Original Article

Clinical Characteristics and Short-Term Outcomes of COVID-19 Positive Hospitalized Hemodialysis Patients

Chowdhury MFH[1], Anwar MR[2], Hossain M[3], Nath PKD[4], Chowdhury KH[5], Akter KD[6], Rana MSA[7], Sumon MAI[8], Saha JV[9]

ABSTRACT

Presentation of Novel Corona virus disease (COVID-19) and its clinical features and outcomes were different in maintenance hemodialysis (MHD) patients than in general population due to relative immunosuppression and high prevalence of co-morbidities in MHD patients. The aim of this study is to identify the clinical characteristics and outcome of MHD patients requiring hospitalization for COVID 19. In this retrospective observational study, a total of 100 adult patients of both sex who were on maintenance hemodialysis therapy having A-V fistula or permanent venous catheter admitted in Nephrology department of Mugda Medical College Hospital due to COVID-19 from April 21, 2020 to April 30, 2021 were included. Demographic data (age, sex, comorbidities), initial clinical presentations (fever, cough, shortness of breath, fatigue), oxygen saturation, chest radiograph and laboratory tests CBC, RBS, Serum Creatinine, SGPT, CRP, LDH, D dimer, Ferritin, Albumin at admission and during hospital stay were retrieved from patient file. Treatment of these hemodialysis patients was given and modified according to the hospital treatment committee including Nephrologist and Medicine specialist. As the patients were followed up from admission in hospital until discharge or death, so they were divided in two groups- Survived and death. All data were compiled and edited meticulously using SPSS version 27 software. The mean age of the patients was 53.8±13.3 (Range 15-90). Male and female ratio was 1.7.1. No significant difference was observed regarding age and sex of the study subjects. Most patients had HTN (78%) followed by DM (52%), IHD (42%), CLD (24%), pulmonary disease (21%) and Stroke (6%). The most common symptoms during admission in hospital were fever 65%, cough 52%, fatigue 43%, SOB 35% and diarrhea 8% respectively. Fever, cough, fatigue and SOB and in case of co-morbidities only IHD were statistically significant. Mean Oxygen saturation during admission was statistically significantly lower in death group (96.0±1.32 vs 90.2±2.9; p<0.001). Regarding biochemical parameters lymphocyte count (1058.4±289.3 vs 2575.9±536.6 p <0.001), albumin (3.38±0.80 vs 3.89±0.57; p<0.001) were statistically significantly low and N:L ratio (10.48±2.77 vs 3.24±0.40; p<0.001), creatinine (9.75±2.28 vs 6.11±2.27; p<0.001), CRP (33.09±12.99 vs 13.29±5.35; p<0.001), LDH (367.09±78.25 vs 294.06±58.1; p<0.001) were significantly high in death group. Lung abnormalities on CXR PA view showed normal CXR in 48.7% patients in survived group and bilateral GGO in 68.2% in death group which were also statistically significant. Outcome of these admitted patients revealed total death rate 22%, ICU admission rate 18% and discharge from hospital rate was 78%. Logistic regression of these risk factors regarding mortality in COVID19

1. Dr. Md. Farhad Hasan Chowdhury, Assistant Professor, Department of Nephrology, Mugda Medical College & Hospital, Dhaka-1214.
2. Dr. Mohammed Rashed Anwar, Associate Professor, Department of Nephrology, Mugda Medical College & Hospital, Dhaka-1214.
3. Dr. Momtaz Hossain, Assistant Professor, Department of Nephrology, Mugda Medical College & Hospital, Dhaka-1214.
4. Dr. Palash Kumar Deb Nath, Assistant Professor, Department of Nephrology, Mugda Medical College & Hospital, Dhaka-1214.
5. Dr. Kowser Hossain Chowdhury, Junior Consultant (Nephrology), DNCC Dedicated COVID-19 Hospital, Dhaka-1212.
6. Dr. Kanij Delara Akter, Medical Officer, Department of Paediatrics, Bangabandhu Sheikh Mujib Medical University, Dhaka-1000.
7. Dr. Muhammad Saiful Ahsan Rana, Medical Officer, Department of Nephrology, Mugda Medical College Hospital, Dhaka-1214.
8. Dr. Md. Aminul Islam Sumon, Medical Officer, Department of Nephrology, Mugda Medical College Hospital, Dhaka-1214.
9. Dr. Jyoti Vaskar Saha, Medical Officer, Department of Nephrology, Mugda Medical College Hospital, Dhaka-1214.

Address of Correspondence: Dr. Md. Farhad Hasan Chowdhury, Assistant Professor**,** Department of Nephrology, Mugda Medical College & Hospital, Dhaka-1214, Bangladesh. Email: hasanfarhad75@gmail.com

showed oxygen saturation (p=0.00), N:L ratio (p=0.00), and CRP (p=0.035) were statistically significant. In this study, we found a high mortality rate in COVID 19 positive hospitalized maintenance hemodialysis patients. Markers of inflammation neutrophil-to-lymphocyte ratio (N:L ratio), CRP and oxygen status are significant predictors of COVID 19 patients' morbidity, highlighting the importance of monitoring these parameters for clinical management and risk stratification.

Keywords: *COVID 19, clinical characteristics, hemodialysis, mortality*

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INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection emerged in Wuhan, China in December 2019 and has spread rapidly worldwide. SARS-CoV-2 is an enveloped, positive-sense RNA virus, and belongs to the â-coronavirus genus that typically causes respiratory damage in humans and animals.[1] On March 11, as the number of COVID-19 cases outside China has increased 13 times and the number of countries involved has tripled with more than 118,000 cases in 114 countries and over 4,000 deaths, WHO declared the COVID-19 a pandemic.[2]

COVID19 primarily manifest as an acute respiratory illness with interstitial and alveolar pneumonia, but it can affect multiple organs such as the kidney, heart, digestive tract, blood, and nervous system.[3] The hyper inflammatory response of the body, coupled with the possible direct effects of severe acute respiratory syndrome on body-wide organs via angiotensin-converting enzyme II, has been associated with complications of the disease like acute respiratory distress syndrome, heart failure, renal failure, liver damage, shock, and multiorgan failure have precipitated death.[4]

Reports from multiple international investigators have identified patient characteristics associated with a higher risk of severe disease and death, including older age, men, underlying cardiac or pulmonary disease, diabetes, and hypertension.[5-7] In addition, underlying CKD has been identified as a risk factor for mortality, with a Chinese cohort demonstrating that elevated baseline serum creatinine was associated with a hazard ratio for death of 3.97.[8] There is a less available evidence about treatment and characteristics of patients on maintenance hemodialysis (MHD) therapy than in the general population. In a retrospective, observational, single-center study in Spain[9], they analyzed the clinical course and outcomes of all maintenance hemodialysis patients hospitalized with COVID-19 from March 12th to April 10th, 2020. They concluded that mortality among hospitalized hemodialysis patients diagnosed with COVID-19 is high (30.5%) than in general population (1.4%-8%)[13,14,15]. In another retrospective study of 114 chronic hemodialysis patients hospitalized at two major hospitals in the Bronx, New York City with COVID-19 from March 9-April 8, 2020, showed the most common comorbidities were diabetes mellitus (66.7%), hypertension (89.5%), coronary artery disease (55.2%) and pulmonary disease (35.1%). The most common symptoms at initial presentation were shortness of breath (50%) and fever (44.7%). Less common symptoms included cough, chest pain, and diarrhea. A total of 15 (13.2%) patients required ICU level care, 19 (16.7%) patients required mechanical ventilation and 18 patients (15.8%) required vasopressors. In-hospital death occurred in 32 (28.1%) patients in that total cohort.[10] In a study of 59 patients with ESKD and COVID-19 receiving dialysis at a New York City medical center, the authors found that although the presentation of patients on dialysis with COVID-19 was similar to that of the general population, these patients have poor outcomes, including 31% overall mortality and 75% mortality among those requiring mechanical ventilation.[11] In a prospective study in Wuhan, China which included 49 hospitalized patients on maintenance hemodialysis and 52 hospitalized patients without kidney failure (controls) with confirmed coronavirus disease 2019 found in terms of common symptoms, there were differences between patients on hemodialysis and controls (fatigue [59% vs. 83%], dry cough [49% vs. 71%], and fever [47% vs. 90%]). Compared with controls, more patients on hemodialysis received noninvasive ventilation (25% vs. 6%, p=0.008). Seven patients on hemodialysis (14%) had died.[12]

The first confirmed case of coronavirus disease 2019 (COVID-19) in Bangladesh was reported on March 8,

2020. At present there is no study regarding clinical characteristics and outcome of a cohort of hemodialysis patients in Bangladesh. This study was conducted in Mugda Medical College Hospital, Dhaka, Bangladesh, which had the largest COVID positive hemodialysis unit in Bangladesh. In this hemodialysis unit there were 33 hemodialysis machines among them 3 for HBsAg positive patients and 3 for AntiHCV positive ESRD patients. The aim of our study was to describe the clinical characteristics, prognostic factors and outcomes of maintenance hemodialysis patients requiring hospitalization for COVID19. We hope this study will help us to early identify the comorbidities of hemodialysis patients and treat them accordingly. Other hemodialysis centers in our country can also use this study observation to treat their patients.

METHODS

A total of 100 adult patients of both sex who were on maintenance hemodialysis therapy having A-V fistula or permanent venous catheter from April 21, 2020 to April 30 of 2021 were included in this retrospective observational single center study. Acute kidney injury patients, hemodialysis less than 3 months and age <18 years were excluded. Hemodialysis patients with COVID 19 confirmed by positive real time reverse transcription-polymerase chain reaction (rRT-PCR) testing admitted in the Department of Nephrology, Mugda Medical College Hospital, Dhaka, Bangladesh, were enrolled and followed up.

Demographic data (age, sex, comorbidities), initial clinical presentations (fever, cough, shortness of breath, throat pain), Oxygen saturation, radiological data of chest x-ray and laboratory tests, e.g., CBC, RBS, serum creatinine, SGPT, CRP, LDH, D dimer, serum ferritin, albumin etc. at admission and during hospital stay were retrieved from the patients' files.

Treatment of these hemodialysis patients was given and modified according to the hospital treatment committee including nephrologist and medicine specialists. Treatment prescription included antibiotic, antiviral therapy, corticosteroid, hydroxychloroquine initially, other immunomodulatory agents, oxygen therapy, other respiratory supports and treatment for comorbidities. Patients got at least 8 hours/week hemodialysis and dialysis prescription was individualized by Nephrologist according to patients' symptoms and clinical evaluation. All patients got thromboprophylaxis. Outcome was measured by discharge from hospital, referred to ICU and death.

As the patients were followed up from admission in hospital until discharge or death, so they were divided in two groups- Survived and death. All data were compiled and edited meticulously using SPSS version 27 software. Continuous variables were presented as mean or median and interquartile range (IQR) according to their distribution. Categorical data were presented as percentages. Group comparisons were performed with unpaired student t-test and Chi-square test as appropriate. Risk factors of mortality from COVID-19 in hemodialysis patients was measured by logistic regression. A p-value of 0.05 or less was considered as statistically significant.

This study was approved by the Institutional Review Board (IRB) of Mugda Medical College, Dhaka, Bangladesh.

RESULTS

A total of 100 maintenance hemodialysis patients suffering from COVID-19 admitted into our hospital were enrolled in this study and divided into two groups - survived and death groups. Table-I shows the comparison of age between two groups; the difference was not statistically significant ($p>0.05$). Male: Female ratio was 1.7:1. No significant difference was observed in sex distribution between survival and death groups (Fig. 1). Table-II shows clinical characteristics of the study subjects. Most patients had hypertension (78%) followed by diabetes mellitus (52%), ischaemic heart disease (IHD) (42%), chronic liver disease (24%), pulmonary disease (21%) and stroke (6%). The most common symptoms during admission in hospital were fever 65%, cough 52%, fatigue 43%, SOB 35% and diarrhea 8% respectively. No statistically significant difference in comorbidities was found except IHD in between two groups. Regarding symptoms fever, cough, fatigue and SOB were statistically significant. Mean oxygen saturation during admission was statistically significantly lower in death group (96.0±1.32 vs. 90.2±2.9, $p<0.001$). Table-III shows biochemical and radiological parameters. Regarding biochemical parameters lymphocyte count (1058.4±289.3 vs 2575.9±536.6 $p<0.001$), albumin (3.38±0.80 vs. 3.89±0.57 $p<0.001$) were statistically significantly low and N:L ratio (10.48±2.77 vs. 3.24±0.40 $p<0.001$), creatinine (9.75±2.28 vs. 6.11±2.27 $p<0.001$), CRP (33.09±12.99 vs. 13.29±5.35 $p<0.001$), LDH (367.09±78.25 vs.

294.06±58.1 p<0.001) were significantly high in death group. Lung abnormalities on chest x-ray P/A view showed 44% patients had GGO bilaterally. In death group, 68.2% patients had ground glass opacities (GGO) bilaterally and 13.6% patients unilaterally, which was statistically significant. Normal chest findings were evident in 48.7% patients in survived group, which was also statistically significant. Table-IV shows outcome of the admitted patients – total death rate was 22%, while ICU admission rate 18% and discharge from hospital after recovery was 78%. Table-V shows the logistic regression of these risk factors regarding mortality in COVID-19 showed oxygen saturation (p=0.00), N:L ratio (p=0.00), and CRP (p=0.035) were statistically significant.

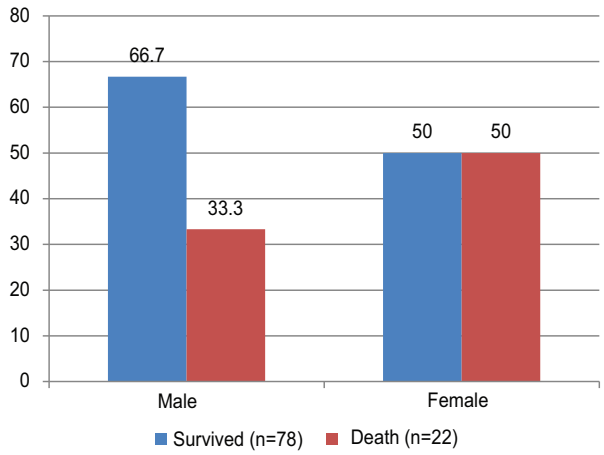

Fig.-1: *Distribution of sex between two groups (N=100).*

Table-I: Comparison of age between two groups (N=100)

Age group(in years)	Survived(n=78) No. (%)	Death(n=22) No. (%)	Total(n=100) No. (%)	p-value
21-30	6(7.7%)	2(9.1%)	8(8.0%)	0.106^{ns}
31-40	7(9.0%)	0(0.0%)	7(7.0%)	
41-50	20(25.6%)	5(22.7%)	25(25.0%)	
51-60	24(30.8%)	5(22.7%)	29(29.0%)	
61-70	17(21.8%)	8(36.4%)	25(25.0%)	
71-80	4(5.1%)	1(4.5%)	5(5.0%)	
81-90	0(0.0%)	1(4.5%)	1(1.0%)	
Total	78(100.0%)	22(100.0%)	100(100.0%)	
Mean±SD	52.7±12.9	57.9±14.2	53.8±13.3	
Range	(15-85) years	(30-90) years	(15-90) years	

Data were expressed as frequency and percentage and mean±SD. Unpaired student t-test was done; ns=not significant

Table-II: *Characteristics of COVID-19 positive MHD patients between two groups (N=100)*

Variables	Survived(n=78) No. (%)	Death(n=22) No. (%)	Total(n=100) No. (%)	p-value
Fever*	45(57.7%)	20(90.9%)	65(65.0%)	0.004^{s}
Fatigue*	29(37.2%)	14(63.6%)	43(43.0%)	0.028^{s}
SOB/Dysponea*	19(24.4%)	16(72.7%)	35(35.0%)	<0.001^{s}
Cough*	34(43.6%)	18(81.8%)	52(52.0%)	0.002^{s}
Diarrhea*	6(7.7%)	2(9.1%)	8(8.0%)	0.831 ^{ns}
HTN*	59(75.6%)	19(86.4%)	78(78.0%)	0.284^{ns}
DM*	40(51.3%)	12(54.5%)	52(52.0%)	0.787^{ns}
IHD*	25(32.1%)	17(77.3%)	42(42.0%)	<0.001^{s}
Pulmonary disease*	16(20.5%)	5(22.7%)	21(21.0%)	0.822^{ns}
Stroke*	6(7.7%)	0(0.0%)	6(6.0%)	0.180^{ns}
CLD*	19(24.4%)	5(22.7%)	24(24.0%)	0.874^{ns}
O2 Saturation**	96.0±1.32	90.2±2.68	94.7±2.9	<0.001^{s}

*Chi-squared Test (χ^2) and **unpaired t-test was done to analyze the data; s=significant, ns=not significant

Table-III: *Comparison of biochemical and radiological parameters between two groups (N=100)*

Parameters	Survived(n=78) Mean±SD	Death(n=22) Mean±SD	Total (n=100) Mean±SD	p-value
Hb Conc.*	10.26±0.68	10.05±0.96	10.2±0.7	0.256^{ns}
ESR*	29.33±7.56	32.77±9.47	31.15±8.56	0.078^{ns}
TC*	11583.1±2466.8	12847.3±3369.6	11861.2±2723.7	0.054^{ns}
Neutrophil *	9717.72±1891.1	10500.9±3225.1	10152.8±2559.5	0.152 ^{ns}
Lymphocyte*	2575.9±536.6	1058.4±289.3	2242.1±800.5	<0.001^{s}
Neutrophil-Lymphocyte ratio*	3.24±0.40	10.48±2.77	4.8±3.3	<0.001^{s}
Platelet*	2.53±0.46	2.39±0.35	2.5±0.5	0.189^{ns}
RBS*	9.59±3.96	11.36±4.37	11.1±4.6	0.073^{ns}
S. creatinine*	6.11±2.27	9.75±2.28	6.9±2.7	<0.001^{s}
SGPT*	56.44±11.90	57.82±14.32	57.9±13.3	0.647^{ns}
CRP*	13.29±5.35	33.09±12.99	17.7±11.2	<0.001^{s}
D dimer *	4.15±1.15	4.50±2.01	4.55±2.0	0.296^{ns}
LDH*	294.06±58.1	367.09±78.25	310.1±69.6	<0.001^{s}
S. ferritin*	1753.1±365.5	1806.6±340.2	1789.8±340.5	0.540^{ns}
S. albumin *	3.89±0.57	3.38±0.80	3.8±0.7	0.001^{s}
CXR Normal**	38(48.7%)	3(13.6%)	41(41.0%)	0.003^{s}
CXR GGO Uni**	11(14.1%)	3(13.6%)	14(14.0%)	0.956^{ns}
CXR GGO Bil **	29(37.2%)	15(68.2%)	44(44.0%)	0.014^{s}

Data were expressed as mean±SD. *Unpaired student t-test and **Chi-squared Test (^{2}) was performed to compare between two groups; s=significant, ns=not significant

Table-IV: Outcome of COVID-19 positive MHD patients (N=100)

Outcome	Admission		p-value
	In ward (n=82) No. (%)	In ICU (n=18) No. (%)	
Death	9(11.0%)	13(72.2%)	
Survived	73(89.0%)	5(27.8%)	<0.001^{s}
Total	82(100.0%)	18(100.0%)	

Chi-square test was done; s=significant

Table-V: *Logistic regression to measure the risk factors of mortality of COVID-19 patients (N=100)*

Model		Unstandardized Coefficients		p-value	95.0% CI for B	
		B-value	Std. Error		Lower Bound	Upper Bound
1	(Constant)	-.717	.609	.243	-1.928	.495
	Fever	.006	.023	.790	-.040	.052
	Fatigue	0.031	0.027	0.651	-.025	.065
	Cough	-.001	.027	.976	-.054	.052
	S.O.B	.029	.029	.326	-.029	.086
	IHD	.017	.026	.527	-.035	.069
	O2.saturation	.035	.006	.000	.023	.047
	Lymphocyte count	-.005	.012	.300	-.007	.000
	NLR	-.059	.006	.000	-.070	-.047
	Creatinine mg/dl	-.005	.005	.353	-.014	.005
	CRP	-.003	.001	.035	-.006	.000
	LDH	.000	.000	.271	-.001	.000
	Albumin	.009	.019	.645	-.028	.045

R= 0.975, R square = 0.950, adjusted R square= 0.941

DISCUSSION

Novel Coronavirus disease (COVID-19) is a newly discovered contagious disease caused by severe acute respiratory syndrome (SARS)–coronavirus (CoV)-2 virus. Due to relative immunosuppression and high prevalence of comorbidities in patients with ESRD on dialysis, there were differences between hemodialysis patients and general population regarding presentation of the disease, clinical features and regarding outcomes.[12-18]

In our study, selected patients mostly belonged to the 41-50 years age group (25%), 51-60 years (29%) and 61-70 years (25%). The mean age in survived group was 52.7±12.9 years and in death group was 57.9±14.2 years. Male and female ratio was 1.7.1. No significant difference was observed regarding age and sex of the study subjects between survived and death group. Comorbidities present in our study were HTN, DM, IHD, Pulmonary disease, Stroke and CLD. Among them only IHD is statistically significant. 77.3% patients in death group had IHD. Stefan et al.[19] showed comorbidities in their study population were arterial HTN, coronary heart disease, DM, COPD, atrial fibrillation and cancer. Among those coronary heart disease (p=0.04) and COPD (p=0.02) were statistically significant. But assessing risk factors associated with in hospital death by hazard ratio revealed no significant relation with these comorbidities with death in hemodialysis patients. Our study supports these result as in logistic regression none of our comorbidities related to increased risk of death.

Initial symptoms during admission were milder than general population cough (52% vs 57.6%), (fatigue 43% vs 45.6%), SOB/dysponea (35% vs 45.6%) with lower rate of fever (65% vs 88.7%).[16] This result is almost similar with findings in MHD patients reported by Rodriguez-Morales et al.[16], Wang et al.[17], Ma et al.[18], Stefan et al.[19]. Lower rate of fever in CKD maintenance hemodialysis patients may have related to immune deficiency and decreased number of lymphocytes and lower serum level of inflammatory cytokines than in general population[18]. GIT symptom diarrhea was lower than Spanish hemodialysis patients (8% vs. 17%)[9] but similar to Romania patients (8% vs. 8%).[19] Oxygen saturation was statistically significantly lower in death group (90.2±2.68) vs survived group (96.0±1.32) in our study (p<0.001). Logistic regression showed lower oxygen saturation is related to increase mortality of COVID19 positive maintenance hemodialysis patients. In several previous studies, it was revealed lower oxygen saturation at admission is a risk factor for mortality[9,18-20].

Regarding laboratory parameters low lymphocyte count, low albumin, increase N:L ratio, creatinine, CRP and LDH were statistically significantly different between survived and death group. Hemoglobin, ESR, total count, neutrophil count, platelet count, SGPT, D-dimer and ferritin level were not significant. Rodriguez-Morales et al.[16] concluded that laboratory abnormalities predominantly found included hypoalbuminemia, elevated inflammatory markers, such as C-reactive protein, LDH, ESR, and lymphopenia, which supports our study findings. In general population, lymphopenia, increase level of CRP, LDH, SGPT, serum creatinine, D-dimer and procalcitonin had been found to be associated with severe disease and mortality in COVID 19.[21] D-dimer level which was a predictor of mortality in general population is not a significant marker of mortality in our cohort as D-dimer normally elevated in dialysis patients and also clearance of this marker during dialysis. On admission, chest x-ray showed normal findings in 48.7% in survived group and only 13.6% in death group, whereas bilateral GGO was present in 68.2% in death group and 37.2% in survived group which were statistically significant. However, our logistic regression analysis showed no relation of chest x-ray findings with increased mortality. This is consistent with previous studies in Spanish and Romania cohort[9,19].

The linear regression model applied to measure risk factors for the morbidity of COVID-19 patients demonstrates a high degree of explanatory power, with an R-squared value of 0.950, indicating that approximately 95% of the variance in patient mortality can be accounted for by the predictors included in the model. Among the predictors examined, oxygen saturation shows the strongest positive association with patient mortality (â= 0.246, p<0.001), followed by neutrophil-to-lymphocyte ratio (N_L_ratio) (â= -0.464, p<0.001) indicating a significant negative association. Other factor such as C-reactive protein (CRP) (â= -0.085, p=0.035) also show statistically significant associations with mortality. In assessing risk factors for mortality of this cohort different study showed oxygen saturation and CRP are common predictors like our study.[9,10,12,19]

ICU requirement in our cohort of COVID positive MHD patients was 18%, which is supported by the findings reported by Rodriguez-Morales et al.[16] For outcome 78 patients were discharged and 22 patients died with a mortality rate of 22%. This result is almost similar with Ma et al. (19%)[18] in China and Stefan et al. (19%)[19] in Romania, but lower than Spanish cohort (30.5%)[9], and Istanbul cohort (31.1%).[20]

There are some limitations of our study. Firstly, it was a single center study. Secondly, as this was a retrospective nature of study, all data like clinical features, laboratory tests were not assessed in a unified method in all patients. Finally, it lacks a prospective design, which would be more reliable.

CONCLUSION

To conclude, we found a high mortality rate in COVID-19 positive hospitalized maintenance hemodialysis patients. Markers of inflammation and oxygen status are significant predictors of COVID-19 patients' mortality, highlighting the importance of monitoring these parameters for clinical management and risk stratification.

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