ORIGINAL RESEARCH

Study of clinical profile and outcome of chronic kidney disease patients on hemodialysis with SARS-CoV-2 infection during pandemic in a tertiary care teaching hospital

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ABSTRACT

Background: Patients suffering from (CKD) are in general at high risk for severe coronavirus disease (COVID-19), but dialysis-dependency (CKD5D) is poorly understood. We aimed to study clinical profile and outcome of CKD patients on hemodialysis with SARS-CoV-2 infection during pandemic in a tertiary care hospital. **Methods:** A total130 consecutive patients of CKD on hemodialysis with SARS-CoV-2 infection aged ≥13 years who attended or were admitted under the Department of General Medicine were included and were studied from Jan 2021 to May 2022. **Results:** The age group affected between 51-60 years (31.5%) with male predominance (57.7%). Generalized body swelling was commonest symptom (76.9%) and tachycardia was commonest sign (84.6%). Clinical profile of these patients showed the most common aetiology as diabetes nephropathy [61(46.9%)] followed by hypertensive nephrosclerosis [37(28.5%)]. The mean duration of dialysis was 4.75 months, ranged from 2 days to 5 years. Majority of the patients were presented in stage 5 CKD (52 patients). The mortality among CKD patients with COVID-19 was found to be 59.3%. Highest mortality (69.2%) was observed in stage 5 patients, in diabetic nephropathy (73.8%), high level of D-dimer (74.4%) and 100% mortality in HIV positive patients. **Conclusion:** CKD patients with severe COVID-19 illness who were treated with early elective intubation had found better outcome. Early hemodialysis and early elective intubation in patients with respiratory failure had good outcome. This study reveals, early use of anticoagulation in patients having tachycardia, tachypnoea and hypoxemia had better outcome. Early detection and effective management of these illnesses can delay the onset, progression of CKD and subsequent morbidity and the requirement of renal replacement therapy, if any.

Key words: Chronic kidney disease, hemodialysis, SARS-CoV-2 infection, diabetes nephropathy

INTRODUCTION

Chronic kidney disease (CKD) has emerged as one of the most prominent causes of death and suffering in the 21st century.[1] Since patients with CKD had greater rates of all-type infections and cardiovascular disease than the general population (with a nearly 10-

fold increased risk for cardiovascular events), it is hypothesised that these patients will have a higher risk of developing the severe disease.[2] Individuals with CKD are three times more likely to develop severe symptoms of COVID-19 than others and also have a higher prevalence of hypertension and diabetes, which are both independently associated with higher mortality with COVID-19. [3, 4]

Patients with CKD have been documented to experience significant immune system changes that result in an immunosuppressed condition and frequent infection consequences. Similarly, persistent systemic inflammation may potentially be a factor in CKD patients' increased morbidity and mortality.[5]

Additionally, a sizable part of them frequently uses hospitals and medical facilities for hem dialysate, which heightens their susceptibility to COVID-19. Patients with CKD had a high documented incidence of severe COVID-19, with fatality rates ranging from 31 to 53.3%.[6]

However, CKD patients have a high proportion of comorbidities and are immune-compromised, making them more susceptible to infections.[7] The first COVID 19 death reported in USA was an ESRD patient on Hemodialysis.[8] Home isolation is not an option as patients on maintenance hemodialysis (MHD) have to visit their dialysis center two to three times a week. Studies have shown mortality rate ranging from 16% to 30.5%.[9, 10] Also, analysis of CKD5D patients on MHD of Wuhan revealed that up to 21.4% patients can be asymptomatic carriers and hemodialysis centers can be high risk settings for spread of infection.[2]

Individuals with stage V CKD (eGFR<15 ml/min/1.73 m^2) have end-stage renal disease (ESRD) and require dialysis. These persons are not only at higher risk if they acquire COVID-19 but they also need to be able to continue their dialysis treatment. It is therefore critical that providers are aware of recommendations on how to continue dialysis services for this population while keeping dialysis patients as safe as possible. It is critical to understand that patients on dialysis face new challenges in the management of their disease in the setting of COVID-19.[11] In this study, we focus on hemodialysis patients with COVID19 infection with emphasis on epidemiology, including clinical features and outcome and its correlation to presenting features.

MATERIAL AND METHODS

After obtaining Institutional Ethical Committee approval and written informed consent from all the patients, this institutional based cross-sectional, descriptive study was conducted in the Department of General Medicine at Tertiary Care Centre during the period from January 2021 to May 2022. A total of 130 consecutive patients of CKD on hemodialysis with SARS-CoV-2 infection aged ≥13 years who attended or were admitted under the department of General Medicine were included. All the patients who have already undergone renal transplants were excluded. A significant proportion of the patients admitted were undergoing maintenance dialysis from other centers (government or private), and once they were COVID positive were referred to tertiary care hospital as exclusive dialysis for COVID positive patients during the first wave were available at very few centers in the city. The diagnostic criteria for COVID-19 infection were a laboratory confirmed SARS-CoV-2 infection, detected in nasopharyngeal and/or oral swab by RT-PCR using methods recommended by the Indian Council of Medical Research, with or without clinical symptoms. As per national guidelines, a policy of mandatory quarantine of all COVID-19 positive patient till 14 days of infection was being observed. Those with underlying comorbidity were advised admission to a hospital instead of a Covid-care center/isolation facility, especially those undergoing regular hemodialysis.

Their demographic data, co morbidities, investigations details including hematologic & biochemical reports, Radiography (X-ray chest &/or CT Chest), SARS-CoV-2 RT PCR reports, treatment details were noted. Clinical course in terms of inotrope requirement, need for oxygen therapy or any other organ dysfunction were recorded. Therapy evolved and changed with time & adopted as per availability, as expected in this new pandemic. They were followed for their entire course of hospital stay. Time required for turning RT PCR negative and final outcomes that is, discharge/mortality, were noted. MOHFW guidelines & precautions for Hemodialysis during COVID pandemic were followed. Regular Heparin was used during dialysis [40 units/kg as bolus & 12 units/kg as maintenance]. Systemic Heparin was used, 5000 units twice daily, in all those needing oxygen. Later group did not receive any heparin during MHD. Complications, during MHD, were noted, if any.

DISCHARGE POLICY: All MHD patients were referrals as they were either symptomatic needing admission or could not be accommodated at their parent centers due to lack of COVID specific shift/isolation facility. To handle this load and ensure that everyone received adequate dialysis, following policy was made. They were discharged if they were asymptomatic for at least 3 days, along with 2 consecutive SARS-CoV-2 RT PCR negative reports and with creatinine less than 10 mg % and serum potassium less than 5.5 meq/L. The outcome of patients during the course of hospitalization in terms of death or discharge and the proportion of patients developing complications (respiratory failure/ myocarditis/AKI/thrombocytopenia/others) were noted. No prospective details were recorded after the patients were discharged.

STATISTICAL ANALYSIS: Data were analyzed using SPSS version 20. The descriptive statistics were calculated. The mean and standard deviation

(SD)/Median (IQR) were calculated for baseline characteristics and biochemical parameters. Student t-test or Manne Whitney U test was applied for comparisons depending upon the use of mean or median for quantitative variables. Chi-square or Fisher's exact test were used for categorical variables. For all comparisons, 5% probability ($p<0.05$) was considered significant. Univariate and multivariate regression analysis was done to identify risk factors for mortality.

RESULTS

Table 1: Age and sex-wise distribution among study subjects

Age Group (in years)	Gender		Total
	Male (%)	Female (%)	
≤20	04 (5.3)	01(1.8)	05 (3.8)
21-30	06 (8.0)	01 (1.8)	07 (5.4)
31-40	14 (33.3)	07 (12.7)	21 (16.2)
41-50	18 (29.6)	19 (34.5)	37 (28.5)
51-60	22 (11.1)	19 (34.5)	41 (31.5)
>60	11 (14.7)	08 (14.5)	19 (14.6)
Total	75 (100%)	55 (100%)	130 (100%)

It was seen from Table 1 that the present study involved 130 consecutive patients of CKD on haemodialysis with SARS-CoV-2 infection during pandemic in tertiary care hospital. The commonest age group affected between 51–60 years (31.5%) with male predominance (57.7%). The mean age of patients was 49.73±13.19 years, ranged from 14 to 82 years.

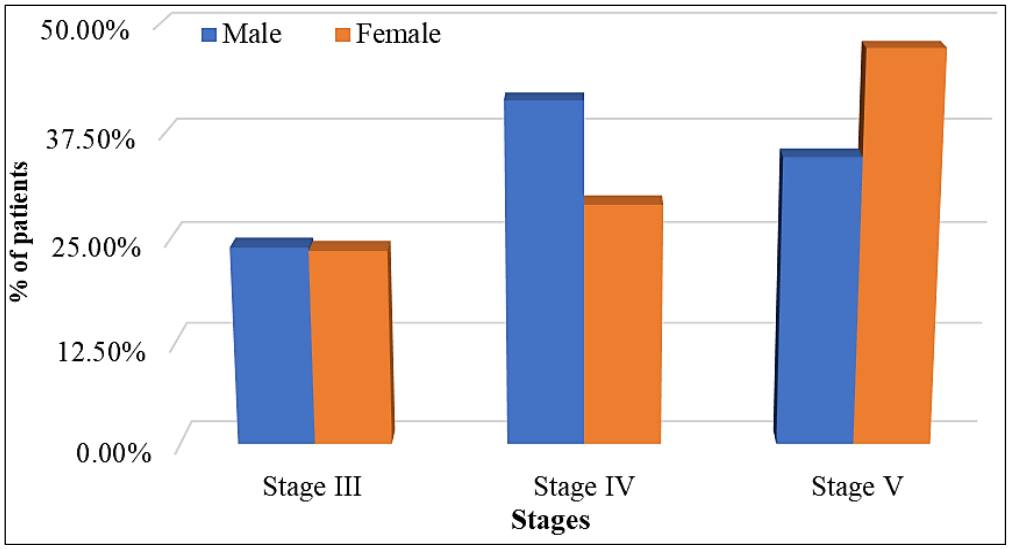


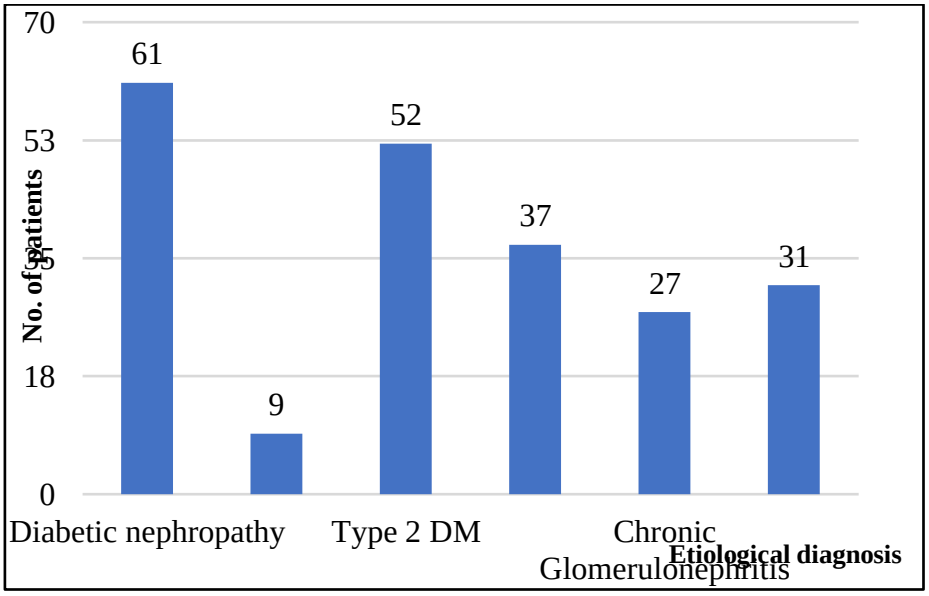
Fig 1: Distribution of cases as per stage of CKD (MDRD Formula)

As seen from Figure 1 that maximum COVID-19 positive patients presented with stage 5 CKD (According to MDRD formula) and almost all had respiratory failure. The majority of the male patients (41.3%) had stage 4 CKD while 47.3% female patients had stage 5 CKD.

Table 2: Duration of illness (CKD) after diagnosis and Hemodialysis details

Parameters	Duration	Frequency	Percentage (%)
CKD after diagnosis (years)	<1	94	72.3
	1-3	21	16.2
	>3	15	11.5
Hemodialysis	≤ 6 months	112	86.2
	6 months	18	13.8
Hemodialysis access	Catheter	95	73.1
	AV fistula	35	26.9
Frequency of hemodialysis	<3 weeks	29	22.3
	≥3 weeks	101	77.7

It was observed from Table 2 that in maximum patients (72.3%) the duration of illness after diagnosiswas less than 1 year, majority of cases (86.2%) undergone hemodialysis from the duration less than 6 months. Preferred dialysis access procedures for CKD patients were dialysis catheter which accounts for 73.1%. The frequency of dialysis was found to be 3 or more per week in 77.7% cases.



*ADPKD, Obstructive Uropathy, Renovascular disease and acute cortical necrosis

Fig 2: Etiological diagnosis

As seen from Figure 2 that the COVID positive CKD patients were more vulnerable for Diabetic nephropathy [61(46.9%)] possibly because of poor glycemic control, followed by Hypertensive nephrosclerosis [37(28.5%)] and chronic glomerulonephritis 98 [27(20.8%)], (Figure 2). No statistically significant difference was observed between etiology and severity of CKD.

Table 3: Distribution of signs and symptoms

Symptoms and signs		Frequency	Percentage
Symptoms	Fever	80	61.5
	Cough	63	48.5
	Breathlessness	76	58.5
	Urinary complaints	38	29.2
	Loose stools	30	23.1
	Chest pain	44	33.8
	Headache	49	37.7
	Sore throat	24	18.4
	Fatigue	35	26.9
	Generalized body swelling	100	76.9
Presenting signs	High blood pressure	94	72.3
	Tachycardia	110	84.6
	Tachypnoea	98	75.3
	Haematuria	07	5.4
	Anemia	102	78.5
	Facial puffiness	32	32.3
	Pedal edema	68	52.3

It was observed from Table 3 that generalized body swelling (76.9%) was commonest presenting symptom, followed by fever (61.5%), and followed by breathlessness (58.5%). Most common clinical sign was tachycardia (84.6%) and tachypnoea (75.3%) followed by high blood pressure (72.3). Majority of the COVID-19 positive CKD patients on haemodialysis presented with comorbidities among which Diabetes (73.75%) was commonest comorbidity to be found followed by Hypertension (43.8%). There were 19 (14.6%) CKD patients had coronary artery disease (CAD), HIV (7.7%) Hepatitis C (4.6%), Hypothyroidism (3.8%), pulmonary Tuberculosis (3.1%).

Cigarette smoking was prevalent in 39.2%, alcohol consumption in 28.5% and tobacco consumption in 33.1%. No statistically significant difference was observed between modifiable risk factors and severity of CKD.

Table 4: Biochemical parameters in chronic kidney disease

Biochemical Parameters	Stages			P-value
	Stage 3	Stage 4	Stage 5	
Hemoglobin (<12g/dl)	11.1±1.52	9.60± 1.79	8.64±1.09	0.000
Blood urea (>45 mg/dl)	67.55±17.26	78.53±20.93	94.63±13.82	0.004
Serum creatinine (>1.35 mg/dl)	4.33± 3.71	6.19 ± 4.77	7.49 ± 4.44	0.000
Potassium (>5 mEq/l)	4.09±1.22	5.06±1.47	5.95±1.51	0.000
Serum albumin (<3.5 mg/dl)	3.86±0.94	3.4±0.40	3.48±0.40	0.005
CRP (mg/dl)	11.28±5.63	15.51± 6.70	15.82±6.96	0.006
D-dimer (µg/ml)	472±62.74	510±79.11	547.63±131.26	0.005

It was observed from Table 4 that the average level of C- reactive protein and D-dimer showed a rising trend with the CKD stages and the standard deviation value has gone up, which indicates more variation in the level of C- reactive protein and D-dimer in stage 5 patients, (Table 4). IL-6 participates in renal instinct cell injury that accelerates the progression of disease. Neutrophil to lymphocyte (N/L) ratio can be used as a measure of systemic inflammation alternatives to many standard biochemical markers. N/L ratio >3.5 denotes severity of COVID-19 illness.

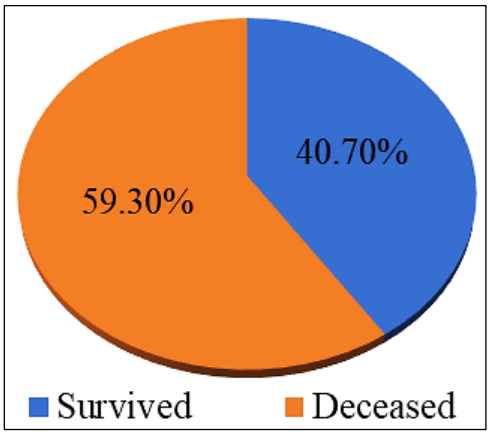


Fig 3: Outcome of the CKD patients

As seen from Figure 3 that the mortality among CKD patients with COVID-19 was found to be 59.3%. Highest mortality (69.2%) was observed in stage 5 patients followed by stage 4 (59.6%) and stage 3 (41.9%). 73.8% mortality observed among the patients with diabetic nephropathy, which was statistically significant, (p=0.002). There was 100% mortality among the patients with type 1 diabetes mellitus who diagnosed with diabetic nephropathy as compared to type 2. However, high level of D-dimer had 74.4% mortality as compared to normal D-dimer level which was statistically significant.

DISCUSSION

In the present study, male predominance was observed as similar to other studies. [12, 13] Age of patients varied between 14 and 82 years, with mean age of 49.73±13.19 years. There is a broad variation in age in this study group highlighting the preponderance of chronic kidney disease across a very large age group. An overwhelming 52 (40%) patients in our study presented for the first time with CKD stage 5. There were 36.2% were in stage 4, 23.8% in Stage 3 and none in Stages 1 or 2, which is consistent with the observations made in the CKD Registry of India Report where 50.3% presented in Stage 5, 24% in Stage 4, 19.1% in Stage 3, 4.4% in Stage 2 and 2.2% in Stage 1. [13] This reflects the lack of awareness about CKD in the public and the failure of the medical practitioners to screen the at risk population and to diagnose CKD at an early stage, which would enable appropriate treatment to be instituted to prevent or reduce the rate of progression of CKD and bring down the huge burden due to mismatch between demand and availability of resources for renal replacement therapy in developing countries like India, especially for low socioeconomic group. In the present study, 46.9% of the patients in the study group had diabetic nephropathy, which was followed by hypertensive nephrosclerosis in 28.5% of cases. 14.8% Type I diabetes was found to be attributed to diabetic nephrosclerosis. The results of the study indicate a higher incidence of diabetes. These findings are correlated with the study conducted by Dash *et al.* [14]

The mean duration of dialysis ranges from 2 days to 5 years with a mean duration of 4.75 months.

The most common symptom in patients from this study group was pedal fever (59.2%), followed by breathlessness (58.5%), cough (48.5%), headache (37.7%), chest pain (33.8%), and urinary complaints (29.2%) like urgency, frequent micturition and fatigability (26.9%). Patients with lower GFR in a subgroup of the NHANES III trial had physical impairment that was eight times worse than that of the overall population, although it was not substantially correlated with renal function.

The mean hemoglobin level in the study population was 9.64±2.01 g/dl. In the study, 95 (73.1%) had anemia (cutoff taken as 11g/dl). It was observed that the prevalence of anemia increased from Stage 3 was (71%) to stage 5 was 95(78.8%). The mean difference of Hb level in different stage was statistically significant. These findings are in accordance with the Canadian Multicenter study and McGonigle RJ *et al*. [15] Although chronic kidney disease frequently results in reduced haemoglobin, there is no quantitative definition of anaemia in this condition because acceptable (normal) Hb values for patients with chronic kidney disease have not been established. [16] The decrease of erythropoietin production in the kidneys and/or the presence of erythropoiesis inhibitors can both lower haemoglobin levels.[18] The length and extent of renal failure are related to the severity of anaemia in chronic kidney disease. Anaemia is more prevalent below a GFR of 60 ml/min/1.73 m2 and its onset and severity are correlated with GFR levels. As the GFR stage advances, it was noticed that more patients were anemic. In the current study, hyperkalemia was seen in 45.3% of CKD patients in this study. In stage 3 patients, the average level of potassium was 4.09±1.22 which kept on increasing with the CKD stage. The mean potassium level of stage 5 was 5.95±1.51mEq/l which shows wide variation of level of potassium in this stage. Hyperkalemia may develop earlier in the course of CKD in patients with hyporeninemic aldosteronism, a complication seen usually with diabetic nephropathy or tubulointerstitial disease. Hyperkalemia may occur in association with dietary indiscretion (e.g. excessive consumption of chocolates, dry fruits, bananas), increased catabolism (as with severe intercurrent illness), or metabolic acidosis. It may also be seen with the use of potassium sparing diuretics, Angiotensin Converting Enzyme (ACE) inhibitors.[18]

The overall mortality of all admitted patients (n=130) at tertiary care center was 59.3%. High mortality rates varying between 11.6% and 31.7% among CKD population have been reported from China and later from other countries.[16,17,19] An analysis of our deaths showed that diabetes nephropathy was found to be most common etiology attributed to death, followed by hypertensive nephrosclerosis. In the present study, among the patients with high level of C-reactive protein and D-dimer, high mortality was observed i.e., 61.3% and 74.4% respectively as compared to normal level.

CONCLUSION

The assessment of clinical profile of CKD patients with COVID-19 showed the most common aetiology as diabetes nephropathy followed by hypertensive nephrosclerosis. CKD patients with severe COVID-19 illness who were treated with early elective intubation had found better outcome. In order to prevent CKD, individuals with one or more co-morbid illnesses (such as hypertension, diabetes mellitus, etc.) must undergo periodic screening. This study reveals, early use of anticoagulation in patients having tachycardia, tachypnoea and hypoxemia had better outcome. Early detection and effective management of these illnesses can delay the onset, progression of CKD and subsequent morbidity and the requirement of renal replacement therapy, if any. The complete range of clinical characteristics and the best method for diagnosing and treating COVID-19 in individuals with severe CKD will require more research and confirmation of these findings in larger cohorts. Our study demonstrates that COVID-19 affects people with CKD, but the outlook may be favorable if quick supportive measures are taken. Positive affirmation and COVID rehabilitation play important role in management. India need more kidney care facility available centers to offer dialysis at root level for the rising CKD population.

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