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CLINICAL CHARACTERISTICS AND SHORT-TERM OUTCOMES IN COVID-19 POSITIVE PATIENTS REQUIRING HEMODIALYSIS AT A TERTIARY HOSPITAL IN A DEVELOPING COUNTRY

Subashri Mohanasundaram*	Senior Resident, Department of Nephrology, Government Stanley Medical College & hospital. *Corresponding Author
Sujit S.	Assistant Professor, Department of Nephrology, Government Stanley Medical College & hospital.
Edwin Fernando	Professor & Head, Department of Nephrology, Government Stanley Medical College & hospital.
Lakshmi Balasundaram	Junior Resident, Department of Pharmacology, JIPMER.

ABSTRACT **Background:** The presence of comorbidities and relative immunosuppression in chronic kidney disease patients on hemodialysis raises concerns that these patients may have an increased risk of severe COVID-19. We aimed to examine the presentation and in-hospital outcomes of COVID-19 patients with end stage renal disease requiring hemodialysis.

Methods: To examine presentation and in-hospital outcomes of COVID-19 in patients with end stage renal disease requiring hemodialysis. The study was conducted in a tertiary care centre from June 2020 to December 2020. We collected clinical & laboratory data of 126 COVID-19 positive in-patients requiring hemodialysis. CKD patients referred to our centre for hemodialysis patients were also included. Patients requiring invasive ventilation and management in intensive care units were excluded. Patients were categorised into two groups based on their outcomes; survivors and non-survivors. Detailed history & biochemistry results were recorded and analysed using SPSS 20.0.

Results: A total of 126 patients were included in our study, with male predominance, n=91(72.2%). The median age of our study population was 53 years. The main presenting complaints were fever, n=78(61.9%); cough, n=69(54.8%), dyspnea, n= 62(49.2%), fatigue, n=102(81%) and myalgia, n=51(40.5%). Eighty nine(70.6%) patients were hypertensives, 48 (38.1%) known diabetics and 13 (10.3%) had pre-existing chronic obstructive pulmonary disease. Lung involvement in CT imaging at the time of admission, were found in 93(85.5%) patients. On comparison between survivor and non-survivors, there was no statistical difference in the biochemical profile, however there was significant chest imaging findings ($p<0.001$) and requirement of ventilator ($p<0.001$) in the non-survivor group.

Conclusion: In our study, mortality was high in patients showing chest imaging findings and also in those requiring non-invasive ventilation even in non-intensive care setting, at admission. The high mortality in CKD patients on hemodialysis emphasizes the need of dedicated COVID hemodialysis units,to prevent interruption in routine outpatient stable dialysis patients.

KEYWORDS : chronic kidney disease, COVID-19, out-patient hemodialysis, mortality

1.INTRODUCTION:

The impact of COVID19, caused by severe acute respiratory syndrome coronavirus 2(SARS-CoV-2) may present with more severe disease course in patients with chronic kidney disease. Although the outcomes in maintenance hemodialysis patients still remain unclear, an earlier small case series by Wang et al suggests a milder course.[1,2] Management of maintenance hemodialysis patients in the context of an epidemic poses several challenges- in the form of transportation to dialysis centres, waiting in crowded places before dialysis session and increased risk of poor outcomes, as most of them are of old age and have co-morbidities.[3] Though the preventive and isolation measures carried out in hemodialysis units will decrease the spread of the virus, little is known about the characteristics of the disease in this population[4-7]. With increasing number of infected patients every day, this study is aimed to address the pattern of presentation, associated comorbidities and short-term outcomes of COVID19 in ESRD patients undergoing hemodialysis in a tertiary care hospital.

2.Aim and objectives

2.1. Aim: To study the clinical symptoms, laboratory profile and short-term outcomes in COVID19 infection in ESRD patients undergoing hemodialysis.

2.2. Primary objective: To assess the predominant clinical symptoms and laboratory parameters in ESRD patients diagnosed with COVID19 infection, undergoing hemodialysis.

2.2.3. Secondary objective: To evaluate the in-hospital mortality in this population.

3. Material and methods:

3.1. Study design:

This study was an observational, prospective single centre study conducted between June 2020 and December 2020.The study was initiated after obtaining Institute Ethics committee approval in the department of Nephrology.Patients were informed about the study and written, informed consent was obtained from individual participants. The study was conducted in accordance with the principles of Declaration of Helsinki and the Good Clinical Practice guidelines of International Conference on Harmonization.

3.2. Patient eligibility criteria:

Adult CKD patients (aged 18 and above but less than 65 years) of either sex who were diagnosed with COVID19 infection (RT-PCR positive) undergoing hemodialysis at our centre, were recruited for participation. We included patients who were on maintenance hemodialysis in other centres, yet got referred to our centre during first wave of COVID. We excluded patients with confirmed diagnosis of COVID19 who required hemodialysis for the treatment of acute kidney injury, patients undergoing peritoneal dialysis, who required invasive ventilation at the time of admission or during hospital stay and patients who were admitted in intensive care setting.

3.3. Study procedure:

Patients with laboratory confirmation of COVID19 infection (RT-PCR) were recruited in this study. Patients were tested for COVID19 based on symptoms such as history of fever>38^0 C, cough, breathlessness and onset within the last 10 days. Demographic data, clinical features, laboratory results, radiological data, treatment and mortality rates were registered. Blood examinations included complete blood count, and serum biochemistry (including renal and liver function tests). Laboratory parameters were measured at the time of admission. During hospital stay, all patients received two four-hour dialysis sessions per week with polysulfone dialysers with medium efficiency with surface 1.3 m^2 and with standard hemodialysis machines. Dialysis prescription was individualized according to patient previous regimes and evolution during admission.

3.4. Statistical Analysis:

Data was analysed using SPSS version 20.0. A p value of <0.05 was considered to be significant. Parametric data was expressed as mean ± SD, non parametric data as median (interquartile range), categorical

data was expressed as number (percentage). Chi square test was used to analyse categorical data, Independent T test was used for continuous variables following normal distribution and Mann Whitney U test for data not following normal distribution.

4. RESULTS:

We identified 126 patients with ESKD on dialysis, who were diagnosed with COVID-19 infection. The median age of our study population was 53 years with male predominance, n=91 (72.2%). A total of 57 (45.2%) patients were smokers, while 32 (25.4%) patients consumed alcohol. Of the entire study population, 89 (70.6%) patients were hypertensives, 48 (38.1%) patients were known diabetics and 13 (10.3%) patients had pre-existing chronic obstructive pulmonary disease (COPD). Among the presenting complaints, 78 (61.9%) patients had fever, 69 (54.8%) patients presented with cough, 62 (49.2%) patients had dyspnoea, 102 (81%) patients presented with fatigue and 51 (40.5%) patients had myalgia. Less commonly, 13 (10.3%) patients presented with diarrhoea and 16 (12.75 %) patients had anosmia. Ninety-three (85.5%) patients had involvement of lungs as evidenced by CT imaging, as either unilateral or bilateral findings at the time of admission. Of the 126 patients, 101 (80.2%) patients required non-invasive ventilator support. Forty three (34.12%) patients were initiated on hemodialysis for the first time during this hospital stay, when they presented with features of uremia, such as acute encephalopathy, volume overload, pulmonary edema.

On analysing the study population, based on in-hospital mortality, mean age among both the groups were comparable. (Table 1). There was no statistical difference in the prevalence of hypertension, diabetes and COPD between the survivors and non-survivors. Neither smoking nor alcohol consumption were found to have an effect on mortality.

With respect to the presenting complaints, the number (percentage) of patients presenting with fever among the survivor and non-survivor groups were 53 (58.9 %) and 25 (69.4 %) respectively. Eighteen (20%) patients in survivor and 8(22%) in non-survivor group presented with diarrhea. Anosmia was documented in 10 (11%) and 6 (16.7%) among the survivor and non-survivor groups respectively. Myalgia was reported in 33 (36.7%) and 18 (50%) among the survivor and non-survivor groups respectively. There was no statistical difference between the two groups with respect to fever, diarrhoea, anosmia and myalgia. Cough and dyspnea was found to be significantly higher ($p<0.001$) in non-survivor group, with all 36 (100%) patients in non-survivor group having the symptoms compared to 33(36.7%) patients having cough and 26 (28.9%) patients having dyspnea in the survivor group. However, fatigue was found to be significantly higher in survivor compared to non-survivor group (93.3% vs 50%, $p<0.001$). Chest imaging, using computed tomography showed either unilateral or bilateral ground glass opacities in 57 (63%) patients in survivor group, whereas 36 (100%) patients who belonged to the non-survivor group had imaging changes at the time of admission.

On analysing the laboratory profile at the time of admission, the median (IQR) haemoglobin among survivors was 8.4 (2) gm% and among the non survivors it was 8.4 (2.3) gm%. The median platelet count was 2.23 lakhs per cu.mm in survivor group compared to 1.9 lakhs per cu.mm in the non-survivor group. Though, neutrophil-lymphocyte ratio (NLR) was elevated (more than 3.7) in 23(63.9%) patients belonging to the non- survivor group, it was not found to be statistically significant (p=0.018). Overall, between survivors and non-survivors , values of random blood glucose (124.5 mg/dL vs 123 mg/dL; p= 0.20), blood urea (77 mg/dL vs 96.5 mg/dL; p=0.26), serum creatinine (6.5 mg/dL vs 7.5 mg/dL; p=0.11), serum sodium (137.2±4.2 mEq/dL vs 137.1±4.4 mEq/dL, p=0.88), potassium (5.7 mEq/dL vs 5.7 mEq/dL; p=0.95), chloride (99 mEq/dL vs 99 mEq/dL, p=0.37) and bicarbonate (15±3.1 mEq/dL vs 15.7±3.3 mEq/dL, p=0.27) were not found to be statistically significant. Among the liver function tests, the values of total protein (mg/dL) and serum albumin (mg/dL) were statistically significant (median, 5.7 vs 5.8 ; p=0.007) and (median, 3.8 vs 3.9; p=0.006) between survivors and non-survivors. Of the study population, the percentage of patients who were required non-invasive form of ventilation ,at the time of admission was 72.2% (65 patients) in survivor group vs 100% (36 patients) in the non-survivor group, which was statistically significant ($p<0.001$). And 30% (27 patients) in survivor group vs 44.4% (16 patients) in non-survivor group were newly initiated on hemodialysis, but the value was not statistically significant. In the non-survivor group, patients died at a median time interval of 6 days (IQR: 4-14) from the time of admission.

Table 1: Comparison of characteristics among survivors vs non-survivors

Sr. No.	Parameter	Survivors (n=90)	Non-survivors (n=36)	P value
	Patient demographics			
1	Age (in years)#	53 (17)	55 (14)	0.3
2	Gender** Males Females	25 (27.8) 65 (72.2)	10 (27.8) 26 (72.2)	1.0
3	Smokers**	39 (43.3)	18 (50)	0.55
4	Alcohol consumers**	25 (27.8)	7 (19.4)	0.37
5	COPD**	7 (7.8)	6 (16.7)	0.19
6	Hypertension**	66 (73.3)	23 (63.9)	0.38
7	Diabetes mellitus**	31 (34.4)	17 (47.2)	0.22
	Presenting complaints			
8	Fever**	53 (58.9)	25 (69.4)	0.31
9	Cough**	33 (36.7)	36 (100)	<0.001
10	Dyspnoea**	26 (28.9)	36 (100)	<0.001
11	Fatigue**	84 (93.3)	18 (50)	<0.001
12	Diarrhoea**	18 (20)	8 (22.2)	0.81
13	Anosmia**	10 (11)	6 (16.7)	0.39
14	Myalgia**	33 (36.7)	18 (50)	0.22
	Chest imaging			
15	Ground glass opacities**	57 (63)	36 (100)	<0.001
	Laboratory investigations			
16	Haemoglobin (gm/dL)#	8.4 (2)	8.4 (2.3)	0.79
17	NLR elevated**	36 (40)	23 (63.9)	0.018
18	Platelet(lakhs per cu.mm)#	2.23 (1)	1.9 (1.2)	0.26
19	Blood glucose(mg/dL)#	124.5 (21)	123 (21)	0.20
20	Blood urea (mg/dL)#	77 (108)	96.5 (107)	0.26
21	Serum creatinine (mg/dL)#	6.5 (6.2)	7.5 (7.5)	0.11
22	Sodium (mEq/dL)*	137.2± 4.2	137.1± 4.4	0.88
23	Potassium (mEq/dL)#	5.7 (0.9)	5.7 (1.6)	0.95
24	Bicarbonate (mEq/dL)*	15± 3.1	15.7± 3.3	0.27
25	Chloride (mEq/dL)#	99 (7)	99 (7)	0.37
26	Total bilirubin (mg/dL)#	0.6 (0.3)	0.6 (0.2)	0.78
27	Direct Bilirubin (mg/dL)#	0.4 (0.3)	0.4 (0.3)	0.26
28	Total Protein (mg/dL)#	5.7 (0.4)	5.8 (0.6)	0.007
29	Serum albumin (mg/dL)#	3.8 (0.3)	3.9 (0.5)	0.006
30	Serum alanine transaminase (IU/L)*	30.2± 7.8	30.9± 7.4	0.19
31	Serum aspartate transaminase (IU/L)*	20± 4.6	21.3± 5.4	0.63
	Requirement of non-invasive ventilation			
32	Ventilated patients**	65 (72.2)	36 (100)	<0.001
	Hemodialysis			
33	Median sessions of hemodialysis#	3 (2)	2 (2)	0.01
34	New induction of hemodialysis**	27 (30)	16 (44.4)	0.14

*values expressed as mean± SD, Independent sample t test was used for analysis

#values expressed as median (IQR), Test of analysis -Mann whitney U test

**values expressed as number (percentage), Test of analysis-chi square test

5.DISCUSSION:

SARS-CoV-2 infection has proven to be a challenge to the healthcare system all over the world. With new information emerging everyday, along with the immunocompromised nature high degree of

comorbidities in patients with chronic kidney disease, make them highly vulnerable population to the disease[8]. Herein, we describe our early experience with COVID infection in ESKD patients in a developing nation with resource constraints.

At our dedicated in-patient dialysis unit, all patients wore surgical or N95 masks throughout their entire dialysis sessions, if they were not on non-invasive ventilator support. The care providers including the technicians and physicians wore personal protective equipment throughout the dialysis session and were under quarantine for a period of seven days, after working for a week in the dialysis unit, and to return to work, had to test negative by COVID-19 RT-PCR, so as to ensure minimal spread of infection through the care-providers at the hospital.

Ferrey et al, described atypical presentation of COVID-19 infection in a hemodialysis patient, who presented with gastrointestinal distress.[9] However, similar to the general population, the most common presenting symptoms were fever (61.9%), cough (54.8%), dyspnea (49.2%), fatigue (81%) and myalgia (40.5%) in our study as well. Majority of the study population (86.5%) had findings in CT chest imaging at the time of admission. Also, 36 (100%) patients who belonged to the non-survivor group had findings on chest imaging compared to 57 (63%) patients belonging to the survivor group, which was statistically significant.[10]

In a study by Mutinelli-Szymanski P, elevated neutrophil-lymphocyte ratio at day 7 was found to be a prognostic marker for predicting severe course of COVID in hemodialysis patient. But, in our study, though the NLR was elevated in non-survivor group (63.9%) compared to the survivor group (40%), it was not found to be statistically significant.[11] Thus NLR at day one of admission may not predict severity of the infection as did on day 7 in other studies. The biochemical parameters of random blood glucose, urea, serum creatinine and electrolytes did not differ much between the survivor and non-survivor groups. Though, there was statistical difference between the values of serum albumin and total protein in the survivor and non-survivor group, it may not have a clinical relevance, as most ESRD patients are malnourished and hence there could have been a low median value of serum albumin and total protein.

About three fourths of the patients (71.4%) in our cohort were discharged by the end of follow-up, which was a median of 8 days after admission. During the study period, a total number of 6112 hemodialysis sessions had taken place catering to the needs of chronic kidney disease patients, out of which, a total of 385 sessions was done for COVID infected patients at our centre. This means that the patients in the study population required a median of two dialysis sessions during their hospital stay, which may be less overall, however it represented our contribution to the need of hemodialysis at a time, during which there was reluctance of many outpatient dialysis units to treat COVID infected patients.[12] The inclusion of these outpatient dialysis patients from other centres could also be reason for the high mortality in our cohort. There was a 100% mortality in patients who were ventilated compared to 72% who did not require ventilator assistance. The difference is found to be statistically significant $p<0.001$.

Also, 43 (34.12%) patients were initiated on hemodialysis for the first time during this hospital stay, which emphasizes the need for repeated education regarding the appropriate measures to be taken in chronic kidney disease patients, who are highly vulnerable to infection in view of their immunocompromised state. In our study, we had high overall morality of 28.5%, which could have been influenced by the participation of maintenance dialysis patients referred from other hemodialysis units. However, the high mortality could be not extrapolated to those who were admitted in intensive care units or patients who were treated with invasive ventilation.

Limitations of our study were that we did not involve patients who required invasive ventilation, or patients admitted to the ICU setting. Since our study setting is in the background of a large public hospital, inflammatory markers such as C-reactive protein, serum ferritin, serum lactate dehydrogenase, Interleukin-6 were not included in the analysis as it could not be performed uniformly in all patients.

In conclusion, ESRD patients with COVID infection showed high mortality, especially those who required ventilatory assistance. This study emphasizes that the need for dedicated dialysis centres, as to avoid delay in the regular schedule of patients who get dialysed on outpatient basis otherwise, as it may add up to the mortality and also regarding educating the "high-risk" chronic kidney disease patients about the infection control measures to prevent the spread of infection.

REFERENCES:

1. Wang R, Liao C, He H, Hu C, Wei Z, Hong Z, Zhang C, Liao M, Shui H. COVID-19 in Hemodialysis Patients: A Report of 5 Cases. Am J Kidney Dis. 2020 Jul;76(1):141-143.
2. Alberici F, Delbarba E, Manenti C, Econimo L, Valerio F, Pola A, Maffei C, Possenti S, Lucca B, Cortinovis R, Terlizzi V. A report from the Brescia Renal COVID Task Force on the clinical characteristics and short-term outcome of hemodialysis patients with SARS-CoV-2 infection. Kidney International. 2020 May 8.
3. Burgner A, Ikizler TA, Dwyer JP. COVID19 and the Inpatient Dialysis Unit: Managing Resources during Contingency Planning Pre-Crisis. Clin J Am Soc Nephrol. 2020 May 7;15(5):720-722.
4. Ikizler TA. COVID-19 in dialysis patients: adding a few more pieces to the puzzle. Kidney Int. 2020 Jul;98(1):17-19.
5. Goicoechea M, Cámara LA, Macías N, de Morales AM, Rojas ÁG, Bascuñana A, Arroyo D, Vega A, Abad S, Verde E, Prieto AM. COVID-19: Clinical course and outcomes of 36 maintenance hemodialysis patients from a single center in Spain. Kidney International. 2020 May 11.
6. Kliger AS, Cozzolino M, Jha V, Harbert G, Ikizler TA. Managing the COVID-19 pandemic: international comparisons in dialysis patients. Kidney Int. 2020 Jul;98(1):12-16.
7. Dudreuilh C, Kumar N, Moxham V, Hemsley C, Goldenberg S, Moutzouris DA. De-isolation of COVID-19-positive hemodialysis patients in the outpatient setting: a single-center experience. Kidney Int. 2020;98(1):236-237.
8. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al.:Clinical course and risk factors formortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. Lancet 395: 1054–1062, 2020.
9. Ferrey A, J, Choi G, Hanna R, M, Chang Y, Tantisattamo E, Ivaturi K, Park E, Nguyen L, Wang B, Tonthat S, Rhee C, M, Reddy U, Lau W, L, Huang S, S, Gohil S, Amin A, N, Hsieh L, Cheng T, T, Lee R, A, Kalantar-Zadeh K: A Case of Novel Coronavirus Disease 19 in a Chronic Hemodialysis Patient Presenting with Gastroenteritis and Developing Severe Pulmonary Disease. Am J Nephrol 2020;51:337-342.
10. Wong HYF, Lam HYS, Fong AH, Leung ST, Chin TW, Lo CSY, Lui MM, Lee JCY, Chiu KW, Chung TW, Lee EYP, Wan EYF, Hung IFN, Lam TPW, Kuo MD, Ng MY. Frequency and Distribution of Chest Radiographic Findings in Patients Positive for COVID-19. Radiology. 2020 Aug;296(2):E72-E78
11. Mutinelli-Szymanski P, Hude I, Merle E, Lombardi Y, Seris P, Abtahi M, Azeroual L, Bourgain C, Ensergueix G, Katerinis I, Kolko A, Kolta A, Maheas C, Mehrbanian S, Morel P, Ossman R, de Préneuf H, Roux A, Saltiel C, Vendé F, Verhoeven AS, Viron B, Laplanche S, Le Monnier A, Ridel C, Ureña-Torres P, Touzot M. Neutrophil:lymphocyte ratio predicts short-term outcome of COVID-19 in haemodialysis patients. Clin Kidney J. 2020 Nov 21;14(1):124-131.
12. Burgner A, Ikizler TA, Dwyer JP: COVID-19 and the inpatient dialysis unit: Managing resources during contingency planning precrisis.Clin J Am Soc Nephrol 15: 720–722, 2020.