Observational Study

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# High dependency renal unit for the management of COVID-19 in patients with severe acute or chronic kidney disease

Sayali Thakare, DM[a], Tulsi Modi, MD[a], Chintan Gandhi, MD[a], Sreyashi Bose, MD[a], Satarupa Deb, MD[a], Abhinav Katyal, DM[a], Nikhil Saxena, DM[a], Ankita Patil, DM[a], Sunil Patil, DM[a], Atim Pajai, DNB[a], Divya Bajpai, DM[a], Pratap Jadhav, Msc[b], Tukaram Jamale, DM[a,*]

**Abstract**

Coronavirus disease 2019 (COVID-19) in patients with severe impairment of kidney function is associated with high mortality. We evaluated the effect of high dependency renal unit (HDRU), with nephrologists as primary care physicians, as a quality improvement initiative for the management of these patients. This was a quasi-experimental observational study conducted at a tertiary care hospital in western India. Patients hospitalized for COVID-19 with pre-existing end-stage-renal-disease and those with severe AKI requiring dialysis (AKI-D) were included. For the first 2 months, these patients were cared for in medical wards designated for COVID-19, after which HDRU was set up for their management. With nephrologists as primary care providers, the 4 key components of care in HDRU included: care bundles focusing on key nephrology and COVID-19 related issues, checklist-based clinical monitoring, integration of multi-specialty care, and training of nurses and doctors. Primary outcome of the study was in-hospital mortality before and after institution of the HDRU care. Secondary outcomes were dialysis dependence in AKI-D and predictors of death. A total of 238 out of 4254 (5.59%) patients with COVID-19, admitted from 28th March to 30th September 2020, had severe renal impairment (116 AKI-D and 122 end-stage-renal-disease). 145 (62%) had severe COVID-19. From 28th May to 31st August 2020, these patients were managed in HDRU. Kaplan–Meier analysis showed significant improvement in survival during HDRU care [19 of 52 (36.5%) in pre-HDRU versus 35 of 160 (21.9%) in HDRU died, $P \leq .01$]. 44 (67.7%) AKI-D survivors were dialysis dependent at discharge. Breathlessness and altered mental status at presentation, development of shock during hospital stay, and leukocytosis predicted mortality. HDRU managed by nephrologists is a feasible and potentially effective approach to improve the outcomes of patients with COVID-19 and severe renal impairment.

**Abbreviations:** AKI = acute kidney injury, AKI-D = acute kidney injury requiring dialysis, CKD = chronic kidney disease, COVID-19 = coronavirus disease 2019, ESRD = end stage renal disease, HCQS = hydroxychloroquine sulfate, HDRU = high dependency renal unit, ICU = intensive care unit, KEMH = King Edward Memorial (VII) Hospital.

**Keywords:** acute kidney injury, COVID-19, dialysis, high-dependency-renal-unit, end-stage-renal-disease

## 1. Introduction

Patients with kidney disease are prone to severe acute respiratory syndrome coronavirus 2 infection, and are more likely to get severe coronavirus disease 2019 (COVID-19) due to highly prevalent risk factors such as advanced age, hypertension, diabetes, and cardiovascular disease.[1–3] COVID-19 in patients with end stage renal disease (ESRD) is associated with high mortality.[4] Similarly, several reports have highlighted the severity of acute kidney injury (AKI) in COVID-19 illness, which is associated with high mortality as well.[5] A significant number of AKI survivors remain on dialysis at the time of discharge from the hospital.[5,6] Treatment of COVID-19 is largely supportive, and except dexamethasone, no therapy has shown survival benefit.[7] Remdesivir was the first drug to be approved for use in COVID-19.[8] Recent evidence has emerged from randomized controlled trials pointing towards the potential benefit of antivirals-molnupiravir,[9]

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*[a] Department of Nephrology, Seth GS Medical College and KEM Hospital, Mumbai, India, [b] Department of Epidemiology and Demography, Seth GS Medical College and KEM Hospital, Mumbai, India.*

**Correspondence: Tukaram Jamale, Department of Nephrology, Seth GS Medical College and KEM Hospital, Ward 34A, 3rd Floor, Old Hospital Building, Mumbai 400012, India (e-mail: tukaramjamale@yahoo.co.in).*

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nirmatrelvir-ritonavir,[10] fluvoxamine,[11] and monoclonal antibodies.[12]

Typically, hospitalized patients with renal impairment have multiple co-morbidities, commonly diabetes and hypertension. They also have medical issues secondary to kidney failure and its complications, for example, fluid-electrolyte disturbances, blood pressure derangements, inadequate dialysis, vascular access dysfunction, and catheter-related blood stream infections. These demand immediate attention by nephrologists even when a patient is hospitalized for reasons not directly related to kidney disease. Failure to address these may contribute to the excess mortality observed with COVID-19 in this population. Close coordination among the admitting and other involved specialties, including paramedical staff and dialysis technicians, is needed to avoid fragmentation of care. Therefore, patients with COVID-19 needing dialysis represent one of the most vulnerable subsets of COVID-19 patients. Strategies to improve outcomes in these patients are needed. We present here our pragmatic experience of a high dependency renal unit (HDRU), which was set up to optimize the management of COVID-19 in patients receiving hemodialysis for acute or chronic kidney disease. Primary outcome of the study was in-hospital mortality before and after institution of the HDRU care. Secondary outcomes were dialysis dependence in severe AKI and predictors of death.

## 2. Methods

Our hospital, the King Edward (VII) Memorial Hospital (KEMH), Mumbai, is an 1800-bedded tertiary care teaching hospital in western India and is one of the largest public hospitals designated for hospitalization of patients with COVID-19. KEMH started admitting patients with COVID-19 and kidney diseases from 28th March 2020. We enrolled consecutive patients with ESRD developing COVID-19 and hospitalized COVID-19 patients developing severe AKI requiring dialysis (AKI-D) for the study. This quasi-experimental observational study was approved by Institutional Ethics Committee, KEMH, Mumbai. Waiver of consent was obtained from the Institutional Ethics Committee (EC/OA/96/2020, dated 10/06/2020) and study was registered at Clinical Trial Registry of India (CTRI/2020/06/026152), date of registration-26/06/2020. Data collection was done from patients' hospital records scrutinized on the day of discharge/death.

For the initial 2 months, that is, from 28th March to 28th May 2020, patients were admitted to either dedicated COVID-19 wards or the COVID-19 intensive care unit (ICU) depending upon the severity of illness. These units were managed by primary care physicians. Patients were evaluated by nephrology service within 2 hours of hospitalization and subsequently, were attended once daily for decisions regarding need of dialysis initiation/discontinuation, fluid therapy, diuretics, drug dosing, and treatment of primary renal disease. Following data were obtained at admission: demographic details, co-morbidities, vital parameters -temperature, heart rate, respiratory rate, blood pressure (supine and sitting/standing position), assessment of hydration, and review of systems. Oxygen saturation on room air, arterial blood gas, and chest x-ray were obtained from all patients. Severe COVID-19 illness was defined as oxygen saturation less than <94% or any need of oxygen therapy. AKI was defined by Kidney Disease Improving Global Outcomes criteria. Routine laboratory evaluation included complete blood count, renal, and liver chemistries. C reactive protein, lactate dehydrogenase, D-dimer, interleukin 6, and ferritin were done for selected cases. High Resolution Computed Tomography of chest was obtained in patients with severe disease or when felt necessary by treating physician. Sudden surge of the cases needing dialysis, need of frequent assessments, decision about initiation and discontinuation of renal support, distribution of patients across various wards and ICUs, limited manpower and dialysis slots, and requirement of patient transfer (when stable) for dialysis created significant logistic challenges in patient management.

At the same time, COVID-19 treatment strategies were continually evolving at international, national and local levels. Following an early 2-month audit of outcomes of all COVID-19 patients, the hospital administration dedicated a 45-bedded ward, COVID-19 HDRU, to the care of COVID-19 patients with acute and chronic renal disease, considering the high volume and specific needs of these patients. HDRU was to be managed primarily by the nephrology team and was located near the 13-bedded COVID-19 dialysis unit for facilitating smooth transfers. Figure 1 gives an overview of the number of patients cared for before and after the institution of HDRU.

HDRU was staffed with 4 staff nephrologists, 3 nephrology fellows, 10 resident medical officers, 14 nurses (including 4 dialysis nurses), 14 patient care assistants and 8 dialysis technicians in shift duties. Duty doctors and nurses received training sessions conducted by staff nephrologists. These were repeated every 2 weeks for the new batch on rotation. The sessions included an overview of management of severe renal impairment, acute dialysis procedure, monitoring during hemodialysis, acute complications related to dialysis, dialysis access care and basic management of COVID-19. Staff and fellows from non-clinical specialties were in charge of logistics of running the unit, provision of essential medical supplies and drugs, management of manpower, duty schedules of fellows, managing daily log and reporting of new cases, deaths, discharges, transfers in and out of the unit and communication with patient's relatives by daily telephonic calls (Figs. 2 and 3).

Upon admission to HDRU, patients were clinically evaluated by fellows on duty every 6 hours. Assessment included subjective assessment, vital parameters, focused review of systems, oxygen saturation, blood glucose, and arterial blood gas if needed. Three staff nephrologists (in 3 duty shifts) evaluated patients daily focusing on vital parameters, volume status, need of fluids or diuretics, indicators of uremia and parameters concerning change in the severity of COVID-19. They made decisions about the conservative management of AKI, need of starting or stopping dialysis, initiation of steroids, antivirals, prophylactic antibiotics, anticoagulants, other anti-inflammatory agents and management of respiratory support. Standard dose modifications for renal impairment were followed for all drugs and antibiotics. Inj. Remdesivir was administered as 200 mg loading dose followed by 100 mg once daily for 5 days (total 600 mg) after written informed consent. Depending upon the severity of hypoxia, patients received oxygen therapy by nasal canula, venturi mask, non-rebreathing mask, high flow nasal cannula or non-invasive ventilation.

Checklist of the key clinical parameters to be monitored every sixth hourly was followed by staff nurses and duty doctors for patient monitoring. Staff nephrologists ensured that the crucial clinical issues (related and unrelated to COVID-19) were addressed as soon as possible after admission by completing the care bundle (Table 1). The unit got priority consultation from radiology, cardiology, chest medicine, surgery, psychiatry, and urology for cross specialty referral care (for e.g., point of care ultrasound imaging of kidneys and urinary tract, inferior vena cava diameter, 2D-echocardiography, respiratory medicine, surgical debridement and dressings, patient counselling, urological evaluation). In-charge nephrologists, who made final decisions on the treatment, acted as primary physicians responsible for close coordination among various specialties.

Patients with worsening hypoxemia, hemodynamic instability, worsening AKI, and severe organ dysfunction were triaged for more intensive monitoring, which included continuous monitoring of oxygen saturation, heart rate, rhythm, respiratory rate and blood pressure. Triaged patients were discussed daily on a telephonic conference call which followed the staff nephrologists' morning clinical rounds. This was attended by all staff nephrologists and fellows to facilitate smooth communication

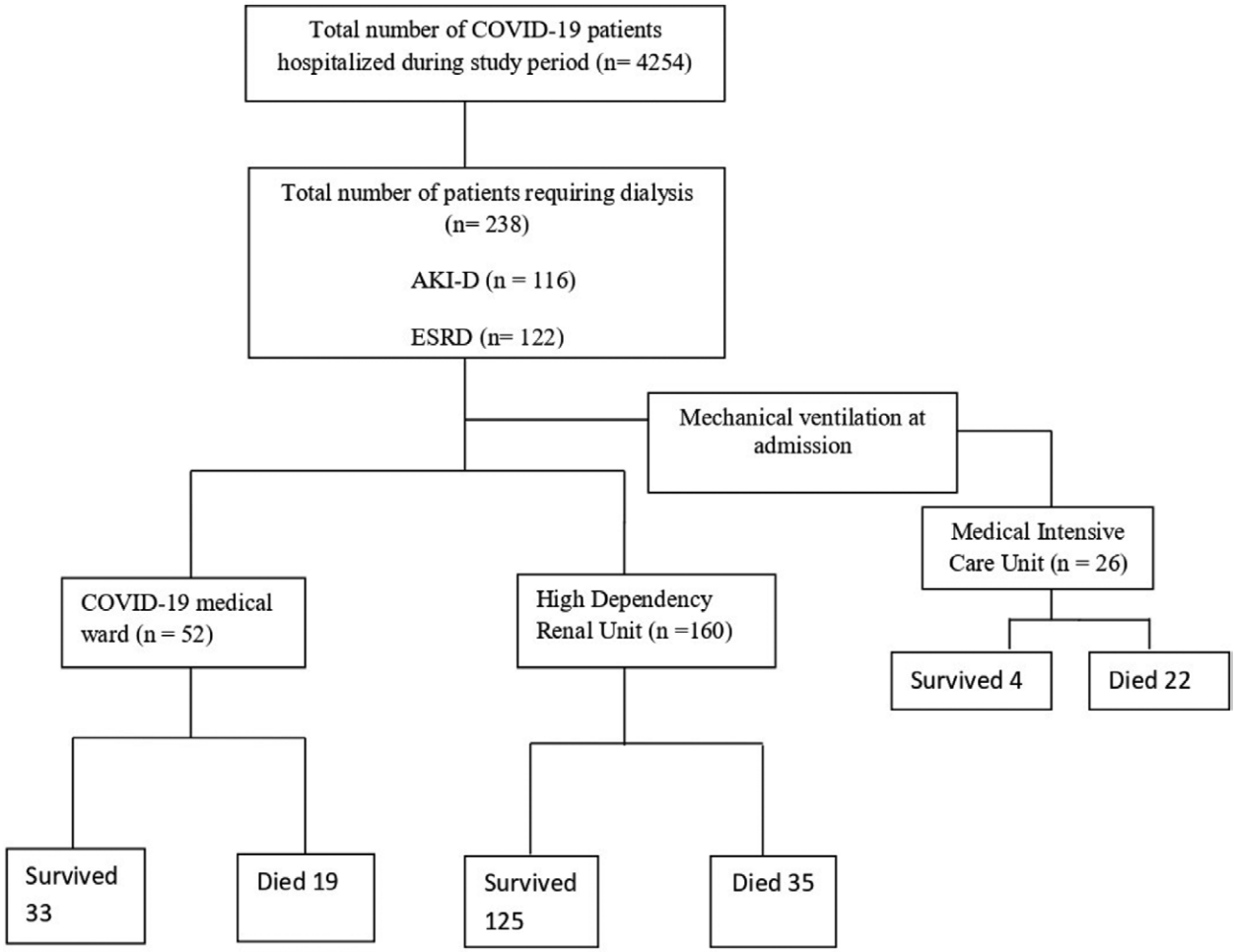


**Figure 1.** Study flow chart. Analysis of predictors of mortality (n = 234, AKI-D-116, ESRD-118), excluding 4 patients in ESRD cohort with missing data (transferred to other centres-3, missing records-1). AKI-D = acute kidney injury requiring dialysis, ESRD = end stage renal disease.

across the duty shifts. Management decisions including initiation of anti-inflammatory and antiviral treatments (steroids, tocilizumab, and remdesivir) were also made during this call conference. In addition, all the patients with severe COVID-19 or with clinical worsening were discussed in an interdisciplinary critical care team meeting daily. This critical care committee consisted of senior physicians from pulmonology, anesthesiology, cardiology, diabetology, and intensive care. Patients needing intubation or invasive mechanical ventilation were transferred to ICUs. Patients were considered for discharge after being asymptomatic for 5 days, room air oxygen saturation above 94% with no subjective sense of breathlessness and documentation of 2 negative Reverse Transcriptase Polymerase Chain Reaction swab tests, done 5 days apart.

### 2.1. COVID-19 hemodialysis unit

A dedicated 13-bedded hemodialysis unit for dialysis of these patients was maintained adjacent to the HDRU. This was staffed with one nephrology fellow, one resident medical officer, one dialysis nurse, and one dialysis technician round the clock. Intermittent hemodialysis was continued for patients on maintenance hemodialysis. Slow low efficiency dialysis (QB 200, QD 300, duration 6–8 hours) was preferred for patients with hemodynamic instability. In patients with AKI, we followed the strategy of delayed initiation of dialysis-initiation only when clinically indicated for any of the following: refractory fluid overload, hyperkalemia, severe metabolic acidosis, alteration of the mental status attributable to uremia, or need of blood transfusion in the setting of oligo-anuria. Alternate daily dialysis was continued until recovery or discharge from the hospital. Hemodialysis unit was equipped with facilities to provide high flow nasal oxygen, non-invasive and invasive ventilation in case of deterioration in oxygen saturation during dialysis treatment. Patients during hemodialysis were monitored for vital parameters, continuous cardiac monitoring, and pulse oximetry.

### 2.2. Statistical analysis

Statistical analysis was done using International Business Management® SPSS® Statistics software version 26 (IBM Corp., Armonk, NY). Quantitative variables were expressed as mean (standard deviation). Qualitative variables were expressed as numbers with percentage. Chi square or Fischer exact test was used for categorical data and independent samples *t* test was used for continuous data. Comparison of baseline, clinical and laboratory parameters between survivors and non-survivors was first done independently for AKI-D and ESRD groups, then for the combined group of all dialysis requiring patients. Comparison of these parameters was done for patients in the total cohort before and after implementation of HDRU. Primary outcome of the study was in-hospital mortality which was compared between pre and post HDRU cohorts. Causes of death were adjudicated by nephrologists treating the patients. Predictors of renal outcome (need of dialysis at discharge from hospital) in AKI-D group were analyzed. Depending on the

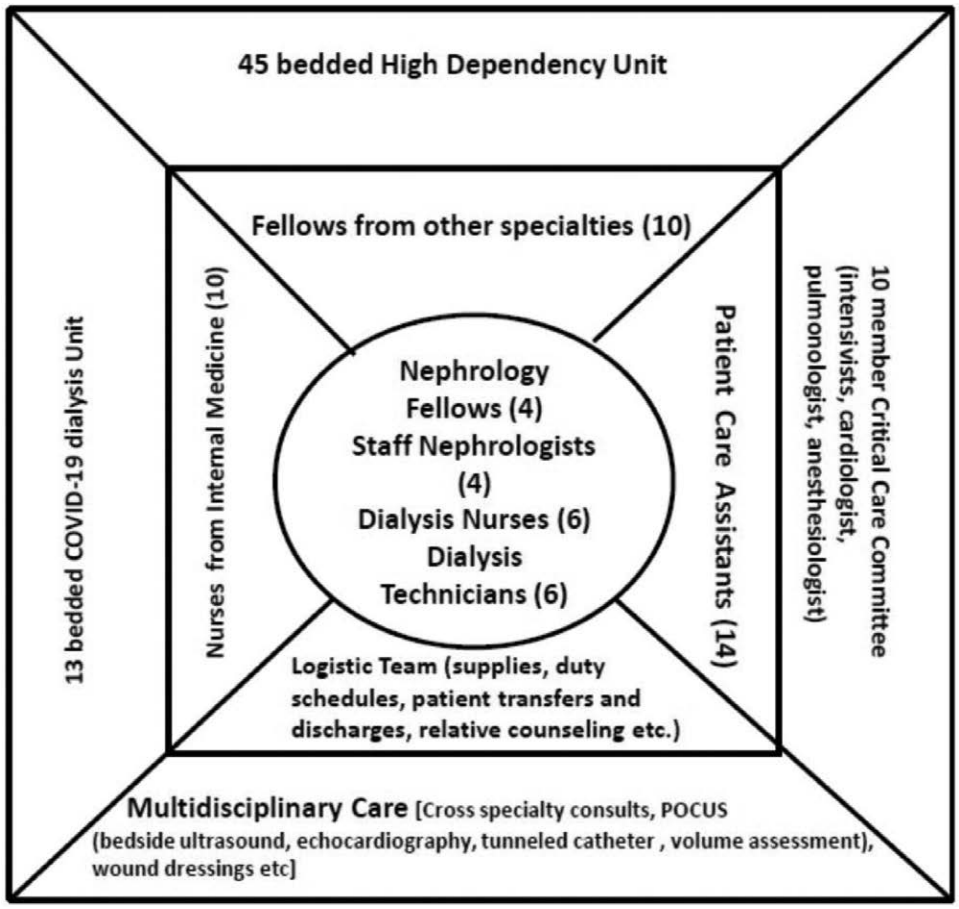


**Figure 2.** Structure of high dependency renal unit. COVID-19= coronavirus disease 2019, POCUS = point of care ultrasound.

nature of the variable, one or 2-sided *P* value < .05 was taken for statistical significance in univariate and multivariate analyses. Kaplan–Meier survival curves were generated for comparing pre and post HDRU survival, and comparison was done using log-rank test. A proportional monthly mortality rate was calculated by entering numerator as number of deaths in a given month and denominator as total number of patients cared for.

## 3. Results

Out of 4254 COVID-19 positive patients admitted to our hospital from 28th March 2020 to 30th September 2020, 238 (5.59%) patients had severe renal impairment (116 AKI-D and 122 ESRD). 52 of these patients were treated in COVID-19 medical wards or ICU from 28th March to 28th May 2020 before the institution of HDRU. From 29th May to 31st August, 160 patients received treatment in HDRU. Baseline characteristics of the entire cohort, AKI-D and ESRD cohorts are summarized in Tables 2, 3 and 4 respectively.

Mean age of the study population was 50.4 years and 152 (64.9%) were men. Hypertension, diabetes, and cardiovascular disease were present in 180 (76.9%), 96 (41.0%), and 41 (17.5%) respectively. Common presenting clinical features included fever 136 (58.1%), breathlessness 132 (56.7%), cough 59 (25.2%), vomiting 44 (18.8%), and diarrhea 30 (12.8%). Severe COVID-19 was present in 145 (62%) of 234 patients during the course of hospitalization. All the patients were treated with intermittent hemodialysis or slow low efficiency dialysis (except 1 patient who was treated with acute peritoneal dialysis).

Shock at presentation, shock during hospital stay and sepsis were present in 19 (8.1%), 57 (24.4%) and 48 (20.5%) patients, respectively. 145 (62%) of all patients required oxygen supplementation at admission or during hospital stay. Oxygen requirements at admission were nasal prongs- 1 (0.43%), face mask- 45 (19.2%), non-rebreathing mask- 45 (19.2%), non-invasive mechanical ventilation- 9 (3.8%), and invasive mechanical ventilation- 4 (1.7%). 24 (20.6%) and 17 (14.4%) patients in AKI-D and ESRD group developed need of respiratory support after admission. 36 (31%) patients with AKI-D and 16 (13.5%) patients with ESRD needed mechanical ventilation during the stay (see Table S1, Supplemental Digital Content 1, http://links.lww.com/MD/H206). Only 3 out of 122 (2.5%) patients in ESRD group had a documented episode of Acute Coronary Syndrome during ward stay, and all recovered with medical management. Steroids, hydroxychloroquine, and remdesivir were given in 142 (61.5%), 111 (46.6%), and 45 (19.2%) patients, respectively.

### 3.1. Outcomes

76 (31.9%) of 238 patients died [AKI-D- 51 (43.9%), ESRD-25 (21.2%)]. 19 (36.5%) and 35 (21.9%) patients died in the pre and post HDRU groups. Comparison of baseline, clinical and laboratory features of the patients treated before and after institution of HDRU is summarized in Table 2. Patients cared for in HDRU were older (51.5 years vs 45.3 years, *P* = .012), were more likely to be diabetic (46.5% vs 25%, *P* = .008) and be symptomatic at admission (92.5% vs 77.1%). They also needed longer oxygen therapy (5.7 days vs 3.8 days, *P* = .029). Kaplan–Meier survival analysis showed that introduction of HDRU led to significant decrease in mortality in overall cohort (Fig. 4) and individually in AKI-D group (see Figure S1, Supplemental Digital Content 2, http://links.lww.com/MD/

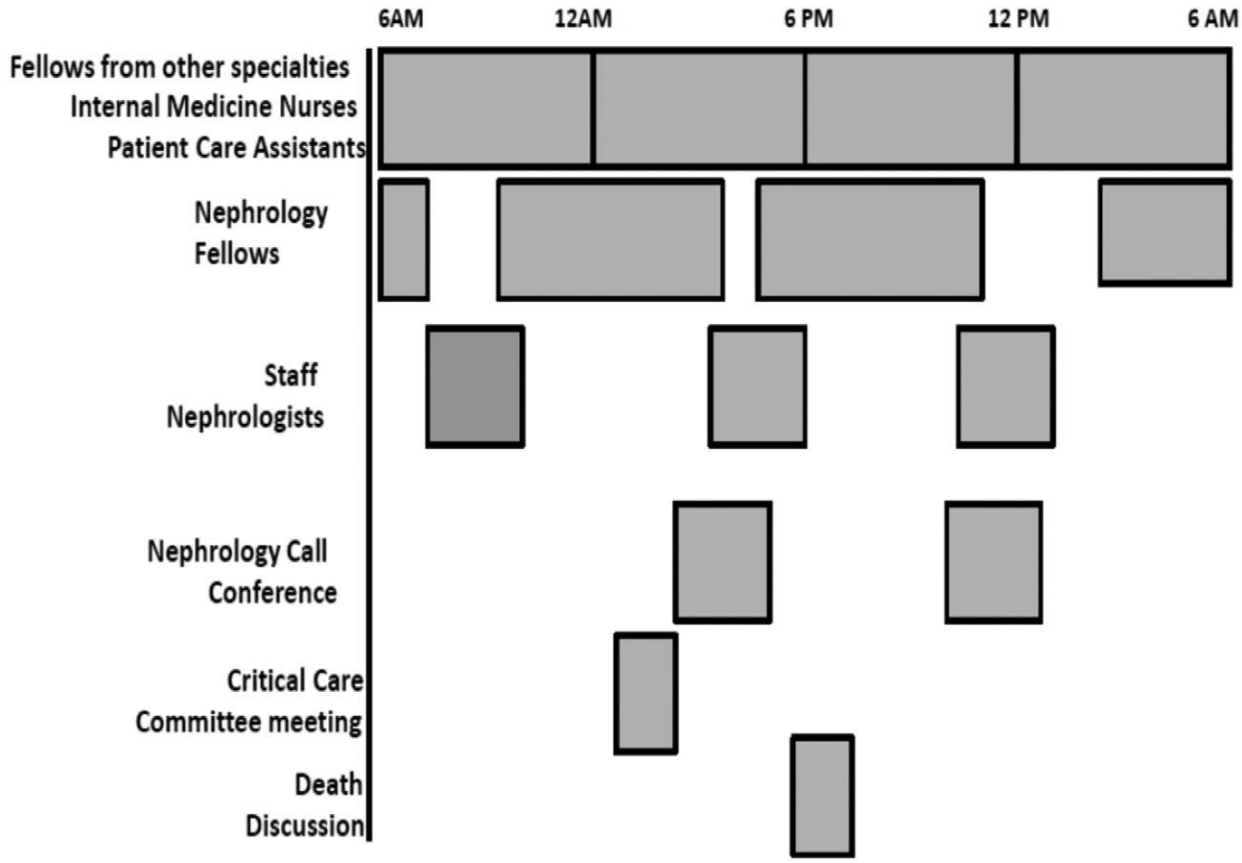


**Figure 3.** Functioning of high dependency renal unit.

H207), and tending towards significance in ESRD group (see Figure S2, Supplemental Digital Content 3, http://links.lww.com/MD/H208). The proportionate monthly mortality for patients is indicated (in Figure S3, Supplemental Digital Content 4, http://links.lww.com/MD/H209). Out of 65 AKI-D survivors, 44 (67.7%) patients remained dialysis dependent. Pre-existing hypertension (77.3% vs 22.7%, $P = .019$) and chronic kidney disease (CKD) (77.6% vs 22.5%, $P = .004$) were associated with dialysis dependence.

### 3.2. Predictors of survival

Among AKI-D cohort, hospitalized patients who expired were more likely to be older (55.8 vs 50.1 years, $P = .040$), have diabetes (56.8% vs 40%, $P = .053$) and cardiovascular disease (27.5% vs 9.2%, $P = .013$). They were more likely to present with breathlessness (74.5% vs 46.9%, $P = .002$), hypoxia (66.7% vs 32.3%, $P = .000$), altered mental status (47.1% vs 10.8%, $P = .000$), leukocytosis ($14{,}311 \times 10^6$/L vs $10{,}116 \times 10^6$/L, $P = .009$), elevated aspartate transaminase (46.24 vs 29.92, $P = .004$), and were more likely to need inotropic support (58.8% vs 15.4%, $P = .000$).

Expired patients in ESRD group were more likely to be older (53.4 years vs 46.8 years, $P = .048$), have cardiovascular disease (32% vs 13.9%, $P = .041$), have breathlessness (76% vs 48.4%, $P = .012$) and cough (48% vs 25.8%, $P = .031$) at admission. They also had lower systolic (122 mm Hg vs 135 mm Hg, $P = .020$) and diastolic (75 mm Hg vs 84 mm Hg, $P = .007$) blood pressures, hypoxia (72% vs 34.8%, $P = .001$), sepsis (28% vs 11.8%, $P = .052$), altered mental status at presentation (20% vs 3.2%, $P = .011$), leukocytosis ($11{,}629 \times 10^6$/L vs $8503 \times 10^6$/L, $P = .009$) and shock during stay (44% vs 6.5%, $P = .000$) as compared to survivors. Severe COVID-19 infection was a risk factor for death in both cohorts in univariate analysis (AKI-D- 82.35% vs 38.46%, $P = .000$, ESRD- 84% vs 38.1%, $P = .001$).

In stepwise forward conditional regression analysis for the entire cohort (see Table S2, Supplemental Digital Content 5, http://links.lww.com/MD/H210), breathlessness and altered mental status at presentation, shock during hospital stay, and leukocytosis were independent predictors of death. For AKI-D cohort, presence of shock at presentation or developing during stay and altered mental status at presentation were the only features predicting mortality. In patients with ESRD, shock at presentation or developing during stay, altered mental status, and severe COVID-19 illness predicted mortality.

### 3.3. Non-COVID-19 issues at admission and cause-specific mortality

49 of 238 patients (20.6%) had significant medical issues apart from COVID-19 at the time of admission, which included tropical infections and sepsis (urinary or dialysis access related) in 28 patients and issues due to underlying medical condition in 21 patients. In ESRD cohort, 35 of 118 (29.6%) had an inter-dialytic interval of >3 days due to missed dialysis sessions prior to admission. 14 (11.9%) had complications related to hemodialysis access at admission. In 25 of 76 (32.9%) patients who died, cause of death was not directly related to COVID-19 acute respiratory distress syndrome. Causes of death in these patients were sepsis (10), cardiac (7), intra-cerebral bleeding (6), malignancy (1), and complications of uremia (1). In patients on Hydroxychloroquine sulphate (HCQS), we did not encounter any cardiac arrhythmias or sudden cardiac deaths, though 7 patients showed QTc

**Table 1**

**Components of high dependency renal unit care.**

| | | Inform If |
|---|---|---|
| Checklist | Heart rate | <60/min or >120/min |
| | Respiratory rate | >30/min |
| | Temperature | >98 F |
| | Oxygen saturation ($sPO_2$) | <94% |
| | Blood pressure, check for orthostasis, relative hypotension | <100 mm Hg or >160 mm Hg systolic or >20 mm Hg fall |
| | Glasgow Coma Scale | Any change |
| | Blood glucose | <70 mg/dL or >250 mg/dL |
| | Urine output | <1 mL/kg/h for 6 hours |
| | Bleeding | Any |
| Care Bundle | *Volume and blood pressure* | |
| | Assess and correct volume depletion/volume overload | |
| | Identify relative hypotension and de-escalate antihypertensive therapy | |
| | *Dialysis and access* | |
| | Ensure dialysis adequacy | |
| | Timely institution and withdrawal of dialysis in AKI-D | |
| | Maintaining functional dialysis access | |
| | Prompt recognition and treatment of CRBSI | |
| | *Therapy related* | |
| | Screen for stress induced hypoxia in patients not on oxygen (6 minutes walk test and ABG analysis) | |
| | Target $O_2$ saturation >94% | |
| | Identify patients for steroids, anticoagulation and remdesivir therapy | |
| | Monitor and treat steroid induced hyperglycemia | |
| Multispecialty care | Fellows from various clinical specialties | |
| | Bedside specialty services (ultrasound, echocardiography, wound management etc) | |
| | Daily Multidisciplinary Critical care committee meeting | |
| | Death discussions | |
| | Daily Teleconferencing among staff and fellow nephrologists | |
| Training | Fellows from other clinical specialties about dialysis basics, monitoring, acute dialysis complications, dialysis access etc | |

ABG = arterial blood gas, AKI-D = acute kidney injury requiring dialysis, CRBSI = catheter related blood stream infection, $sPO_2$ = oxygen saturation.

prolongation (480 milliseconds), which necessitated stopping of HCQS.

## 4. Discussion

Our data suggest that COVID-19 in patients with severe acute or chronic kidney disease requiring dialysis (AKI-D and ESRD) is associated with significant mortality and morbidity. It is feasible for a dedicated nephrology team to deliver high dependency care, implementation of which can lead to improvement in survival. Presence of leukocytosis, breathlessness, altered mental status at presentation, and development of shock during hospital stay identified patients at high risk of death. In patients with AKI, survivors had a high risk of dialysis dependence which was significantly associated with pre-existing CKD and hypertension. To our knowledge, this is the first report of care in a high dependency set up, as a quality improvement initiative led by nephrologists, leading to improved outcomes.

Key components of HDRU, that are, checklist-based close clinical monitoring, care bundle approach focusing on key clinical issues, and integration of multispecialty care by primary care physician-nephrologists, most likely underlie the observed benefits of HDRU. Sudden and unexpected clinical deterioration in an apparently stable patient is not uncommon in COVID-19.[13] In a report from Italy, patient with ESRD and COVID-19 assigned to outpatient management based upon initial evaluation, experienced late clinical deterioration and associated mortality (19% of initially stable patients developed new onset/worsening of interstitial pneumonia, 8% died during follow-up).[14] 41 of 234 (17.5%) patients in our cohort were not hypoxic at admission, but developed deterioration of respiratory status during hospitalization, highlighting the need of monitoring.

Checklist of the key clinical parameters enabled us to quickly identify such patients and triage them for intensive monitoring. Use of checklists for the management of critically ill patients can reduce the errors of omission and improve outcomes[15] and in our experience, their use by medical and nursing staff is feasible and serves as an effective measure. This also simplified the relatively complex process of caring for hospitalized patients on dialysis. Bundle care approach which focused on prompt optimization of hemodynamics, dialysis adequacy, resolution of dialysis access issues, and therapy of COVID-19 ensured that key clinical needs were addressed as soon as possible after admission, saving crucial time in identification and implementation.

20.6% of the patients had major medical issues apart from COVID-19 at admission and 32.9% the deaths were not directly related to COVID-19 acute respiratory distress syndrome. Multi-specialty consultation is required for patients with both CKD and COVID-19 for management of existing co-morbidities,[16,17] which, when unconcerted, can potentially lead to fragmentation of care and contribute to adverse clinical outcomes. Coordination across specialties can be challenging, especially during the time of a pandemic. Daily conference call and critical care committee meeting facilitated direct communication within the team and across the specialties, thus preventing fragmentation of care.

Hospitalized patients with ESRD and AKI-D also pose unique challenges such as management of vascular access, dialysis adequacy, or fluid-electrolyte abnormalities which can be primary reasons for adverse outcomes if not tackled in time. These issues are indeed best managed by attending nephrology teams. For instance, to cite an everyday scenario, relative hypotension, which in critically ill patients is associated with Major Adverse Kidney Events,[18] was observed more often in our study patients who died of severe COVID-19. Staff nephrologists ensured that this was promptly identified and such patients were monitored closely for further deterioration. Such situations make a strong case for involvement of nephrologists as primary care physicians in the management of COVID-19 with associated severe renal function impairment.

Our cohort of AKI-D patients had a high rate of dialysis dependence at discharge, which possibly could be due to high prevalence of CKD at baseline. However, this could also be due to higher survival and discharge rates in our cohort as compared to the reported literature of AKI associated with COVID-19. Large number of patients needing transfer to chronic dialysis also highlights the role of a nephrologist who can plan and counsel regarding modalities of renal support, dialysis access, and follow-up care. High mortality to the tune of 54.5% in the first year, and as high as 22.5% in the first month, early after dialysis initiation has been reported in elderly patients with comorbidities.[19] This highlights importance of the critical period of "transition to renal replacement therapy" where nephrologists play a crucial role.

Higher risk of death reported in men with COVID-19 in general population[17,20] has not been observed in our study. Shock during hospital stay was likely related to severe systemic inflammation at presentation and development of sepsis, which also contributed to mortality. This finding is further supported by association of leukocytosis with mortality. While bacterial sepsis in not a common feature of COVID-19, reported as 3.8% in a series,[21] 21 (9%) of our patients had sepsis at presentation. Patients with CKD and ESRD are 100 to 300 times prone to sepsis associated mortality.[22] Altered mental status at presentation was associated with mortality. This association may be attributable to multisystem involvement in severe COVID-19,

**Table 2**

**Characteristics for pre and post HDRU groups.**

| Variable | Total (n = 234) | Pre-HDRU (n = 48) | HDRU (n = 160) | *P* value |
|---|---|---|---|---|
| Demographic characters and co-morbidities | | | | |
| Age (yr) | 50.4 (15.1) | 45.3 (15.3) | 51.5 (14.9) | .012 |
| Gender, male (%) | 152 (64.9) | 28 (58.3) | 103 (64.8) | .495 |
| Hypertension (%) | 180 (76.9) | 37 (77.1) | 127 (79.9) | .687 |
| Diabetes mellitus (%) | 96 (41.0) | 12 (25) | 74 (46.5) | .008 |
| Cardiovascular disease (%) | 41 (17.5) | 9 (18.8) | 24 (15.1) | .510 |
| Clinical features at admission | | | | |
| Symptomatic at admission (%) | 210 (89.7) | 37 (77.1) | 147 (92.5) | .007 |
| Fever (%) | 136 (58.1) | 28 (58.3) | 90 (56.6) | .869 |
| Cough (%) | 59 (25.2) | 13 (27.1) | 41 (25.8) | .853 |
| Breathlessness (%) | 132 (56.7) | 26 (54.2) | 89 (56.3) | .869 |
| Vomiting (%) | 44 (18.8) | 7 (14.6) | 33 (20.8) | .409 |
| Diarrhoea (%) | 30 (12.8) | 5 (10.4) | 20 (12.6) | .804 |
| Sepsis at presentation (%) | 48 (20.5) | 7 (14.6) | 31 (19.5) | .527 |
| Shock at presentation (%) | 19 (8.1) | 3 (6.3) | 11 (6.9) | 1.000 |
| Altered mental status (%) | 39 (16.7) | 9 (19.1) | 22 (13.8) | .362 |
| Hypoxia at admission (%) | 130 (55.6) | 21 (43.8) | 66 (41.5) | .868 |
| Laboratory parameters at admission | | | | |
| Hemoglobin (g/dL) | 8.6 (2.5) | 8.7 (2.5) | 8.5 (2.6) | .680 |
| Total leukocyte count (cells $\times 10^6$/L) | 10,571 (7116) | 9505 (6680) | 10,285 (6755) | .506 |
| Platelets (cells $\times 10^9$/L) | 206 (97.6) | 186 (99.9) | 206 (83.8) | .210 |
| Blood urea nitrogen (mg/dL) | 72.7 (48.3) | 63.7 (25.4) | 74.3 (51.5) | .076 |
| Creatinine (mg/dL) | 9.7 (5.4) | 11.3 (5.4) | 9.6 (5.6) | .065 |
| Sodium (meq/L) | 131.7 (6.4) | 132.1 (5.7) | 131.1 (6.4) | .392 |
| Potassium (meq/L) | 4.9 (1.1) | 5.2 (1.0) | 4.9 (1.1) | .073 |
| AST (IU/L) | 37.8 (27.5) | 36.1 (19.7) | 36.9 (27.5) | .858 |
| ALT (IU/L) | 34.5 (68.2) | 22.6 (15.8) | 37.1 (77.6) | .260 |
| Treatment and course of stay | | | | |
| Inotrope use (%) | 57 (24.4) | 12 (25) | 36 (22.6) | .702 |
| Requirement of blood transfusions (%) | 93 (40.4) | 18 (37.5) | 68 (43.3) | .508 |
| Steroids (%) | 142 (61.5) | 28 (58.3) | 94 (59.9) | .868 |
| Remdesivir (%) | 45 (19.2) | 0 (0) | 35 (22) | .000 |
| Heparin (%) | 78 (33.8) | 16 (33.3) | 50 (31.8) | .861 |
| HCQS (%) | 111 (48.1) | 44 (91.7) | 62 (39.5) | .000 |
| COVID-19 stage | | | | .000 |
| Mild (%) | 89 (38.0) | 17 (35.4) | 68 (42.5) | |
| Severe (%) | 145 (62.0) | 31 (64.6) | 92 (57.5) | |
| Duration of $O_2$ requirement (d) | 5.3 (7.1) | 3.8 (4.2) | 5.7 (7.9) | .029 |

ALT = alanine transaminase, AST = aspartate transaminase, COVID-19 = coronavirus disease 2019, HCQS = hydroxychloroquine sulphate, HDRU = high dependency renal unit, $O_2$ = oxygen.

severe uremia due to missed regular dialysis sessions or sepsis itself. 35 (28.5%) patients missed their scheduled dialysis sessions after diagnosis of COVID-19 as indicated by a long interval of >3 days from their last dialysis session. This highlights the importance of rapid evaluation and management of sepsis (with antimicrobials or access removal) and optimization of dialysis dose in these patients.

Our study has limitations. Being an observational study, definite conclusions about survival benefits of HDRU cannot be made. Imbalances in the baseline characteristics of the patients were noted in the pre and post HDRU cohorts. Patients in post-HDRU cohort were older, more likely to be diabetic, present with symptoms, need oxygen for longer duration, were less likely to receive HCQS, and more likely to receive remdesivir. All the aforesaid factors (except availability of remdesivir) indicate a sicker HDRU cohort, and yet better outcomes were observed against this unfavorable baseline. With respect to remdesivir therapy, large data showed only reduction in the time to recovery, with no effect on mortality, and hence its use is unlikely to be the sole cause for better outcomes observed in HDRU.[23] Patients receiving HCQS were monitored regularly for QT interval and arrhythmias, and sudden cardiac deaths were not observed in these patients. Therapy of COVID-19 evolved during the study period and learning curve issues rather than drugs used in the management of disease, might underlie the observed higher mortality in pre-HDRU cohort. Treatment protocols were modified with time as per the available evidence, and despite the time dependent, non-randomized nature of this study, the difference in mortality is noticeable. Causality with improved care delivery comes forth as a plausible mechanism through these observations. Pre HDRU AKI-D cohort in our study was small (9% of total); however, our post-HDRU cohort had far lower mortality rate in AKI-D than that reported in a large study (43.9% vs 64%).[24] Similarly, mortality

**Table 3**

**Characteristics and comparison between survivors and non-survivors in patients with Acute kidney injury requiring dialysis**

| Variable | Total (n = 116) | Survived (n = 65) | Expired (n = 51) | *P* value |
|---|---|---|---|---|
| Demographic characters and co-morbidities | | | | |
| Age (yr) | 52.6 (14.8) | 50.1 (14.6) | 55.8 (14.5) | .040 |
| Sex, male (%) | 74 (63.8) | 39 (60) | 35 (68.6) | .437 |
| Hypertension (%) | 76 (65.5) | 44 (67.7) | 32 (62.7) | .694 |
| Diabetes mellitus (%) | 55 (47.4) | 26 (40) | 29 (56.8) | .053 |
| Chronic kidney disease (%) | 81 (69.8) | 48 (73.8) | 33 (64.7) | .195 |
| Cerebrovascular disease (%) | 10 (8.6) | 3 (4.6) | 7 (13.7) | .083 |
| Coronary artery disease (%) | 10 (8.6) | 3 (4.6) | 7 (13.7) | .083 |
| Clinical features at admission | | | | |
| Symptoms present at admission (%) | 111 (95.7) | 60 (92.3) | 51 (100) | .051 |
| Duration of symptoms (d) | 6.93 (7.0) | 7.10 (7.7) | 6.75 (6.1) | .792 |
| Fever (%) | 64 (55.2) | 33 (50.8) | 31 (60.8) | .187 |
| Cough (%) | 23 (19.8) | 13 (20) | 10 (19.6) | .574 |
| Breathlessness (%) | 68 (58.6) | 30 (46.9) | 38 (74.5) | .002 |
| Vomiting (%) | 27 (23.3) | 16 (24.6) | 11 (21.6) | .437 |
| Diarrhoea (%) | 17 (14.7) | 8 (12.3) | 9 (17.6) | .292 |
| Heart rate (beats/min) | 92.18 (15.77) | 90.72 (15.94) | 94.04 (15.52) | .263 |
| Systolic blood pressure (mm Hg) | 130.32 (23.98) | 129.12 (21.67) | 131.84 (26.79) | .547 |
| Diastolic blood pressure (mm Hg) | 80.59 (13.00) | 80.40 (12.67) | 80.84 (13.55) | .856 |
| Admission $sPO_2$ ($sPO_2$%) | 90.85 (12.46) | 94.63 (6.78) | 86.04 (16.01) | .001 |
| Hypoxia at admission (%) | 55 (47.4) | 21 (32.3) | 34 (66.67) | .000 |
| Sepsis at presentation (%) | 30 (25.9) | 14 (21.5) | 16 (31.4) | .162 |
| Shock at presentation (%) | 10 (8.6) | 6 (9.2) | 4 (7.8) | .532 |
| Oliguria at presentation (%) | 55 (47.4) | 27 (41.5) | 28 (54.9) | .107 |
| Altered mental status (%) | 31 (26.7) | 7 (10.8) | 24 (47.1) | .000 |
| Laboratory parameters at admission | | | | |
| Hemoglobin (mmol/L) | 5.37 (1.68) | 5.14 (1.71) | 5.65 (1.61) | .109 |
| Total leukocyte count (cells $\times 10^6$/L) | 12,010 (8366) | 10,116 (7435) | 14,311 (8916) | .009 |
| Platelets (cells $\times 10^9$/L) | 214.50 (107.10) | 201.16 (92.47) | 230.71 (121.55) | .145 |
| Blood urea nitrogen (mmol/L) | 30.7 (20.1) | 28.9 (16.7) | 33.0 (24.0) | .341 |
| Creatinine (μmol/L) | 872.7 (571.2) | 969.1 (658.7) | 752.5 (411.2) | .043 |
| Sodium (mmol/L) | 131.49 (7.03) | 131.45 (7.10) | 131.54 (7.02) | .944 |
| Potassium (mmol/L) | 4.89 (1.09) | 4.76 (1.03) | 5.05 (1.16) | .165 |
| AST (IU/L) | 36.82 (27.20) | 29.92 (17.86) | 46.24 (34.04) | .004 |
| ALT (IU/L) | 32.02 (38.02) | 26.92 (33.46) | 38.78 (42.78) | .111 |
| Treatment and course of stay | | | | |
| Inotrope use (%) | 40 (34.5) | 10 (15.4) | 30 (58.8) | .000 |
| Requirement of PCV transfusions (%) | 51 (43.9) | 33 (50.7) | 18 (35.3) | .069 |
| Steroids (%) | 73 (62.9) | 35 (53.85) | 38 (74.51) | .033 |
| Remdesivir (%) | 29 (27.1) | 13 (21.3) | 16 (34.8) | .092 |
| Heparin (%) | 41 (35.34) | 17 (26.15) | 24 (47.06) | .031 |
| HCQS (%) | 50 (43.1) | 26 (40) | 24 (47.06) | .457 |
| Severe COVID-19 (%) | 79 (68.1) | 32 (40.5) | 47 (59.5) | .000 |
| Hospital stay (d) | 16.67 (12.77) | 20.86 (12.33) | 11.41 (11.38) | .000 |
| **Variable** | **Total (n = 65)** | **Dialysis independent at discharge (n = 21)** | **Discharged on dialysis (n = 44)** | ***P* value** |
| Renal survival (dialysis independence at discharge) | | | | |
| Hypertension (%) | 44 (67.7) | 10 (22.7) | 34 (77.3) | .019 |
| Diabetes mellitus (%) | 26 (40.0) | 10 (22.7) | 16 (36.4) | .275 |
| Chronic kidney disease (%) | 49 (75.4) | 11 (22.5) | 38 (77.6) | .004 |
| Oliguria (%) | 28 (43.1) | 10 (47.6) | 18 (40.9) | .403 |
| Severe COVID-19 (%) | 24 (36.9) | 10 (47.6) | 14 (31.8) | .168 |

ALT = alanine aminotransferase, AST = aspartate aminotransferase, COVID-19 = coronavirus disease 2019, HCQS = hydroxychloroquine, PCV = packed cell volume, $sPO_2$ = oxygen saturation.

**Table 4**

**Characteristics and comparison between survivors and non-survivors in patients with end stage renal disease.**

| Variable | Total (n = 118) | Survived (n = 93) | Expired (n = 25) | *P* value |
|---|---|---|---|---|
| Demographic characters and co-morbidities | | | | |
| Age (yr) | 48.2 (15.2) | 46.8 (15.7) | 53.4 (12.3) | .048 |
| Sex, male (%) | 78 (66.1) | 59 (63.4) | 19 (76) | .341 |
| Hypertension (%) | 104 (88.1) | 82 (88.2) | 22 (88.0) | 1.000 |
| Diabetes mellitus (%) | 41 (34.7) | 31 (33.3) | 10 (40) | .346 |
| Cerebro-vascular disease (%) | 6 (5.1) | 4 (4.3) | 2 (8.0) | .488 |
| Coronary artery disease (%) | 10 (8.5) | 3 (3.2) | 7 (2.8) | .043 |
| Dialysis characteristics | | | | |
| Dialysis vintage (mo) | 30.8 (38.2) | 27.6 (33.9) | 42.5 (50.6) | .105 |
| Dialysis vintage | | | | .349 |
| <1 yr | 49 (48.5) | 40 (51.2) | 9 (39.1) | |
| >1yr | 52 (51.5) | 38 (48.7) | 14 (60.9) | |
| Arterio-venous fistula (%) | 73 (64.6) | 59 (67.0) | 14 (56) | .329 |
| Temporary catheter (%) | 24 (21.2) | 16 (18.2) | 8 (32) | |
| Tunnelled cuffed catheter (%) | 16 (14.2) | 13 (14.8) | 3 (12) | |
| Frequency of HD-3/wk* (%) | 82 (74.5) | 67 (77.9) | 15 (62.5) | .183 |
| Missing HD sessions > 3d (%) | 35 (29.7) | 24 (26.7) | 11 (45.8) | .070 |
| Clinical features at admission | | | | |
| Symptoms present at admission (%) | 99 (83.9) | 74 (79.6) | 25 (100) | .007 |
| Duration of symptoms (d) | 4.45 (4.2) | 4.3 (4.4) | 4.9 (3.6) | .569 |
| Fever (%) | 72 (61.0) | 58 (62.4) | 14 (56) | .361 |
| Cough (%) | 36 (30.5) | 24 (25.8) | 12 (48.0) | .031 |
| Breathlessness (%) | 64 (54.2) | 45 (48.4) | 19 (76.0) | .012 |
| Vomiting (%) | 17 (14.4) | 13 (13.9) | 4 (16) | .508 |
| Diarrhoea (%) | 13 (9.6) | 9 (9.7) | 4 (16) | .283 |
| Heart rate (beats/min) | 91.9 (11.7) | 91.92 (12.02) | 91.76 (11.42) | .952 |
| Systolic blood pressure (mm Hg) | 132.3 (25.2) | 135.18 (24.70) | 121.80 (26.58) | .020 |
| Diastolic blood pressure (mm Hg) | 81.8 (13.9) | 83.49 (13.47) | 75.00 (14.36) | .007 |
| Admission $sPO_2$† ($sPO_2$%) | 92.4 (11.5) | 94.18 (6.79) | 90.00 (9.26) | .014 |
| Hypoxia at admission (%) | 49 (42.9) | 31 (34.8) | 18 (72) | .001 |
| Sepsis at presentation (%) | 18 (15.3) | 11 (11.8) | 7 (28) | .052 |
| Shock at presentation (%) | 9 (7.6) | 5 (5.4) | 4 (16) | .094 |
| Altered mental status (%) | 8 (67.8) | 3 (3.2) | 5 (20) | .011 |
| Laboratory parameters at admission | | | | |
| Hemoglobin (mmol/L) | 5.34 (1.43) | 5.22 (1.41) | 5.65 (1.58) | .195 |
| Total leukocyte count (cells $\times 10^6$/L) | 9108 (5207) | 8503 (4721) | 11,629 (6270) | .009 |
| Platelets (cells $\times 10^9$/L) | 196 (86.5) | 200.61 (93.97) | 201.16 (87.36) | .981 |
| Blood urea nitrogen (mg/dL) | 60.1 (34.9) | 56.55 (33.20) | 72.48 (39.88) | .059 |
| Creatinine (mg/dL) | 9.6 (4.2) | 9.29 (10.56) | 10.56 (6.24) | .368 |
| Sodium (mmol/L) | 132.1 (5.6) | 131.7 (5.7) | 133.1 (5.1) | .343 |
| Potassium (mmol/L) | 5.0 (1.0) | 5.1 (1.1) | 4.9 (1.0) | .657 |
| AST (IU/L) | 38.7 (27.8) | 36.66 (28.90) | 47.76 (24.84) | .110 |
| ALT (IU/L) | 37.1 (88.8) | 40.55 (101.01) | 27.20 (15.57) | .549 |
| Treatment and course of stay | | | | |
| Inotrope use (%) | 17 (14.4) | 6 (6.5) | 11 (44) | .000 |
| Sepsis during stay (%) | 22 (19.3) | 14 (15.7) | 8 (32.0) | .066 |
| Requirement of PCV transfusions (%) | 42 (36.8) | 36 (40.0) | 6 (25) | .132 |
| Steroids (%) | 69 (60.0) | 51 (56.0) | 18 (75) | .106 |
| Remdesivir (%) | 16 (13.6) | 10 (10.7) | 5 (23.8) | .103 |
| Heparin (%) | 37 (32.17) | 23 (25.3) | 14 (58.33) | .003 |
| HCQS (%) | 61 (53.0) | 46 (50.5) | 15 (62.5) | .361 |
| Severe COVID-19 (%) | 66 (55.9) | 43 (65.2) | 23 (34.8) | .000 |
| Hospital stay (d) | 16.9 (12.2) | 18.6 (10.5) | 11.6 (16.2) | .013 |

ALT = alanine aminotransferase, AST = aspartate aminotransferase, COVID-19 = coronavirus disease 2019, HCQS = hydroxychloroquine, HD = hemodialysis, PCV = packed cell volume, $sPO_2$ = oxygen saturation.
*Frequency of maintenance hemodialysis sessions was < 3/wk in the others.
†Best maintained $sPO_2$ at admission.

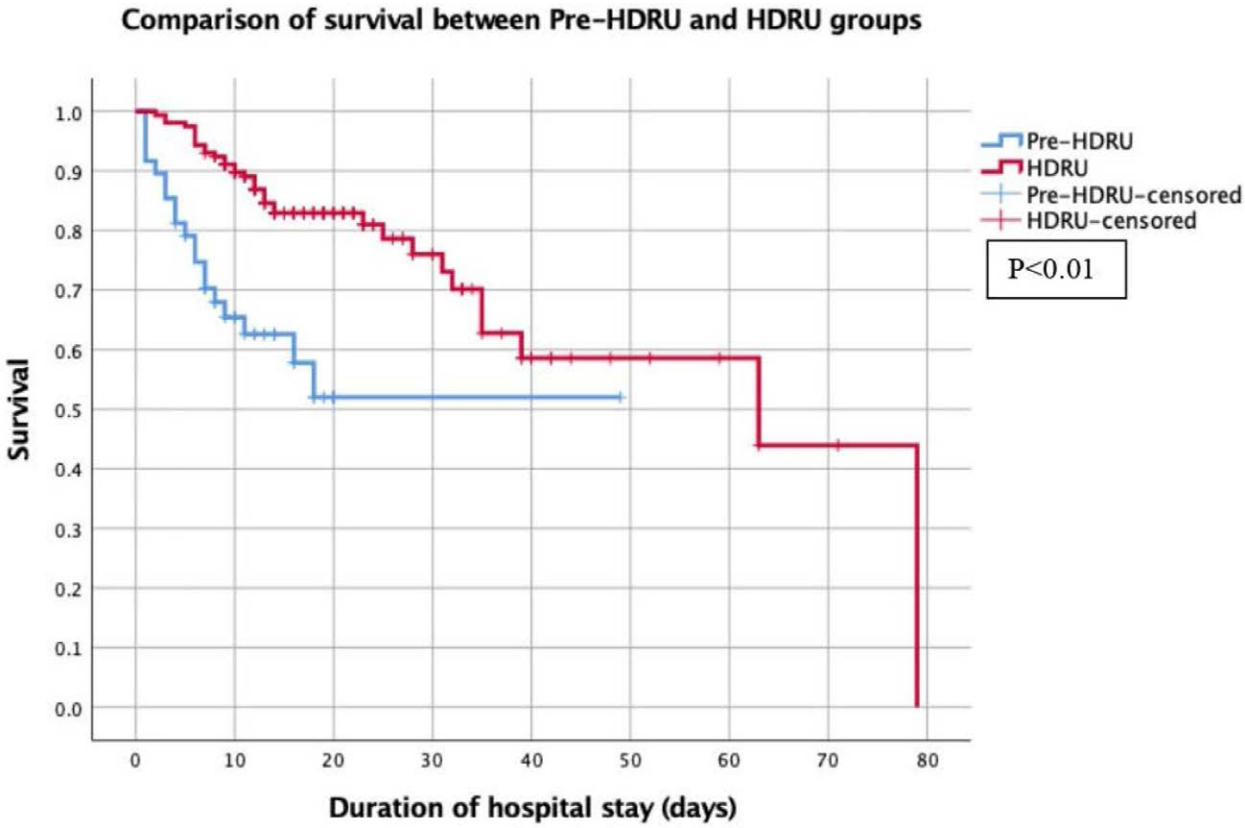


**Figure 4.** Kaplan–Meier survival curves for pre-HDRU and HDRU groups. HDRU = high dependency renal unit.

in the post-HDRU ESRD cohort is lower than that reported in India[25] (37%) and elsewhere (31%,[4] 27.3%[26]). These observations support the beneficial effect of HDRU care delivery on outcomes.

In conclusion, it is feasible for nephrologists to deliver high dependency renal care to hospitalized patients with COVID-19. Pandemics like COVID-19 typically result in disruption of routine health services, pressurize existing resources and cause fragmentation of medical care in patients with multiple co-morbidities, all of which contribute to overall morbidity and mortality. Our experience highlights the potential utility of an HDRU set-up in decreasing mortality with COVID-19 in one of the most vulnerable of patient subsets. As the COVID-19 pandemic continues despite mass vaccination programs and global measures to control its spread, we believe our experience will benefit many hospitals, especially in resource limited settings. Further evaluation of this approach is needed.

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## Author contributions

CG, TM, SD, and SB evaluated the patients upon admission and informed to AP, ST DB, and TJ. DB, TJ and AP made final decisions about evaluations and treatments. ST and TJ designed the study, monitored data collection, adjudicated causes of death and wrote first draft. DB trained the fellows, DB and TJ supervised overall activities of the HDRU, AP, SP, and AP supervised activities of the hemodialysis unit, AP monitored bedside dialysis activities. NS, AK, SD, SB, TM, and CG collected the first evaluation data. AK, CG collected data during ward stay. PJ did statistical analysis. ST wrote initial draft and TJ wrote the final draft.

**Conceptualization:** Sayali Thakare, Tukaram Jamale.
**Data curation:** Sayali Thakare, Tulsi Modi, Chintan Gandhi, Sreyashi Bose, Satarupa Deb, Abhinav Katyal, Nikhil Saxena, Ankita Patil, Sunil Patil, Atim Pajai, Divya Bajpai, Tukaram Jamale.
**Formal analysis:** Sayali Thakare, Pratap Jadhav, Tukaram Jamale.
**Investigation:** Sayali Thakare, Tulsi Modi, Chintan Gandhi, Sreyashi Bose, Satarupa Deb, Abhinav Katyal, Nikhil Saxena, Ankita Patil, Sunil Patil, Atim Pajai, Divya Bajpai, Tukaram Jamale.
**Methodology:** Sayali Thakare, Tulsi Modi, Chintan Gandhi, Sreyashi Bose, Satarupa Deb, Abhinav Katyal, Nikhil Saxena, Ankita Patil, Sunil Patil, Atim Pajai, Divya Bajpai, Pratap Jadhav, Tukaram Jamale.
**Project administration:** Sayali Thakare, Tulsi Modi, Chintan Gandhi, Sreyashi Bose, Satarupa Deb, Abhinav Katyal, Nikhil Saxena, Ankita Patil, Sunil Patil, Atim Pajai, Divya Bajpai, Tukaram Jamale.
**Resources:** Tukaram Jamale.
**Supervision:** Sayali Thakare, Atim Pajai, Divya Bajpai, Tukaram Jamale.

**Validation:** Tukaram Jamale.
**Visualization:** Tukaram Jamale.
**Writing – original draft:** Sayali Thakare.
**Writing – review & editing:** Sayali Thakare, Tukaram Jamale.

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