Original Article

Clinical presentation and outcomes of chronic kidney disease patients with COVID-19 admitted to the intensive care unit of a teaching hospital of Northern India during the third wave of the pandemic: A retrospective study

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Abstract

Introduction: Chronic kidney disease (CKD) patients have impaired immune status; that's why these patients are prone to develop infection-related complications. The current study compares non-haemodialysis chronic kidney disease and end-stage renal disease (NO-HD-CKD and ESRD, respectively) patient outcomes, the data of which is sparse. **Methods:** Patients diagnosed with COVID-19 infection through reverse transcriptase polymerase chain reaction (RT-PCR) were retrospectively studied using electronic health records. Patients were divided into three categories: non-chronic kidney disease (NO-CKD), NO-HD-CKD, and ESRD, and the outcome was assessed. **Results:** Out of 745 patients, 92 (12.34%) had NO-HD-CKD and 31 (4.16%) had ESRD. CKD patients who were not on haemodialysis had higher rates of comorbidities and D-dimer and C-reactive protein (CRP) values compared to ESRD patients. The overall unadjusted mortality rate was found to be 17.44%, and it was 10.45% in case of NO-CKD patients, 58.69% for NO-HD-CKD patients, and 48.39% for ESRD patients. It was observed that patients having NO-HD-CKD had greater odds ratio of overall expiry in comparison to those without CKD in univariate analysis (OR: 1.58; 95% CI: 1.31–1.91). It was not significant in fully adjusted models (OR: 1.11; 95% CI: 0.88–1.40). **Conclusions:** During the third wave of COVID-19, we found higher mortality rates for cases with NO-HD-CKD and, to a lower extent, ESRD. However, patients with ESRD were observed to have good outcomes in comparison to those with NO-HD-CKD. Primary care physicians are the first point of contact for patients. Hence, it is critical for them to manage and to do proper referral of comorbid patients to higher centres.

Keywords: CKD, COVID-19, ESRD, haemodialysis, third wave pandemic

Introduction

The current pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that emerged from Wuhan city of China in December 2019 is having a significant impact on global health

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worldwide,[1,2] affecting more than 39 million people and causing more than 5,757,562 deaths (as of 9 February 2022, WHO Corona virus Disease Dashboard. Multiple organs like the lungs, heart, nervous system, or the kidney involvement is found.[3,4] Till now, the reported COVID-19 mortality rates are subject to wide variability, with initial reports from China pointing to fluctuating infection-associated death rates between 11% and 45% among hospitalized patients.[5–7] Age, pre-existing conditions such as cardiovascular, cerebrovascular or other underlying diseases, and abnormal inflammatory markers such as low absolute lymphocyte count or elevated D-dimer, C-reactive protein (CRP), or interleukin-6 (IL6) have been associated with increased risk of death.[6,7] Those at highest risk for adverse outcomes include the elderly and those with pre-existing health conditions.[8–10] This is especially true for patients with end-stage renal disease (ESRD), who are more susceptible to sepsis[11] and are presumably at greater risk of contracting SARS-CoV-2 due to more frequent encounters with the healthcare system.[12-15] Although acute kidney injury (AKI) portends unfavourable outcomes,[13,16] data concerning pre-existing chronic kidney disease (CKD) in relation to COVID-19 are more limited and discordant. Reports specifically from the ESRD community in Europe, USA, and China have generally demonstrated a high mortality rate (nearly 30%).[17–21] In this study, we examined clinical presentations and outcomes among Indian patients hospitalized with COVID-19 from December 2021 to mid-February 2022. The first contact doctor is the primary care physician for the patient. Hence, it is critical for them to understand and to do proper referral of patients at higher centres. The current study was done to assess the outcome of kidney disease during the third wave of the COVID-19 pandemic.

Material and Methods

Study Population

A retrospective study on patients admitted to the COVID intensive care unit (COVID-ICU) of King George's Medical University, Lucknow, was done. This institution includes a tertiary care facility, admitting the patients from urban as well as rural areas. The study included all patients over the age of 18 years, hospitalised with positive reports for SARS-CoV-2 via real-time RT-PCR assay of nasopharyngeal and oro-pharyngeal swab specimens between December 2021 and mid-February 2022. Patients who did not have a creatinine report or who were not hospitalised specifically for COVID-19 [Figure 1] were excluded from the study.

Covariates

All data were collected and analysed using Statistical Package for the Social Sciences (SPSS) version 20 (SPSS, Chicago, IL). Diagnosis codes for stage 3–5 CKD and ESRD from the problem list and past medical history of the patient, and a Chronic Kidney Disease Epidemiology Collaboration eGFR of 60 ml/min per 1.73 m^2, considering the latest outpatient creatinine (if available), within the last six months before admission, was considered to classify CKD and ESRD. The charts of all patients were reviewed, who were managed by renal replacement therapy (RRT), or those who expired within the first 72 hours of hospitalization, to ensure there was no misclassification of cases with ESRD.

Patient data was also collected for medical comorbidities (chronic obstructive pulmonary disease, hyperlipidaemia, hypertension, coronary artery disease, congestive heart failure, asthma, type 1 and type 2 diabetes, malignancy), demographics (age, sex), lab values, body mass index, vitals during admission and significant hospitalization events like intensive care unit (ICU) admission, intubation, RRT, mortality, etc., AKI was explained as per creatinine criteria, given by the Acute Kidney Injury Network, by considering the hospitalization creatinine value as the baseline.

Statistical analyses

The evaluation of baseline characteristic features was assessed by CKD status, applying medians with inter-quartile ranges for continuous variables, and frequencies for categoric variables. Logistic regression model was used to compare patients with non-haemodialysis chronic kidney disease (NO-HD-CKD) and those with ESRD for overall hospital mortality. Logistic regression models were also used to exclude patients with NO-CKD and directly compared those with ESRD to those with NO-HD-CKD for the results of ICU expiry, and ICU admission. Two-sided *P* values less than 0.05 were taken as statistically significant.

Ethical approval was taken from the institution and consent was taken from each patient during admission.

Results

Baseline Characteristics of Inpatients with COVID-19

This study included 745 patients, who were classified as non-chronic kidney disease (NO-CKD), NO-HD-CKD, and ESRD. The median age for the study patients was 64 years; 59.78% were men, 36.89% were diabetic, 60.72% were hypertensive, and 83.9% were having a major chronic illness. There were 92 patients (12.34%) with NO-HD-CKD, and 31 patients (4.16%) with ESRD. Patients with NO-HD-CKD status had a greater median age (72 years) than those with either ESRD (63 years) or those without CKD (62 years) [Table 1]. The NO-HD-CKD and ESRD patients had raised D-dimer levels and had a chronic medical condition, particularly diabetes, hypertension, hyperlipidaemia, and heart disease, during hospitalization. It was also found that the ESRD subgroup had decreased admission C-reactive protein values, less obesity, and more hypotension in comparison to those without CKD [Table 2],

Outcomes

The overall unadjusted mortality rate was found to be 17.44%, and it was 10.45% in case of NO-CKD patients, 58.69% for NO-HD-CKD patients, and 48.39% for ESRD patients**.** It was

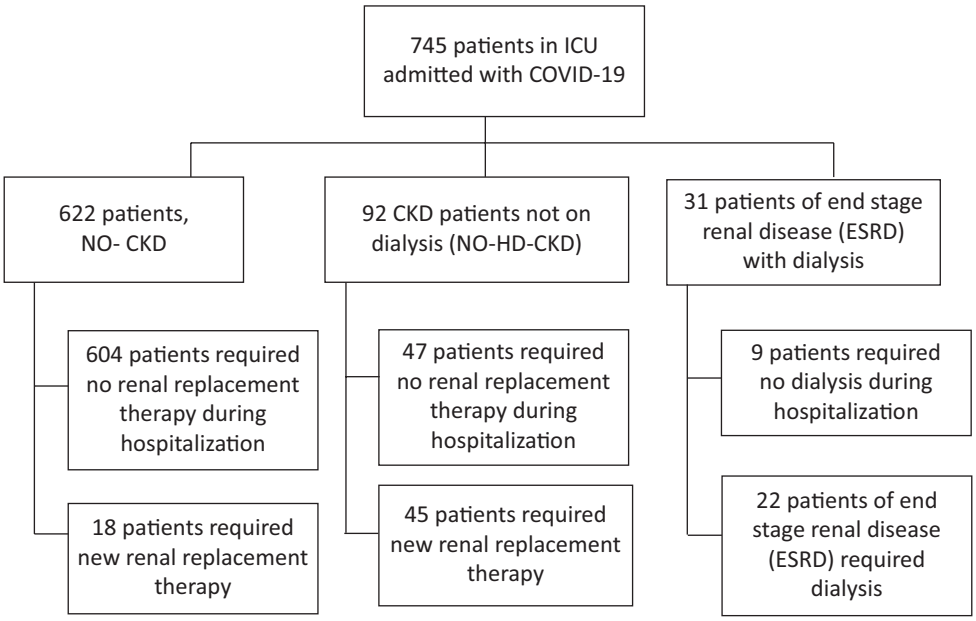

Figure 1: COVID-19 patient flowchart

Table 1: Characteristic features of COVID-positive patients during the third wave

Patient characteristics	Total no. of patients (*n*=745)	NO-CKD patients (*n*=622)	NO-HD-CKD patients (*n*=92)	ESRD patients on haemodialysis (*n*=31)
Age (years), median	64 (52-76)	62 (50-70)	72 (64-80)	63.3 (54-73)
19-44	89 (11.85%)	87 (13.85%)	2 (1.8%)	2 (6%)
45-54	104 (13.9%)	93 (14.9%)	6 (6.7%)	5 (15.78%)
55-64	156 (20.6%)	137 (21.5%)	13 (13.7%)	6 (20%)
65-74	179 (25%)	143 (22.7%)	27 (28.8%)	9 (27.65%)
>75	217 (29.9%)	162 (25.9%)	44 (49%)	9 (29%)
Male	447 (59.78%)	377 (60.9%)	51 (57%)	20 (65.88%)
Obesity				
BMI of 40 kg/m^2	59 (8%)	50 (8%)	9 (9.89%)	2 (7%)
BMI of 30-40 kg/m^2	246 (32.78%)	205 (32.78%)	30 (33%)	8 (25%)
BMI of 25-30 kg/m^2	246 (32.76%)	199 (31.87%)	32 (34.88%)	10 (31.87%)
BMI of <25	171 (22.9%)	143 (22.89%)	20 (21%)	11 (34.75%)
Unknown	23 (3%)	25 (3.78%)	1 (1%)	0
Chronic illness	626 (83.9%)	504 (80.9%)	92 (100%)	30 (98.78%)
Coronary artery disease	119 (15.8%)	75 (12%)	31 (33.83%)	12 (38.9%)
Heart failure	82 (10.9%)	37 (6%)	27 (29%)	13 (41%)
Hypertension	454 (60.72%)	336 (54%)	81 (87.88%)	25 (94.57%)
Diabetes mellitus	276 (36.89%)	199 (31.77%)	52 (57%)	21 (68%)
Hypercholesteremia	343 (46%)	249 (40%)	69 (74.96%)	21 (68.8%)
Asthma or chronic obstructive pulmonary disease	127 (16.71%)	93 (14.79%)	26 (28%)	5 (16%)
Malignancy	89 (11.88%)	62 (9.9%)	18 (19.90%)	4 (12%)
Haemodynamic parameters				
SpO_2 <88% at admission	119 (15.9%)	99 (15.89%)	12 (12.96%)	5 (14%)
Systolic BP <100 mmHg at admission	75 (9.9%)	37 (6%)	7 (8%)	4 (11.84%)

observed that mortality decreased in the preceding months in case of all strata of patients. It was probably because the pandemic wore on. ICU hospitalization was slightly on the higher side in case of NO-CKD patients compared with NO-HD-CKD and ESRD. Furthermore, duration of hospital stay was almost equal in all three groups as well as in case of use of high-flow nasal oxygenation (HFNO). A higher proportion of cases with ESRD did need mechanical ventilation [Table 1]. AKI was developed commonly in NO-HD-CKD in comparison to NO-CKD (56.98% versus 27.78%) [Table 2]. Patients admitted in ICU had outcomes in terms of discharge or deceased [Table 3]. NO-HD-CKD had the highest crude expiry rates (59%). Higher mortality was found in the ESRD group in comparison to NO-CKD group. ESRD status was observed to have no significant increase in

Table 2: Laboratory findings of patients

Laboratory data, median value (IQR)	Total no. of patients (*n*=745)	NO-CKD patients (*n*=622)	NO-HD-CKD patients (*n*=92)	ESRD patients on haemodialysis (*n*=31)
D-dimer (ng/ml)	409 (249-726)	400 (240-756)	432 (289-899)	450 (334-1045)
Potassium (mEq/l), maximum	4.2 (3.8-4.6)	4.5 (3.8-4.8)	4.6 (3.9-4.9)	4.8 (4.05-5.3)
Sodium (mEq/l), maximum	136 (133-139)	136 (133-139)	137 (134-140)	137 (133-139)
Creatinine (mg/dl), baseline	1.1 (0.8-1.46)	0.94 (0.79-1.21)	1.67 (1.2-2.64)	7.013 (4.2-9.465)
eGFR (ml/min./1.73m^2)	NA	>60 (56-60)	42 (25.4-54.2)	NA
CRP (mg/dl)	100 (48.6-156)	119.23 (51.6-164)	106.2 (49.8-166)	78.8 (28.78-130.2)
Bicarbonate (mmol/l), minimum	23 (21-26)	24 (23-26)	22 (17-24)	21 (20-28)
Ph	7.36 (7.35-7.55)	7.40 (7.35-7.55)	7.32 (7.26-7.40)	7.34 (7.30-7.40)
LDH (U/L)	530 (300-1000)	550 (300-900)	603 (350-950)	590 (360-920)
AKI	231 (30.9%)	174 (27.78%)	52 (56.98%)	NA
Use of HFNC	60 (8%)	50 (8%)	7 (8%)	2 (7%)
Mechanical ventilation	164 (21.67%)	131 (20.88%)	20 (21.99%)	8 (26.87%)
Duration of hospital stay (days)	8 (4-12)	7 (3-12)	8 (4-13)	8 (4-11)

mortality risk, in comparison to NO-CKD group, in fully adjusted regression models (OR: 0.82; 95% CI: 0.51–1.32) [Table 4]. It was also observed that NO-HD-CKD had the highest expiry rates, and on univariate analysis, it was associated with higher mortality (OR: 1.57; 95% CI: 1.31–1.91), while in fully adjusted model, it was found to be insignificant (OR: 1.10; 95% CI: 0.88–1.40). Lastly, we directly compared ESRD to NO-HD-CKD in fully adjusted models; ESRD had decreased odds of overall mortality (OR: 0.57; 95% CI: 0.33–0.95).

Table 3: Outcomes of NO-CKD, NO-HD-CKD and ESRD groups in ICU care

CKD status	Discharged to home *n* (%)	Expired *n* (%)	*P*
NO-CKD (622)	557 (89.54%)	65 (10.45%)	0.539
NO-HD-CKD (92)	38 (41.30%)	54 (58.69%)	
ESRD (31)	16 (51.61%)	15 (48.39%)	

Table 4: Logistic regression models for ICU-admitted COVID patients during the third wave of the pandemic

Mortality	Odds ratio estimate (95% CI)	*P*
NO-HD-CKD vs NO-CKD		
Unadjusted	1.57 (1.31-1.91)	<0.001
Model 2	1.05 (0.85-1.32)	0.60
Fully adjusted	1.10 (0.88-1.40)	0.36
ESRD vs NO-CKD		
Unadjusted	1.14 (0.77-1.69)	0.47
Model 2	0.78 (0.50-1.23)	0.30
Fully adjusted	0.82 (0.51-1.32)	0.43

Model 2 includes adjustment for age, sex, race/ethnicity, smoking status, obesity, coronary artery disease, heart failure, hyperlipidaemia, hypertension, diabetes, pulmonary, and cancer. Fully adjusted includes adjustments in model 2 and adjustments for oxygen saturation, temperature, systolic BP, D-dimer, and week of admission

Discussion

In this study during the third wave of the COVID-19 pandemic, it was observed that there was increased incidence of severe illness and comparatively low mortality among patients hospitalized with COVID-19 infection. Comparison of outcomes between NO-HD-CKD and ESRD in the third wave of the COVID-19 pandemic was observed. Here, it was found that mortality was highest among those with NO-HD-CKD, whereas patients with ESRD not only had decreased mortality than those with NO-HD-CKD, but they also had higher ICU mortality compared with NO-CKD group.

Overall, these observations support the idea that the presence of ESRD does not independently increase the risk of death or COVID-19-related critical illness, and that the high mortality rates reported in this population are likely due to the presence of unfavourable demographics and comorbidities. Although patients with NO-HD-CKD and who have COVID-19 in this study had substantially increased mortality rates than those with NO-CKD, variations in age and comorbidities eliminated the increased risk, highlighting the importance of age and comorbid conditions in outcomes for this subset of patients. This may attribute to the fact that this group was, on an average, 10 years older than patients without CKD, and comorbidities such as diabetes, heart disease, and chronic obstructive pulmonary disease were nearly two to three times more prevalent. Unexpectedly, we found that patients with ESRD had a lower incidence of mortality than individuals with NO-HD-CKD. CKD has been proven to be a significant risk factor for the development of AKI in patients with hypertension, diabetes, or after major surgery.[22,23] CKD may induce increased propensity toward developing AKI through chronic inflammation, mitochondrial and vascular dysfunction, or abnormal cell signalling and autophagy.[24] In this study, overall mortality rate among admitted patients with ESRD was 17.44%, while in other studies from New York, Spain, and Italy, mortality rates were 28%–31%.[25] Of note, the time period of study in our population was significantly less, and there was improvement in mortality in later months. When compared with patients with NO-HD-CKD, patients with ESRD in our study group were younger and had lower obesity rates and less comorbidities. The relative reduction in mortality risk versus those with NO-HD-CKD persisted in models adjusting for these factors. It is tempting to hypothesize that patients with ESRD, who have an impaired immune response in the setting of uraemia, may have a less profound cytokine storm, but this

hypothesis needs further study. Although patients with ESRD had higher overall mortality rates than patients with NO-CKD—as with patients with NO-HD-CKD—these differences were no longer significant after adjusting for confounders.

This underscores the importance of demographics and comorbidities as greater determinants of COVID-19 outcomes. Furthermore, our findings imply that the presence of ESKD does not increase the risk of mortality among patients admitted with COVID-19, and may, in fact, be associated with reduced mortality compared to NO-HD-CKD. As per our knowledge, only few studies have reported individual outcomes for both NO-HD-CKD and ESRD in the same patient population, or compared the two directly; perhaps, by mixing these groups together in prior studies, it might have masked important and differential effects of these CKD stages on the outcomes associated with COVID-19 illness.

Our study has numerous strengths, including a diverse patient population, the capture of admissions over a period from December 2021 to February 2022, demonstrating changes in mortality over time, individual reporting of outcomes for NO-HD-CKD and ESRD on a variety of characteristics and outcomes, within a single cohort and the focus being on patients admitted primarily for COVID-19 and not those who incidentally tested positive on admission for other medical conditions.

Limitations

There were several limitations to our study, including the study being retrospective; urinalysis and kidney images were not routinely analysed because they were not regularly available in the pandemic; and data was collected using electronic health records. It is possible that the patients were more likely to be labelled as NO-HD-CKD at more severe CKD stages; therefore, milder forms of CKD could be missed and this could potentially increase the magnitude of effect of NO-HD-CKD on mortality, although this may not explain our findings regarding the lack of association of ESRD with adverse outcomes. It might be possible that patients with preadmission, community-acquired AKI were also misclassified as having CKD, which would tend to bias our results because AKI is more likely to be associated with adverse outcomes. Still, this would not affect the results demonstrating a similar ICU mortality between patients with ESRD and those with NO-CKD.

Conclusion

In view of these results, we consider that all spectrum of CKD patients are exposed to considerably higher risk of death during hospitalization due to COVID-19. CKD patients requiring hospitalization due to COVID-19 suffer from significantly increased risk of death due to higher incidence of AKI during the episode, which considerably worsens prognosis.

To summarise, we found that crude hospital mortality from COVID-19 was highest among patients with NO-HD-CKD, followed by those with ESRD, and then those with NO-CKD. Patients with ESRD had reduced odds of mortality versus those with NO-HD-CKD, whereas the risk of mortality was lower in those without CKD in fully adjusted analyses. Further studies are required to substantiate as mortality, regardless of CKD status, improved significantly in later months of the third wave of the pandemic.

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Key points

1. Each and every COVID-19 wave affected the practice of primary care physicians. Unawareness of various complications and their management and proper referral lead to unsatisfactory results.
2. CKD patients have impaired immune status, which is why these patients are prone to develop infection-related complications that further cause increased morbidity, mortality, and worsening of COVID-19 outcomes in comparison to the general population.
3. NO-HD-CKD patients have overall highest mortality in comparison to NO-CKD and ESRD patients. Reduced kidney function causes increased risk of COVID-19 infection.
4. In this COVID times, it is the responsibility of all primary care physicians to be trained and have proper knowledge of infection prevention, control and proper referral of the patients to higher centres.
5. We require a sustainable and integrated global infrastructure to recognize evidence-based approaches to reduce transmission of infection and worse results.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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