Use of Remdesivir in Patients With COVID-19 on Hemodialysis: A Study of Safety and Tolerance

Dhanapalan Aiswarya1, Venkatesh Arumugam1, Thanigachalam Dineshkumar1, Natarajan Gopalakrishnan1, Tanuj Moses Lamech1, Govindasamy Nithya1, Bhagavatula V.R.H. Sastry1, Paulpandian Vathsalyan1, Jeyachandran Dhanapriya1 and Ramanathan Sakthirajan1

1Institute of Nephrology, Madras Medical College, Chennai, India

**Background:** There are scarce data regarding the use of remdesivir in patients with severe acute respiratory distress syndrome coronavirus 2 (SARS-CoV-2) and end-stage renal disease as US Food and Drug Administration cautions against its use in patients with an estimated glomerular filtration rate <30 ml/min/1.73m² unless the potential benefits outweigh the potential risks. We studied the compassionate use and safety profile of remdesivir in patients with end-stage renal disease and moderate to severe SARS-CoV-2 infection.

**Methods:** We conducted an observational prospective study in 48 dialysis-dependent patients with SARS-CoV-2 infection who received remdesivir as part of institutional treatment protocol. During the treatment period, 100 mg of remdesivir was given 4 hours before hemodialysis sessions. Liver function tests, inflammatory markers such as serum C-reactive protein, serum ferritin and lactate dehydrogenase levels, and oxygen requirement before and after remdesivir treatment were compared.

**Results:** There were no events of significant liver function test alterations with the administration of 2 to 6 doses of remdesivir. A significant decline in serum C-reactive protein level ($P<0.001$) was noted. More than two thirds (68.57%) of patients showed an improvement in oxygen requirement. Early administration of remdesivir within 48 hours of hospital admission shortened the duration of hospitalization by a mean of 5.5 days ($P=0.001$).

**Conclusion:** Remdesivir was well tolerated and found safe in our study. If initiated within 48 hours of hospitalization, it reduces recovery time. Assessing the mortality benefits of remdesivir in these patients requires a randomized controlled trial with a larger population.

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KEYWORDS: COVID-19; dialysis; ESRD; remdesivir; SARS-CoV-2

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evidence. There are scarce data regarding the safety profile and usage of remdesivir in patients with ESRD. Thakare et al. studied 36 patients on hemodialysis (16 patients with ESRD and 20 patients with acute kidney injury) and found that remdesivir was well tolerated in this group. We studied the compassionate use and safety profile of remdesivir in patients undergoing dialysis who were admitted to our center with SARS-CoV-2 infection.

METHODS

This observational prospective study was conducted at the Institute of Nephrology, Madras Medical College, a tertiary care center in Chennai, India, after approval from the institutional ethics committee (no. 46042020).

Study Population

All patients with CKD requiring hemodialysis who tested positive for SARS-CoV-2 infection from analysis of nasopharyngeal swab by reverse transcription polymerase chain reaction with moderate or severe infection and who received ≥1 dose of remdesivir according to our institutional protocol through September 2020 were included. Patients with mild disease and underlying chronic liver disease were excluded.

Institutional Management Protocol

All patients with ESRD requiring renal replacement therapy were admitted. The blood investigations conducted on admission included a complete hemogram, renal function test, liver function tests, and serum C-reactive protein (CRP), ferritin, and lactate dehydrogenase (LDH) levels. All patients were subjected to computed tomography (CT) scans of the chest, and the severity of lung involvement was graded as <25%, 25% to 50%, 50% to 75%, and >75% (grades 1, 2, 3, and 4, respectively). These investigations were repeated as clinically indicated. According to the hospital protocol, mild disease was defined as having any one of the following: oxygen saturation on room air >94%, a respiratory rate of <24 breaths/minute, a neutrophil lymphocyte ratio between 3.13 and 5, a serum CRP level between 10 and 50 mg/dl, a serum ferritin level between 400 and 600 ng/ml, a serum LDH level between 220 and 300 IU/ml, a serum interleukin-6 level of 20 to 100 pg/ml, or a CT scan of the chest showing <25% lung involvement (Supplementary Table S1). Moderate disease was defined as having any one of the following: oxygen saturation on room air <94% requiring oxygen, a respiratory rate of >24 to 30 breaths/minute, a neutrophil lymphocyte ratio >5, a serum CRP level of 50 to 100 mg/dl, a serum ferritin level of 600 to 1500 ng/ml in males and 500 to 1000 ng/ml in females, a serum LDH level of 300 to 500 IU/ml, a serum interleukin-6 level of 20 to 100 pg/ml, or a CT scan of the chest showing 25% to 75% lung involvement (grades 2 or 3). Severe infection was defined as having any one of the following: oxygen saturation on room air <90% requiring oxygen, a respiratory rate of >30 breaths/minute, a neutrophil lymphocyte ratio >7, a serum CRP level of >100 mg/dl, a serum ferritin level of >1500 ng/ml in males and >1000 ng/ml in females, a serum LDH level of >500 IU/ml, a serum interleukin-6 level of >100 pg/ml, or a CT scan of the chest showing >75% lung involvement (grade 4).

Administration of Remdesivir

Remdesivir was given at a dose of 2.5 mg/kg of edema-free body weight (dry weight) up to a maximum dose of 100 mg on day 1 in patients undergoing hemodialysis 4 hours before the session. Subsequent doses up to a maximum of 6 doses were given 4 hours before each hemodialysis session. Liver function tests were monitored daily and further doses were withheld if there was alanine aminotransferase (ALT) elevation ≥5 times the upper limit of normal or if ALT elevation was accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or prothrombin time international normalized ratio. Once the ALT decreased to <5 times the upper limit of normal, further doses were administered, depending on the clinical and laboratory parameters. A loading dose of the drug was not given to our study population.

In addition to remdesivir, patients also received low molecular weight heparin 40 mg subcutaneously and intravenous dexamethasone 8 mg for 5 days, extended up to 10 days in patients with severe disease. Low molecular weight heparin was skipped on the day of dialysis and standard anticoagulation using unfractionated heparin was used during dialysis (a 2500-unit bolus followed by 750 units/hour). For all patients with grade 3 or above pulmonary involvement, a third-generation cephalosporin was added to cover bacterial superinfection. Hemodialysis was given every 48 to 72 hours as decided by the treating physician based on clinical assessment and laboratory parameters.

Nasopharyngeal swabs for SARS-CoV-2 by reverse transcription polymerase chain reaction were repeated every 72 hours after admission, until a negative result occurred. Criteria for discharge included clinical recovery along with a single negative nasopharyngeal swab for SARS-CoV-2.
Statistical Methods
Statistical analysis was performed using SPSS software (version 23; IBM Corp., Chicago, IL). Qualitative variables are expressed as absolute numbers and percentage. Quantitative variables are expressed as mean ± standard deviation or as median and interquartile range (IQR). Pairwise deletion of missing data was performed during analysis. Appropriate tests for statistical significance were used for comparisons between various groups: the χ² or Fisher exact test for qualitative data, the independent samples t test for continuous variables, and the Mann–Whitney U test for nonparametric data. Comparison of parameters before and after the course of remdesivir treatment were done using the paired sample t test for continuous variables or the Wilcoxon rank sum test for nonparametric data. For categorical variables, χ² or Fisher exact tests were conducted. A 2-sided P < 0.05 was considered statistically significant.

RESULTS
Baseline Characteristics
Forty-eight consecutive patients who received ≥1 dose of remdesivir between July 2020 and September 2020 were included. The mean age of the study population was 50.1 ± 12.2 years. Men predominated the study population (n = 38, 79.2%). The study participants presented to us with a median duration of symptoms of 3 days (IQR 2–4 days). The median duration of hospital stay was 9 days (IQR 6–12 days). Twenty patients (41.7%) were diabetic and 41 (85.4%) were hypertensive (Tables 1 and 2). The clinical severity of the disease was moderate in 21 (43.8%) patients and severe in 27 (56.2%) patients. Twenty-three patients received 2 doses of remdesivir and another 11 patients received 3 doses of remdesivir over a course of 5 days. A 10-day course consisting of 4 doses and 5 doses was administered for 6 and 2 patients, respectively. One patient received 6 doses of remdesivir over 11 days. Ten patients died during the study period.

Clinical and Laboratory Characteristics
The median neutrophil lymphocyte ratio, CRP, and ferritin of the study population were 6.3 (IQR 3.7–10.6), 149.2 mg/dl (IQR 71.2–250.8 mg/dl), and 1271 ng/ml (IQR 824–2000 ng/ml), respectively. The median serum LDH was 481.7 ± 202 IU/ml. CT findings suggestive of COVID-19 were present in 44 patients, and 15, 17, and 8 patients had 25% to 50%, 50% to 75%, and >75% lung involvement, respectively (Table 1). Due to the continuous requirement of high-flow oxygen therapy, 2 patients on high-flow nasal oxygen (HFNO) therapy and 1 on continuous positive airway pressure (CPAP) therapy could not be mobilized to

### Table 1. Baseline characteristics of the study population

| Parameters | Baseline characteristics, n = 48 | Discharged, n = 38 | Death, n = 10 | P value |
|------------|---------------------------------|-------------------|--------------|---------|
| Age, yr, mean ± SD | 50.1 ± 12.2 | 49.8 ± 12.6 | 51.2 ± 11.1 | 0.75 |
| Age < 50 yr, n (%) | 24 (50) | 19 (50) | 5 (50) | 1.00 |
| Male sex, n (%) | 38 (79.2) | 32 (84.2) | 6 (60) | 0.18 |
| Hypertension, n (%) | 20 (41.7) | 14 (36.8) | 6 (60) | 0.28 |
| Diabetes, n (%) | 41 (85.4) | 33 (86.8) | 8 (80) | 0.63 |
| Duration of symptom before admission, days, median (IQR) | 3 (2–4) | 3 (2–3.3) | 4 (2.5) | 0.13 |
| Duration of hospitalization, days, median (IQR) | 9 (6–12) | 9 (6.8–11.3) | 7 (4–12.5) | 0.22 |
| Day of initiation of remdesivir, median (IQR) | 2 (1–3) | 2 (1–4) | 2 (1–3) | 0.24 |
| Doses, median (IQR) | 2 (2–3) | 2 (2–3) | 3.5 (1–5) | 0.20 |
| Median laboratory values, median (IQR) | | | | |
| NLR | 6.3 (3.7–10.6) | 6.1 (3.1–9.8) | 6.8 (6.0-21.5) | 0.13 |
| ALT, IU/l | 18.5 (12–33.3) | 23 (12–34) | 17 (11–23.5) | 0.33 |
| AST, IU/l | 33 (19.5–47) | 35 (19.8–58.8) | 28 (19–40) | 0.45 |
| ALP, IU/l | 116 (88.5–160.3) | 112.5 (88.5–160.3) | 137 (84.5–184.8) | 0.64 |
| CRP, mg/dl | 149.2 (71.2–250.8) | 138.7 (67.1–243.4) | 166.5 (102.5–329.0) | 0.32 |
| LDH, IU/l | 438 (340–635) | 422 (339.5–585.5) | 476 (329–703.3) | 0.66 |
| Ferritin, ng/ml | 1271 (824–2000) | 1584 (850–2000) | 1050.3 (605.9–2237.3) | 0.40 |
| Deraigned LFT, n (%) | 6 (12.5%) | 4 (10.5) | 2 (20%) | 0.77 |
| CT scan of the chest, n (%) | | | | |
| None | 1 (2.1) | 1 (2.6) | 0 | 0.023 |
| Grade 1 | 4 (8.3) | 4 (10.5) | 0 | |
| Grade 2 | 15 (31.3) | 14 (36.8) | 1 (10) | |
| Grade 3 | 17 (35.4) | 13 (34.2) | 4 (40) | |
| Grade 4 | 8 (16.7) | 6 (15.8) | 2 (20) | |

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; CT, computed tomography; IQR, interquartile range; LDH, lactate dehydrogenase; LFT, liver function test; NLR, neutrophil lymphocyte ratio; SD, standard deviation.

*Fisher exact test.
undergo a CT scan of the chest. Nine patients (18.7%) had elevated aspartate aminotransferase (>45 IU/l) and 6 patients (12.5%) had elevated ALT levels (>55 IU/l) with a median ALT level of 66 IU/l (IQR 57.3–99.3 IU/l) at the time of admission. Among those with deranged ALT values, 2 patients received 2 doses of remdesivir, 2 patients received 3 doses of remdesivir, and 1 patient received 5 doses of remdesivir over 10 days. Remdesivir was withheld after 1 dose in a patient in whom worsening of known behavioral disorder was suspected.

In our cohort, 24 patients (50%) were >50 years of age. The comorbidities in our study population were diabetes (41.7%) and hypertension (85.4%). There was no difference in the levels of neutrophil lymphocyte ratio, CRP, and LDH between patients who were <50 or >50 years of age (P = 0.22, 0.48, and 0.93, respectively). There was no significant difference in lung involvement as evidenced by CT scan (P = 0.59) or mortality (P = 1) between the groups and the number of days taken to become swab-negative among survivors (P = 0.61).

**Respiratory Support During Remdesivir Therapy**

At the time of admission, only 3 patients (6%) were on room air, and the remaining 45 patients (84%) required some form of oxygen support. Seven (14%) needed oxygen masks, 30 (62%) needed nonrebreathing masks, 6 (13%) needed HFNO therapy, and 2 needed CPAP support. Two patients on each modality (CPAP, HFNO, and nonrebreathing mask) died during treatment (Figure 1). One of the 6 patients (16.7%) requiring HFNO at the initiation of remdesivir improved, requiring a nonrebreathing mask at the end of remdesivir therapy, and this patient was later discharged on room air; the other 5 (83.3%) patients died. Nine patients who died during the study period were put on mechanical ventilation as respiratory failure ensued. Among those requiring nonrebreathing masks, 20 (66.7%) patients were weaned off oxygen support, 8 (26.7%) patients had improving respiratory status, and 2 (6.7%) deteriorated and died at the end of remdesivir therapy. One of the 7 patients who required minimal respiratory support via facemask at the start of remdesivir therapy deteriorated rapidly, requiring HFNO at the end of treatment course, and later died (Supplementary Figure S1).

**Remdesivir and Clinical Severity**

There were no significant differences in the baseline demographic characteristics, duration of hospitalization, number of doses, and timing of initiation of remdesivir therapy in those with moderate and severe disease (Table 2) (Supplementary Figure S2). However, the time taken for a swab to be negative was significantly higher in those with severe illness (P = 0.03). Serum levels of aspartate aminotransferase, ALT, LDH, and ferritin were comparable in both the groups (Table 2). Serum level of CRP was significantly higher in those patients with severe disease (P = 0.027). ALT levels >55 IU/l were present in 3 patients in each group (P = 0.57). The lung involvement and mortality were higher in those with severe disease (P = 0.03 and 0.016, respectively). The mortality in patients with moderate disease was 48% and in those with severe disease it was 33.3%.

**Efficacy and Safety of Remdesivir**

A significant decrease in the serum level of CRP was observed after remdesivir therapy (P < 0.001). However, there was no significant difference in the levels of serum LDH and ferritin. Serum levels of transaminases

### Table 2. Comparison of clinical parameters across disease severity

| Parameters                        | Moderate disease, n = 21 | Severe disease, n = 27 | P value |
|-----------------------------------|-------------------------|------------------------|---------|
| Age, yr, mean ± SD                |                         |                        | 0.47    |
| Age <50 yr, n (%)                 |                         |                        |         |
| Male sex, n (%)                   |                         |                        |         |
| Diabetes, n (%)                   |                         |                        | 0.66    |
| Hypertension, n (%)               |                         |                        | 0.00    |
| Duration of symptom before admission, days, median (IQR) | 3 (2–3.5) | 3 (2–4) | 0.31 |
| Duration of hospitalization, days, median (IQR) | 8 (6–10) | 9.5 (7–14.5) | 0.20 |
| Day of initiation of remdesivir, median (IQR) | 2 (1–3) | 2 (1–4) | 0.96 |
| Doses, median (IQR)              | 2 (1–3) | 2.5 (2–4) | 0.16 |
| Days to swab negative, median (IQR) | 5 (2.5–8) | 8 (6.5–11) | 0.03 |
| Median laboratory values, median (IQR) | | | |
| Ferritin, ng/ml                   | 1170 (825.4–1703) | 1183 (735.5–2034) | 0.35 |
| CRP, mg/dl                        | 98.4 (47.7–277.8) | 170.3 (106.6–277.8) | 0.027 |
| LDH, IU/l                         | 384 (334.5–498.5) | 492.5 (352.5–703.3) | 0.13 |
| Deranged LFT, n (%)               | 3 (14.3) | 3 (11.1) | 0.57 |
| CT scan of the chest, n (%)       |                         |                        |         |
| None                              | 1 (4.8) | 0 |
| Grade 1                           | 4 (19) | 0 |
| Grade 2                           | 9 (42.9) | 6 (22.2) | 0.03 |
| Grade 3                           | 6 (28.6) | 11 (40.7) |
| Grade 4                           | 1 (4.8) | 7 (25.9) |
| Death, n (%)                      | 1 (4.8) | 9 (33.3) | 0.016 |

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; CT, computed tomography; IQR, interquartile range; LDH, lactate dehydrogenase; LFT, liver function test; NLR, neutrophil lymphocyte ratio; SD, standard deviation.

*Fisher exact test.
did not show any significant change in patients after remdesivir therapy (Table 3). No patient in our cohort reported any immediate adverse effects after infusion of remdesivir. One patient had acute coronary syndrome 6 hours after the first dose of remdesivir and 1 had worsening of behavioral disorder after 15 hours of remdesivir initiation leading to withdrawal of the drug in the second patient. The decrease in serum CRP levels with remdesivir therapy was consistent in the study population among various subgroups, based on age, disease severity, and timing of initiation of the drug. There was no significant change in the levels of the transaminases and LDH among various subgroups (Table 3). Patients >50 years of age had a significant fall in the levels of serum ferritin ($P = 0.005$). A trend toward decrease in levels of serum ferritin with remdesivir therapy was seen in patients in whom the drug was initiated within 48 hours of admission, although this was not statistically significant ($P = 0.06$). In those 6 patients with raised baseline serum ALT levels at admission, remdesivir therapy was not associated with any worsening of the transaminitis ($P = 0.35$).

**Timing of Initiation of Remdesivir with Outcome**

Remdesivir was initiated within 48 hours of admission in 29 patients and after 48 hours in 19 patients. The distribution of moderate and severe cases was comparable between the 2 groups ($P = 0.85$). Among the survivors, the mean duration of hospitalization was significantly shorter in patients who received remdesivir within 48 hours compared with those who received remdesivir after 48 hours of therapy, with a mean difference of 5.5 days ($P = 0.001$). The mean number of days to have a negative swab result after initiation of the first dose was significantly lower in

![Figure 1. Respiratory support of the study population during the course of remdesivir treatment. CPCP, continuous positive airway pressure; HFNO, high-flow nasal oxygen; NRM, nonrebreathing mask.](image)

**Table 3. Comparison of biochemical parameters before and after remdesivir therapy**

| Parameters          | Before remdesivir | After remdesivir | $P$ value |
|---------------------|-------------------|------------------|-----------|
| CRP, mg/dL         | 149.2 (71.2–250.8) | 44.6 (28.2–116)  | <0.001    |
| LDH, IU/L          | 438 (340–635)     | 436.5 (298–573.5) | 0.10      |
| Ferritin, ng/mL    | 1264.5 (821–2000) | 1268 (599.3–2000) | 0.047     |
| ALT, IU/L          | 18.5 (12–33.3)    | 25 (13.8–40.8)   | 0.14      |
| AST, IU/L          | 33 (19.5–47)      | 29 (19.5–45.3)   | 0.37      |
| ALP, IU/L          | 116 (88.5–160.3)  | 110.5 (82–142.8) | 0.61      |
| Deranged ALT, n=6  |                   |                  |           |
| ALT, IU/L          | 66.6 (57.3–99.3)  | 53 (41.5–128.8)  | 0.35      |
| Remdesivir initiated within 48 hours, n=29 | | | |
| AST, IU/L          | 37 (19.8–67)      | 29 (21–55)       | 0.69      |
| ALT, IU/L          | 18.5 (12–32)      | 28 (15.5–47)     | 0.08      |
| CRP, mg/dl         | 129.7 (89.2–226.2) | 63 (36.4–119)    | 0.002     |
| LDH, IU/L          | 451 (339.5–640)   | 437 (326.5–301.5) | 0.34      |
| Ferritin, ng/mL    | 1584 (822–2017)   | 1381 (761.2–2000) | 0.06      |
| Remdesivir initiated after 48 hours, n=19 | | | |
| AST, IU/L          | 27 (20–39)        | 29 (16–33)       | 0.29      |
| ALT, IU/L          | 19 (12–34)        | 24 (12–38)       | 0.74      |
| CRP, mg/dl         | 152.2 (72.9–260.5) | 33 (22.7–123)    | 0.002     |
| LDH, IU/L          | 437 (326.5–801.5) | 386 (275–574)    | 0.15      |
| Ferritin, ng/mL    | 1381 (761.2–2000) | 1058 (553–2000)  | 0.26      |

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; LDH, lactate dehydrogenase.

Values presented as median (interquartile range).
those who had the first dose within 48 hours (\(P = 0.041\)). However, no benefit in terms of mortality was observed in patients who had their therapy initiated within 48 hours of admission (\(P = 0.34\)). No significant difference in posttreatment CRP levels was seen between the groups (Table 4).

### DISCUSSION

The presumed toxicity in patients with decreased renal function is attributed to both remdesivir and accumulation of its solubilizing excipient sulfobutylether-betacyclodextrin (SBECD).\(^8\) Remdesivir is a weak inhibitor of mammalian DNA and RNA polymerases and has a low potential to cause mitochondrial toxicity especially at the Emergency Use Authorization–prescribed dose for a period of 5 to 10 days. SBECD is hepatotoxic at supraclinical doses of 3000 mg/kg—about 50 times the dose administered in humans—resulted in vacuolization of renal tubules and the liver.\(^9\) The volume of distribution of SBECD corresponds with extracellular water with an elimination half-life of about 2 hours and is readily removed by dialysis. One hundred milligrams of lyophilized powder of remdesivir contains 3 g of SBECD, which is below the maximum recommended daily dose.\(^1\)

In this observational study, 48 patients with CKD undergoing dialysis were studied with a median duration of dialysis therapy (pre–COVID-19) of 1 year (IQR 0.15–3.5 years). Our cohort was comprised of relatively younger patients, with mean age of 50.1 ± 12.2 years. In a cohort of 61 patients with severe disease by Grein et al.,\(^10\) the median age was 64 years. This difference could be attributed to two reasons. First, our study population included patients with both moderate and severe disease, and advanced age is a risk factor for severe disease in the general population. Second, CKD itself is a risk factor for SARS-CoV-2 infection, making all our patients vulnerable to infection irrespective of the age group. In our cohort, higher age was not found to be a risk factor for severe disease or mortality. Even though none of the patients in our cohort required invasive ventilation on admission, 45 patients (93.7%) needed oxygen supplementation by various modalities (CPAP, \(n = 2\); HFNO, \(n = 6\); non-rebreathing mask, \(n = 30\); and facemask, \(n = 7\)). At the end of remdesivir therapy, 33 patients (68.75%) showed an improvement in oxygen requirement in the ordinal scale score (Figure 1). However, this improvement was significant in patients requiring a lower modality of oxygen support at admission. Patients on high-flow oxygen and noninvasive ventilation at the initiation of remdesivir therapy were not found to have any clinical benefit.

Among the biochemical markers, CRP correlated with disease severity. Serum levels of CRP were significantly higher in patients with severe disease, similar to other studies.\(^11,12\) Even though there was a trend toward increased levels of serum LDH and serum ferritin in patients with severe disease, these trends were not statistically significant. CKD and dialysis are chronic inflammatory states. Serum ferritin level may not be a good marker of inflammation in patients on dialysis due to supplemental iron therapies and blood transfusions. These patients have higher serum ferritin levels than the general population.\(^13\)

The total number of doses of remdesivir administered in this study ranged from 2 to 6 over a duration of 5 to 11 days, as subsequent doses were administered depending on the clinical assessment and biochemical parameters. After administration of remdesivir there was a significant decline in serum CRP levels across all subgroups based on age, disease severity, and timing of drug administration. In our study population, early initiation of remdesivir (within 48 hours of hospital admission) was shown to decrease the mean duration of hospitalization by 5.5 days (\(P = 0.001\)) compared with those who received it after 48 hours. This delay of 48 was unintentional and was mainly caused by delays in obtaining consent, therapeutic decision making, and logistic reasons. The time taken for the swab test to become negative was significantly lower in those who received the first dose of remdesivir within 48 hours of admission. These results are similar to the final reports of the Adaptive COVID-19 Treatment Trial, where the recovery time was reduced by 5 days in patients who received remdesivir compared with those who did not.\(^14\) The median duration of hospitalization in our study population was 9 days (IQR 6–12 days) whereas the median recovery time in the remdesivir group of Adaptive COVID-19 Treatment Trial was 10 days.

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**Table 4.** Comparison of parameters between those who received remdesivir <48 hours and >48 hours of admission

| Parameters | Initiation before 48 hours, \(n = 29\) | Initiation after 48 hours, \(n = 19\) | \(P\) value |
|------------|--------------------------------------|--------------------------------------|-------------|
| Day of initiation, median (IQR) | 1 (0.5–2) | 4 (3–8) | 0.34 |
| Days to swab negative, mean ± SD | 5.4 ± 3.3 | 8 ± 3.5 | 0.041 |
| Days to discharge, mean ± SD | 7.7 ± 2.7 | 13.2 ± 5.2 | 0.001 |
| CRP after remdesivir, mg/dl, median (IQR) | 63 (36.4–119) | 33 (22.7–123) | 0.13 |
| Severe, \(n\) (%) | 16 (55.2) | 11 (57.9) | 0.85 |
| Moderate, \(n\) (%) | 13 (44.8) | 8 (42.1) | 0.65 |
| Death, \(n\) (%) | 7 (24.1) | 3 (15.8) | 0.34 |

CRP, C-reactive protein; IQR, interquartile range; SD, standard deviation.
However, these results could not be translated into any benefit when mortality was considered. The mortality in our cohort was 20.8% compared with 17.9 % in the entire population of patients with ESRD with SARS-CoV-2 infection who received dialysis in our center (unpublished data). This difference could be caused by the presence of more asymptomatic patients as well as those with milder disease in the latter group. Compared with other studies in patients with ESRD, the mortality in our study population is considerably lower.1–5

The knowledge regarding the pharmacokinetics and safety profile of SBECID in patients with decreased renal function is obtained from studies conducted on patients receiving intravenous voriconazole. Luke et al.13 studied the pharmacokinetics of SBECID in 7 patients requiring dialysis and 6 patients with normal GFR treated with intravenous voriconazole and showed that the mean half-life of SBECID was 2.1 ± 0.4 hours in normal subjects and 79.1 ± 24.5 hours in patients undergoing dialysis. Dialysis shortened the elimination half-life of SBECID to 5.0 ± 1.4 hours and removed about 46% of the total body load of SBECID.13 A case report by Lê et al.16 showed that a single 4-hour session of hemodialysis can decrease the concentration of the metabolite of remdesivir by 59%. In our study, remdesivir was administered intravenously 4 hours before dialysis, which is 2 to 4 plasma half-lives of the parent molecule. This allows time for distribution of 75% to 93% of the compound to the tissues and release of carrier molecule, which is later considerably removed by hemodialysis. However, a loading dose of the drug was not administered as no evidence of safety in patients with ESRD was available during the study period. Grein et al.10 reported hepatic enzyme derangement in 23% of patients during the course of remdesivir, but they could not attribute it to either remdesivir or underlying disease because liver dysfunction commonly occurred with COVID-19 infection. Other adverse effects reported during remdesivir use from various studies include diarrhea, rash, hypotension, and acute kidney injury.10,17 Although 6 patients had deranged LFTs on admission in our study group, none of the patients developed a significant elevation of ALT or aspartate aminotransferase on treatment with remdesivir across subgroups based on age or disease severity that warranted its discontinuation, similar to the study by Thakare et al.7 The adverse effects reported in our cohort included a single case of acute coronary syndrome and a case of worsening of behavioral disorder. No immediate infusion-related hypersensitivity reactions were reported.

The strength of our study is that this is the only large cohort to date reporting the use of remdesivir in patients with CKD who require dialysis. The limitations of our study are its small sample size, observational study design, and variable dosing of remdesivir. Therapeutic drug levels were not monitored, and a loading dose was not given to our patients. Due to the observational study design, a head-to-head comparison of remdesivir with various therapeutic modalities could not be made. There is no available gold standard therapy for COVID-19, hence the efficacy of remdesivir could not be compared. Due to the short follow-up period, the long-term effects of remdesivir could not be identified.

CONCLUSION

Our study showed that remdesivir use in patients with ESRD is safe and was not associated with any serious adverse effects. Early initiation of remdesivir appears to confer clinical benefits in terms of shorter time to recovery and discharge. Remdesivir may be considered as a therapeutic option in the ESRD population with COVID-19 infection.

DISCLOSURE

All the authors declared no competing interests.

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SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Institutional protocol for categorization and management of patients with COVID-19

Figure S1. Comparison of oxygen requirement of patients during hospitalization

Figure S2. Survival of patients admitted with moderate and severe disease

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