID in the general population in our cohort of patients, with fever, cough, and breathlessness being the most common manifestations. We also found that patients with severe disease were more likely to die, with the relative risk of mortality being 7.37 times higher in patients with severe COVID than those with mild/moderate disease. The presence of comorbidities also increased the risk of severe COVID and mortality. This observation was not different from the death pattern reported in nondialysis patients.[28,29] The elderly or patients with comorbidities were more susceptible to COVID-19, and the incidence of severe cases and the risk of death were high.[30]

The relatively high mortality in the present study could be due to the inclusion of only symptomatic patients, indicative of relatively more severe manifestations of infection. MHD patients are more susceptible to acquire an infection due to an immunosuppressed state because of uremia. However, they may not manifest fever and other symptoms because of an immunosuppressed condition and inability to mount effective cellular immune response following invasion of SARS-CoV-2.[19,20] A recent study showed that compared with the general population, the T cells and their cytokine response in SARS-CoV-2 infected MHD patients remain relatively low in comparison with non-MHD patients with SARS-CoV-2 infection.[14,17,20] In such a scenario, any degree of cytokine storm may indicate severe COVID, worsening condition, and death.[20] In our study, 19.01% of patients received glucocorticoids, and the majority in severe categories, and those died. It suggests that glucocorticoids had been used only in desperate situations in our patients. While a number of agents have been tried, the RECOVERY trial showed that glucocorticoids reduce mortality in patients with severe disease.[31] However, the systematic review and meta-analysis did not show any mortality benefit.[32] Given the immunosuppressed state, the use of steroids should be considered carefully.[31,32] More data are needed to make a conclusive recommendation about the benefit of glucocorticoids in MHD patients with COVID-19. Another reason for the higher mortality in our cohort could be an association with comorbidities, which had been independently associated with COVID-related mortality. In our study, 97% of those who died had some associated comorbidities.

5 | STRENGTH AND LIMITATION OF THE STUDY

The multicentric nature of the study is the major strength of the study. The study propitiously pinpointed the dialysis specific predictor of mortality like CVC as vascular access and severity of the COVID-19. The study included only symptomatic patients. The outcome of asymptomatic patients on MHD remains undetermined. The cardiac enzyme data were not collected from all centers. The mortality of non-COVID patients on MHD during the same study period in the dialysis unit was not analyzed. The effect of antiviral like remdesivir on COVID pneumonia was not analyzed in the present study.

6 | CONCLUSION

COVID-19 in MHD is associated with higher mortality than the general population with COVID-19. Patients with comorbidities developed severe COVID. The mortality risk is elevated in patients with severe COVID-19 and patients with CVC as vascular access.

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CONFLICT OF INTEREST

The authors declared none. The results presented in this paper have not been published previously in whole or part.

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