Complications of remdesivir in COVID 19 patients with kidney diseases

Hamid Tayyebi khosroshahi, MD, professor of nephrology

Safety and effectiveness of Remdesivir in patients with kidney diseases

Coronavirus 2019 (COVID-19), rapidly spread worldwide and lead to a global pandemic by the end of 2019.

Most individuals infected with the virus experience mild-to-moderate respiratory illnesses and recover without requiring specific treatment.

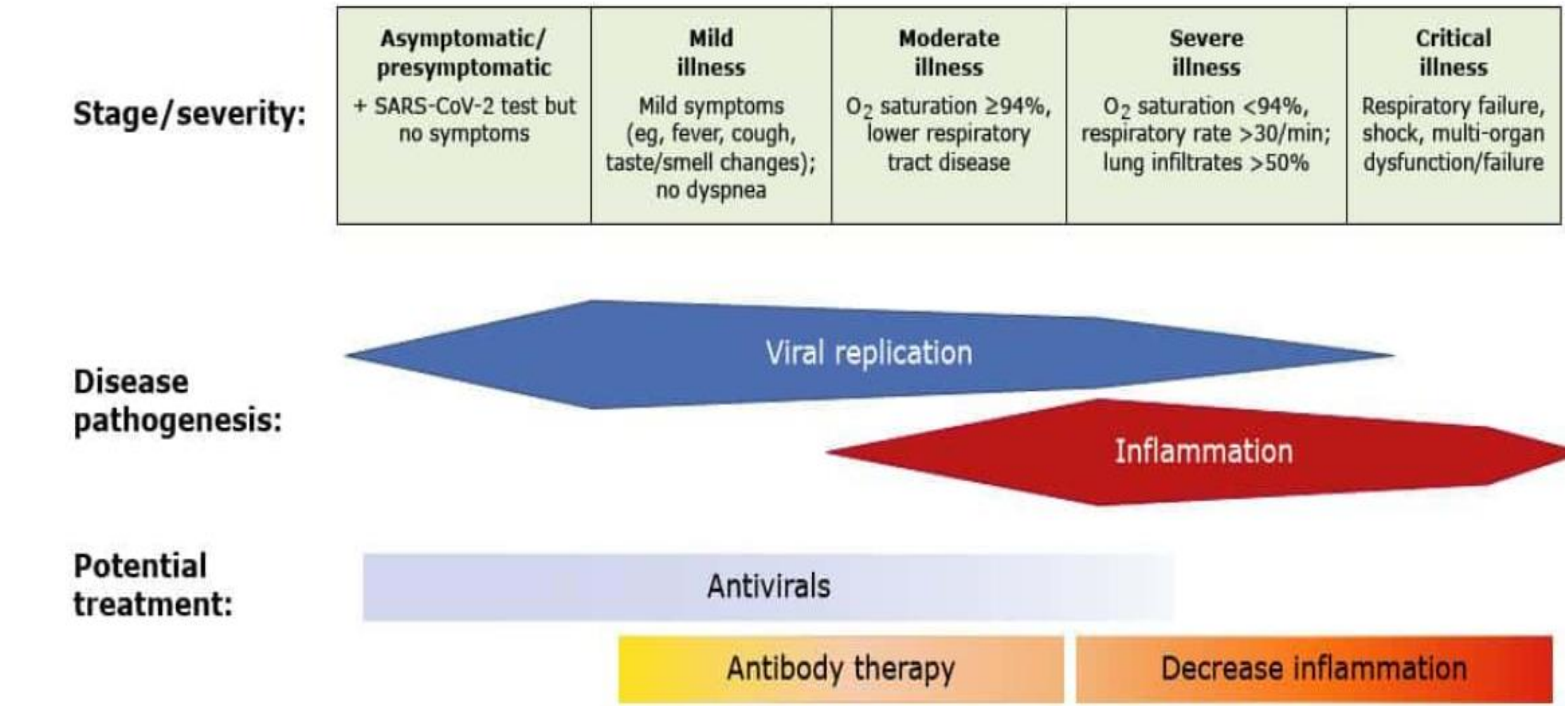
However, older adults and individuals with underlying conditions such as cardiovascular disease, diabetes, chronic respiratory diseases, kidney disease, or cancer are more susceptible to severe illness with COVID-19.

Based on data from the World Health Organization (WHO), as of **June** 7, 2023, over 6.9 million individuals have died from COVID-19 worldwide.

Title:

Potential targets of COVID-19 therapies by stage of infection

Potential targets of COVID-19 therapies by stage of infection



Remdesivir is an RNA-dependent polymerase inhibitor, and previous studies have demonstrated its effectiveness in reducing recovery time and lowering respiratory tract symptoms in patients with COVID-19. Guidelines established by the Infectious Diseases Society of America (IDSA) and the National Institutes of Health (NIH) also recommend the use of remdesivir in patients with COVID-19,

It was issued an emergency use authorization by the U.S. Food and Drug Administration in May 2020.

Although remdesivir has been shown to be effective in treating COVID-19, it is known to have side effects, including nausea, vomiting, elevated transaminase levels, anemia, hyperglycemia, and in some cases, bradycardia.

Dosing:

Kidney Impairment: Adult. The renal dosing recommendations are based upon the best available evidence and clinical expertise.

1- Altered kidney function: No dosage adjustment necessary for any degree of kidney impairment.

2- Hemodialysis, intermittent (thrice weekly): Not significantly dialyzable: No supplemental dose or dosage adjustment necessary; may be administered without regard to timing of dialysis sessions.

3- Peritoneal dialysis: Unlikely to be significantly dialyzable: No dosage adjustment needed.

4- CRRT: No dosage adjustment necessary.

5- PIRRT (eg, sustained, low-efficiency diafiltration): No dosage adjustment necessary.

Dosing: Liver Impairment: Adult

Note: Although randomized, controlled trials excluded patients with baseline ALT/AST ≥5 times ULN, remdesivir has been successfully used in a limited number of patients with baseline AST/ALT >5 times ULN.

While AST/ALT elevations have been observed in patients treated with remdesivir (requiring discontinuation in ~3% of patients) an exploratory analysis to determine the risk of remdesivir-induced liver injury (defined as one of the following: total bilirubin, ALT or AST >2 times ULN, or INR >1.7) did not find an increased risk of remdesivir-induced liver injury following exposure.

Additionally, elevated transaminases are a known clinical feature of COVID-19 infection, and therefore, use of remdesivir should not be avoided solely based on the presence of elevated liver chemistries.

Hepatic impairment prior to treatment initiation:

Initial or dose titration in patients with preexisting liver cirrhosis: Note:

Baseline liver chemistries should be obtained prior to initiation in hospitalized patients and periodically (eg, every 1 to 2 days) during treatment and as needed in outpatients if clinically indicated.

Child-Turcotte-Pugh class A to C: No dosage adjustment necessary.

Dosage adjustment in patients with chronic, worsening hepatic function during treatment (eg, progression from Child-Turcotte-Pugh class A to B):

Progression from baseline to Child-Turcotte-Pugh class A to C:

ALT ≤10 times ULN: No dosage adjustment necessary.

ALT >10 times ULN: Consider discontinuation of remdesivir.

If therapy is continued, no dosage adjustment necessary; however, in patients also experiencing signs/symptoms of liver inflammation, remdesivir therapy should be discontinued.

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Acute hepatotoxicity during treatment (eg, requiring hospitalization) : Note:

Baseline liver chemistries should be obtained prior to initiation in hospitalized patients and periodically (eg, every 1 to 2 days) during treatment and as needed in outpatient if clinically indicated (Ref).

ALT ≤10 times ULN: No dosage adjustment necessary; however, in patients also experiencing signs/symptoms of liver inflammation, must weigh risks/benefits of continuation of remdesivir therapy.

ALT >10 times ULN: Consider discontinuation of remdesivir. If therapy is continued, no dosage adjustment necessary; however, in patients also experiencing signs/symptoms of liver inflammation, remdesivir therapy should be discontinued

Adverse Reactions

The following adverse drug reactions and incidences are derived from product labeling unless otherwise specified. Reported adverse reactions are for adolescents and adults. >10%:

1- **Endocrine & metabolic**: Increased serum glucose (grades 3/4: 3% to 11%)

2- **Renal**: Decreased creatinine clearance (grades 3/4: 2% to 19%), increased serum creatinine (grades 3/4: 3% to 15%)

1% to 10%:

3- **Dermatologic**: Skin rash (<2%)

4- **Gastrointestinal**: Nausea, pancreatitis (3% to 7%)

5- **Hematologic & oncologic**: Decreased hemoglobin, lymphocytopenia , prolonged prothrombin time (grades 3/4: 9%)

6- Hepatic: Increased serum alanine aminotransferase (2% to 7%), increased serum aspartate aminotransferase (3% to 6%) Increased serum alkaline phosphatase
7- Hypersensitivity: Hypersensitivity reaction (<2%)
8- Nervous system: Seizure (<2%)Frequency not defined:
9- Local: Erythema at injection site
10- Cardiovascular: Bradycardia (including severe bradycardia and sinus bradycardia) (Gubitosa 2020, Jacinto 2021, Touafchia 2021), heart failure (Wang 2020), hypotension (Touafchia 2021)

Drug Interactions

Using this medicine with any of the following medicines is usually not recommended, but may be required in some cases. If both medicines are prescribed together, your doctor may change the dose or how often you use one or both of the medicines.

- **Chloroquine**
- **Everolimus**
- **Hydroxychloroquine**
- **Tacrolimus**
- **Warfarin**

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Adverse events following remdesivir administration in moderately ill COVID-19 patients - A retrospective analysis

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Remdesivir, an antiviral drug, received an emergency use authorization for treating coronavirus disease 2019 (COVID-19) patients. Though many studies have reported the safety aspects of this antiviral agent, most of them were observed in severely ill COVID-19 patients, making very less data available in the moderately ill patients. The present study was conducted with an objective of finding the adverse events (AEs) associated with remdesivir in moderately ill COVID-19 patients.

Methodology:

A retrospective observational study was conducted by collecting data of demographic details and details of remdesivir, laboratory investigations, and AEs from the patient medical records from May to July 2021 and analyzed by using the appropriate statistics.

Results:

Out of the 160 COVID-19 patients, 32 were moderately ill (males: 29, females: 03) and were treated with remdesivir along with steroids and low molecular weight heparin (LMW) heparin. The average number of administered remdesivir doses was 4, with a loading dose of 200 mg and a maintenance dose of 100 mg. A total of 41 AEs were observed out of which 17 were adverse drug reactions (ADRs) (a significant increase in the alanine transaminase (ALT) [$P < 0.001$]) and 23 AEs (a significant rise in random blood sugars, RBS [one of the AEs] [$P = 0.007$]). The AEs were more commonly seen in the hypertensive patients. An increased oxygen requirement was a major serious AE observed in four patients.

Conclusion:

Remdesivir caused a significant increase in the liver enzymes. Increased blood sugar levels were the most common AE and increased oxygen requirement was the major serious AE observed.

Conclusion

From our study, we observed that the elevation of liver enzymes, increased oxygen requirement, and hyperglycemia were common AEs in moderately ill COVID-19 patients treated with remdesivir.

The raised liver enzymes could be attributable to remdesivir and the increased blood sugar levels could be due to the concomitant steroid use whereas the increased oxygen requirement could be due to disease progression.

Clinical Pharmacology & Therapeutics

Brief Report

Remdesivir and Acute Renal Failure: A Potential Safety Signal From Disproportionality Analysis of the WHO Safety Database

Correction(s) for this article

Alexandre O. Gérard, Audrey Laurain, Audrey Fresse, Nadège Parassol, Marine Muzzone, Fanny Rocher, Vincent L.M. Esnault, Milou-Daniel Drici

First published: 19 December 2020 | https://doi.org/10.1002/cpt.2145 | Citations: 48

Abstract

A decrease of the creatinine clearance associated with remdesivir has been inconstantly reported in clinical trials with unclear relevance.

Despite these uncertainties, we searched for a potential signal of acute renal failure (ARF) in pharmacovigilance postmarketing data. An analysis of the international pharmacovigilance postmarketing databases (VigiBase) of the World Health Organization (WHO) was performed, using two disproportionality methods. Reporting odds ratio (ROR) compared the number of ARF cases reported with remdesivir, with those reported with other drugs prescribed in comparable situations of COVID-19 (hydroxychloroquine, tocilizumab, and lopinavir/ritonavir).

VigiBase is the WHO global database of adverse event reports for medicines and vaccines

Clinical pharmacology and therapeutics 19 dec 2020

The combination of the terms “acute renal failure” and “remdesivir” yielded a statistically significant disproportionality signal with 138 observed cases instead of the 9 expected.

ROR of ARF with remdesivir was 20-fold (20.3; confidence interval 0.95 [15.7–26.3], $P < 0.0001$]) that of comparative drugs.

Based on ARF cases reported in VigiBase, we detected a statistically significant pharmacovigilance signal of nephrotoxicity associated with remdesivir.

Meanwhile, as recommended in its Summary of Product Characteristics, **assessment of patients with COVID-19 renal function should prevail before and during treatment with remdesivir in COVID-19**.

Clinical pharmacology and therapeutics 19 dec 2020

Safety of Remdesivir in Patients With Acute Kidney Injury or CKD

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Patients with chronic kidney disease (CKD), especially those with end-stage renal disease (ESRD), are susceptible to the development of severe coronavirus disease 2019 (COVID-19), which is associated with high mortality.[1] Apart from respiratory support depending upon the severity of the respiratory involvement, management of COVID-19 is largely supportive. Remdesivir is a nucleotide analog that inhibits viral RNA-dependent

median age of these patients was 53.1 years (range 15–84 years) and 30 (65.2%) were male. Renal diagnoses were ESRD in 16 (34.7%) and AKI in 30 (65.2%%) patients. Eight (17.4%) of 46 patients were recipients of live donor kidney transplants. Of 30 patients with AKI, 3 (6.5%), 2 (4.3%), and 25 (83.3%) patients had Kidney Disease: Improving Global Outcomes AKI stages 1, 2, and 3, respectively. Notably, all patients with stage 1

One hundred fifty-seven patients with COVID-19 who were admitted to the intensive care unit or our nephrology high dependency unit between July 7 and September 22, 2020 had either AKI or CKD.
Forty-six of 157 (29.3%) cases were treated with remdesivir.
The median age of these patients was 53.1 years (range 15– 84 years) and 30 (65.2%) were male.
Renal diagnoses were ESRD in 16 (34.7%) and AKI in 30 (65.2%%) patients. Eight (17.4%) of 46 patients were recipients of live donor kidney transplants.
Of 30 patients with AKI, 3 (6.5%), 2 (4.3%), and 25 (83.3%) patients had Kidney Disease: Improving Global Outcomes AKI stages 1, 2, and 3, respectively

Comorbidities included hypertension in 35 (76%) patients, diabetes in 26 (56.5%) patients, coronary artery disease in 4 (8.7%) patients, nephrolithiasis in 3 (6.5%) patients, and HIV in 1 (2.2%) patient.

Twelve (26%) patients were treated in the intensive care unit. At the time of initiation of remdesivir, oxygen requirements were as follows: noninvasive ventilation (n = 7), high flow nasal canula (n = 1), nonrebreathing mask (n = 11), face mask (n = 15), and nasal prongs (n = 12).

Further in the course of illness, 9 (19.5%) patients required invasive mechanical ventilation.

Remdesivir was administered as a total dose of 600 mg (200 mg on day 1, followed by 100 mg/day), which was extended in 2 patients to 1200 mg because satisfactory clinical improvement was not observed.

The median number of days from hospital admission to starting remdesivir was 5 days (range 1–26 days).

The median duration of follow-up was 15.5 days (range 6– 81 days).

Thirty-six (78.2%) patients were on dialysis (ESRD [n = 16] and AKI [n = 20]) at the time of initiation of therapy.

Therapy could not be completed in 6 patients who died. Remdesivir was discontinued early because of clinical improvement in 2 patients, and therapy is ongoing in 2 patients.

Transient behavioral changes were noted in 5 cases and acute gout was observed in 1 patient while they were undergoing therapy (World Health Organization–Uppsala Monitoring Center causality category:possible).

Baseline liver function test abnormalities (elevated aspartate aminotransferase [AST]/alanine aminotransferase [ALT] levels) were noted in14 (30.4%) cases before starting remdesivir—grade 1 elevation in 13 patients (AST in 4, ALT in 1, and both AST and ALT in 8) and grade 2 elevation in 1 patient, which improved by the end of therapy in 12 cases.

Liver function remained stable in 28 (60.9%) cases.

No patient had a severe rise in AST/ALT >5 times the upper limit of normal, therefore therapy was not required to be discontinued for this reason in any of the patients.

No renal function abnormalities attributable to drug were observed .

Fourteen (30.4%) patients died, 24 (52.2%) patients were discharged from the hospital after recovery, and 8 (17.3%) cases are still admitted, of which 2 are still undergoing treatment.

This is the first report of the use of remdesivir in patients with severely reduced kidney function, and our findings suggest that it is tolerated well.

Mild derangement in the liver function tests at baseline improved post-treatment. Although it is not possible to attribute such improvement to drug use, it suggests that **mild elevations in transaminases should not be considered as a contraindication**.

In conclusion, remdesivir was well tolerated in patients with AKI and CKD including those on hemodialysis.
Larger, well-controlled studies evaluating its
safety and efficacy in patients with kidney diseases are
needed.

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RESEARCH LETTER

Clinical Effectiveness and Safety of Remdesivir in Hemodialysis Patients with COVID-19

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Kidney Int Rep (2022) **7,** 2522–2525; https://doi.org/10.1016/j.ekir.2022.08.031
KEYWORDS: COVID-19; hemodialysis; mortality; remdesivir; severity; side effect

Results

In total, 118 patients with COVID-19 who are on hemodialysis were included in the study, and 44 patients (37.3 %), were administered remdesivir during hospitalization.

The **mean age was 68.5 ± 12.8 years, and 66.1% were male.**

The remdesivir group had a tendency of more severe disease ($P = 0.058$), and the NEWS on the day of hospitalization was significantly higher in the remdesivir group ($P = 0.026$). The incidence of comorbid diseases did not differ between the 2 groups.

The patients in the remdesivir group showed substantially higher lactate dehydrogenase levels and proportion of bilateral lung infiltration at admission.

Clinical Course and Outcomes

The proportion of patients who received oxygen therapy, a high-flow nasal cannula, and mechanical ventilation did not differ between the 2 groups.

The composite outcome of mortality, use of a high-flow nasal cannula, and transfer to the intensive care unit occurred less frequently in the remdesivir group (1 [2.3%] vs. 10 [13.5%], *P* = 0.042).

Disease severity aggravation rate was also lower in the remdesivir group (3 [6.8%] vs. 15 [20.3%], *P* = 0.049).

No anaphylaxis or hypersensitivity reaction was observed after the use of remdesivir.

The incidence of elevation of liver enzymes during hospitalization did not differ between the remdesivir and non-remdesivir groups (22.7% vs. 17.6%, $P = 0.494$;.

In conclusion, remdesivir use in patients with COVID-19 who are on hemodialysis reduced the risk of composite of mortality, high-flow nasal cannula use, and intensive care unit transfer.

In addition, the risk of severity worsening decreased in patients treated with remdesivir.

No significant side effects, including liver function test derangement, were observed after remdesivir use.

Remdesivir may be used in patients with COVID-19 who are on hemodialysis after considering its benefits and risks.

Clin Kidney J. 2022 Nov; 15(11): 2056–2062.
Published online 2022 Aug 23. doi: 10.1093/ckj/sfac185
PMCID: PMC9452122
PMID: 36320364

Comparison of safety and outcomes related to remdesivir treatment among dialysis patients hospitalized with COVID-19

Kirollos E Zaki, Cheng-Wei Huang, Hui Zhou, Joanie Chung, David C Selevan, Mark P Rutkowski, and John J Sim✉

Associated Data

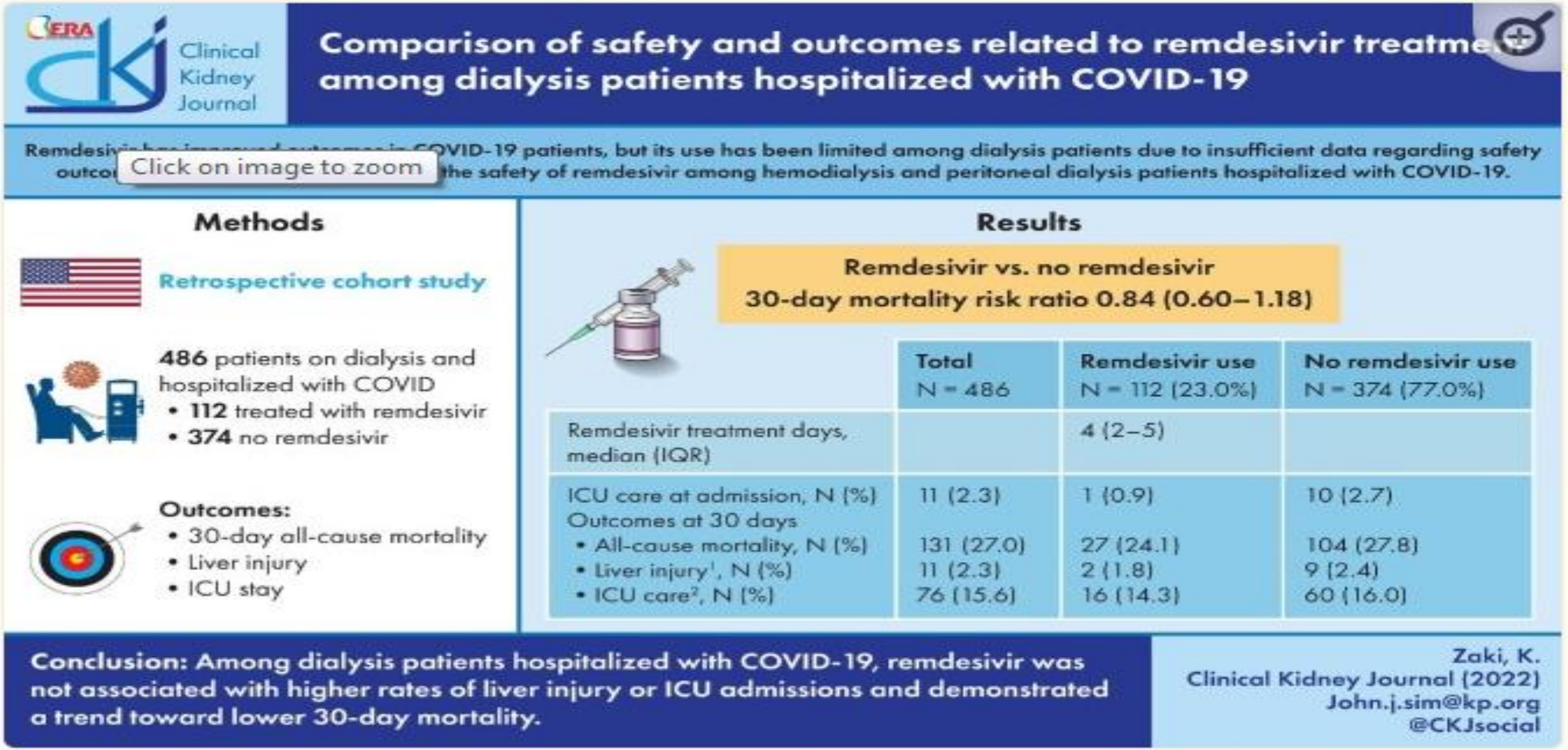
- **Supplementary Materials**
- **Data Availability Statement**

ABSTRACT

Go to: ▸

Background

Patients with end-stage kidney disease (ESKD) are highly susceptible to coronavirus disease 2019 (COVID-19) infection and its complications. Remdesivir has improved outcomes in COVID-19 patients but its use has been limited among ESKD patients due to insufficient data regarding safety outcomes. We sought to evaluate the safety of remdesivir among dialysis patients hospitalized with



nical Abstract

CONCLUSION

Our study demonstrated that remdesivir treatment in both peritoneal and hemodialysis patients hospitalized with COVID-19 was not associated with worsened transaminitis, ICU and mortality outcomes compared with patients who did not receive remdesivir. Furthermore, remdesivir-treated patients demonstrated a trend toward improvement in 30-day mortality.

Remdesivir Administration in COVID-19 Patients With Renal Impairment: A Systematic Review

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Farhad Najmeddin, PharmD,[1] and Mojtaba Mojtahedzadeh, PharmD[1]*

Background: Remdesivir (RDV) is the main antiviral for the treatment of moderate to severe forms of Coronavirus disease 2019 (COVID-19). Several studies revealed a shortening time to clinical improvement of COVID-19 and mortality benefits in patients receiving RDV. The patients with renal disease were excluded from large clinical trials of RDV, and the probable nephrotoxicity of the drug, its metabolites, and the vehicle (sulfobutylether-β-cyclodextrin) have led to the recommendation against using RDV in patients with an estimated glomerular filtration rate of <30 mL/min.

Areas of Uncertainty: This systematic review aimed to collect data about the necessity and safety administration of RDV in the setting of renal impairment.

Data Sources: Search through databases including MEDLINE, ScienceDirect, Cochrane Library, and PubMed was performed. The studies were carried out in adults and enrolled patients with different types of renal impairment (ie, acute kidney injury, chronic kidney disease, kidney transplant, and renal replacement therapy) were included. Eligible studies were assessed, and required data were extracted.

Results: Twenty-two cross-sectional studies, cohorts, case reports, and case series were included in this review. The mortality rate was between 7.3% and 50%, and various severity of COVID-19 was included in the studies. None of them reported an increase in adverse effects attributed to RDV administration. A decrease in inflammatory mediators and other benefits were obvious.

Conclusions: Although the manufacturer's labeling does not recommend RDV administration in patients with severe renal impairment, it seems that nephrotoxicity is less concerning in the population of these patients. Moreover, RDV may be helpful in acute kidney injury induced by the viral invasion of COVID-19. To the best of our knowledge, this is the first systematic review of the use of RDV in kidney failure. Larger, well-designed, and pharmacokinetic studies are required to have a

American Journal of Therapeutics 29, e520–e533 (2022)

Conclusions:

Although the manufacturer's labeling does not recommend RDV administration in patients with severe renal impairment, it seems that nephrotoxicity is less concerning in the population of these patients.

Moreover, RDV may be helpful in acute kidney injury induced by the viral invasion of COVID-19.

To the best of our knowledge, this is the first systematic review of the use of RDV in kidney failure. Larger, well-designed, and pharmacokinetic studies are required to have a safe and logical recommendation about the use of RDV in patients with renal disorders.

American Journal of Therapeutics 29, e520–e533 (2022)

Men's Health Journal. 2023; 7(1): e7

ORIGINAL RESEARCH

Clinical Outcomes of Remdesivir in COVID-19 Patients with Acute Kidney Injury or Chronic Kidney Disease: A Randomized Clinical Trial

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Abstract: **Background:** remdesivir is an RNA polymerase inhibitor approved to treat moderate to severe Coronavirus Disease 2019 (COVID-19); however, it has not yet been authenticated to apply to patients with acute kidney injury (AKI) or chronic kidney disease (CKD). Regarding some positive results obtained from previous studies, we aimed to evaluate the efficacy and safety of remdesivir in patients with COVID-19 with severe renal impairment.
Methods: In a randomized clinical trial, remdesivir was added to the standard regimen of treating patients with COVID-19 with AKI or CKD. 200 mg remdesivir was given on the first day of admission to 50 patients followed by 100 mg every other day until resolution of the symptoms. Clinical and paraclinical evaluation was performed daily and the findings were compared with the 50 patients on standard treatment regimen.
Results: the rates of intensive care unit (ICU) admission (P: 0.02), and mortality (P: 0.007) were significantly reduced in patients who received remdesivir. Moreover, a substantial decrease of aspartate transaminase (AST) (P: 0.004), lactate dehydrogenase (LDH) (P: 0.004), ferritin (P: 0.007), erythrocyte sedimentation rate (ESR) (P<0.0001), alkaline phosphatase (ALP) (P: 0.006) were observed in the patients receiving remdesivir compared to the baseline values which was absent in case of non-remdesivir group. No serious side effects were observed, except for one patient who showed elevated liver enzymes.
Conclusion: remdesivir appears to be well tolerated in patients with AKI and CKD. Administration of this drug resulted in reduced mortality and ICU admission as well as clinical and paraclinical improvement in these patients.

Methods: In a randomized clinical trial, remdesivir was added to the standard regimen of treating patients with COVID-19 with AKI or CKD. 200 mg remdesivir was given on the first day of admission to 50 patients followed by 100 mg every other day until resolution of the symptoms. Clinical and paraclinical evaluation was performed daily and the findings were compared with the 50 patients on standard treatment regimen.

Results: the rates of intensive care unit (ICU) admission (P: 0.02), and mortality (P: 0.007) were significantly reduced in patients who received remdesivir. Moreover, a substantial decrease of aspartate transaminase (AST) (P: 0.004), lactate dehydrogenase (LDH) (P: 0.004), ferritin (P: 0.007), erythrocyte sedimentation rate (ESR) (P<0.0001), alkaline phosphatase (ALP) (P: 0.006) were observed in the patients receiving remdesivir compared to the baseline values which was absent in case of non-remdesivir group. No serious side effects were observed, except for one patient who showed elevated liver enzymes.

Conclusion:

remdesivir appears to be well tolerated in patients with AKI and CKD. Administration of this drug resulted in reduced mortality and ICU admission as well as clinical and paraclinical improvement in these patients

Mens Health J. 2023; 7(1): e7.

antibiotics

MDPI

Article

Efficacy and Safety of Remdesivir in COVID-19 Positive Dialysis Patients

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Methods: **The sample population consisted of 83 dialysis patients with COVID-19 who were administered Remdesivir at a dose of 100 mg before hemodialysis, as per hospital protocol**. After the treatment with Remdesivir, we assessed the outcomes across two endpoints, namely primary (surviving vs. dying) as well as clinical and biochemical changes (ferritin, liver function test, C-reactive protein, oxygen requirements, and lactate dehydrogenase levels) and secondary (adverse effects, such as diarrhea, rise in ALT). In Kaplan–Meier analysis, the survival probabilities were compared between patients who received Remdesivir within 48 h of diagnosis and those who received it after 48 h. Cox regression analysis was employed to determine the predictors of outcome. (4)

Results:

Of the 83 patients, 91.5% survived and 8.5% died.

Remdesivir administration did not reduce the death rate overall.

Hospital stays were shorter (p = 0.03) and a nasopharyngeal swab for COVID-19 was negative earlier (p = 0.001) in survivors who had received Remdesivir within 48 h of diagnosis compared to those who had received Remdesivir after 48 h.

The only variables linked to the 30-day mortality were serum CRP (p = 0.028) and TLC (p = 0.013). No major adverse consequences were observed with Remdesivir.

Conclusions: Remdesivir has the potential to shorten the recovery time for dialysis patients if taken within 48 h of onset of symptoms, without any adverse effects.

Available online at www.sciencedirect.com

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journal homepage: www.e-jmii.com

Original Article

Safety and effectiveness of remdesivir for the treatment of COVID-19 patients with end-stage renal disease: A retrospective cohort study

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Abstract Background: Remdesivir has been used to treat severe coronavirus 2019 (COVID- 19); however, its safety and effectiveness in patients remain unclear. This study aimed to investigate the safety and effectiveness of remdesivir in patients with COVID-19 with endstage renal disease (ESRD).

Methods:

This retrospective study used the Chang Gung Research Database (CGRD) and extracted data from 21,621 adult patients with COVID-19 diagnosed between April 2021 and September 2022.

The patients were divided into groups based on their remdesivir use and the presence of ESRD.

The adverse effects of remdesivir and their outcomes were analyzed after propensity score matching.

Results:

There were no statistically significant differences in heart rates, blood glucose levels, variations in hemoglobin levels and liver function, before and after remdesivir use, or between the two groups after remdesivir use.

A comparison was made between patients with ESRD using remdesivir and those not using remdesivir after propensity score matching (N = 44)

Conclusions

Our study demonstrates the safety of remdesivir in patients with ESRD and COVID-19.

Common adverse effects of remdesivir, including anemia, hyperglycemia, abnormal liver function, and bradycardia, were not higher in patients with ESRD than in patients without ESRD.

Although remdesivir use in patients with COVID-19 and ESRD appears to improve some clinical conditions, its effectiveness remains uncertain and could not be proved in our study.

Further studies are required to explore the effects of remdesivir in the treatment of patients with COVID-19 and

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RESEARCH Open Access

Adverse effects of remdesivir for the treatment of acute COVID-19 in the pediatric population: a retrospective observational study

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Abstract

Background Although the severity of coronavirus disease 2019 (COVID-19) tends to be lower in children, it can still lead to severe illness, particularly among those with chronic medical conditions. While remdesivir (RDV) is one of the few approved antiviral treatments for COVID-19 in children in many countries, the available data on the safety of RDV in this population is limited.

Methods To address this knowledge gap, a multicenter study involving 65 patients retrospectively analyzed the clinical data from individuals aged ≤18 who were hospitalized due to severe COVID-19 (defined as $SpO_2 < 94\%$ or requiring supplemental oxygen) and received at least one dose of RDV. Additionally, the study encompassed 22 patients with mild-moderate COVID-19 who were considered at high risk of developing severe disease.

Results Nineteen children (29%) experienced mild-to-moderate adverse events (AEs) attributed to RDV, including transaminitis in 20% of children, bradycardia in 8%, and hypotension in 5%. AEs did not require discontinuation of RDV, except in one patient who developed premature ventricular contractions. The rate of AEs did not differ between patients with severe COVID-19 and those with mild-moderate COVID-19 but at high risk for severe disease. All but one patient were discharged within 23 days of admission, and no fatalities were recorded. Among high-risk patients with mild-moderate disease, only 2 (9%) progressed to the point of needing supplemental oxygen.

Conclusions Our data suggests that RDV is safe in children, with no reported serious AEs. However, the absence of a control group limits the extent to which conclusions can be drawn. RDV may contribute to clinical improvement, particularly in high-risk patients.

Conclusions Our retrospective study of RDV in children with COVID-19 demonstrates the safety of this pharmacotherapy in the pediatric population, as all AEs were either mild or moderate and rarely necessitated discontinuation of the drug.

The most commonly observed AE was transaminitis, followed by bradycardia and hypotension.

A similarly favorable adverse effect profile was seen in high-risk children with mild-moderate COVID19. Rates of clinical improvement in the overall cohort at one month were extraordinarily high, and very few high-risk patients progressed to require supplemental oxygen once started on RDV. While placebo-controlled trials are warranted to establish definite conclusions about its safety and efficacy, our study provides a valuable contribution to the growing literature supporting the safety and tolerability of RDV in pediatric patients with COVID-19.

Clinical Infectious Diseases

MAJOR ARTICLE

Efficacy and Safety of Remdesivir in People With Impaired Kidney Function Hospitalized for Coronavirus Disease 2019 Pneumonia: A Randomized Clinical Trial

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Background. Few antiviral therapies have been studied in patients with coronavirus disease 2019 (COVID-19) and kidney impairment. Herein, the efficacy, safety, and pharmacokinetics of remdesivir, its metabolites, and sulfobutylether-β-cyclodextrin excipient were evaluated in hospitalized patients with COVID-19 and severe kidney impairment.

Methods. In REDPINE, a phase 3, randomized, double-blind, placebo-controlled study, participants aged ≥12 years hospitalized for COVID-19 pneumonia with acute kidney injury, chronic kidney disease, or kidney failure were randomized 2:1 to receive intravenous remdesivir (200 mg on day 1; 100 mg daily up to day 5) or placebo (enrollment from March 2021 to March 2022). The primary efficacy end point was the composite of the all-cause mortality rate or invasive mechanical ventilation rate through day 29. Safety was evaluated through day 60.

Results. Although enrollment concluded early, 243 participants were enrolled and treated (remdesivir, n = 163; placebo, n = 80). At baseline, 90 participants (37.0%) had acute kidney injury (remdesivir, n = 60; placebo, n = 30), 64 (26.3%) had chronic kidney disease (remdesivir, n = 44; placebo, n = 20), and 89 (36.6%) had kidney failure (remdesivir, n = 59; placebo, n = 30); and 31 (12.8%) were vaccinated against COVID-19. Composite all-cause mortality or invasive mechanical ventilation rates through day 29 were 29.4% and 32.5% in the remdesivir and placebo group, respectively ($P = .61$). Treatment-emergent adverse events were reported in 80.4% for remdesivir versus 77.5% for placebo, and serious adverse events in 50.3% versus 50.0%, respectively. Pharmacokinetic plasma exposure to remdesivir was not affected by kidney function.

Conclusions. Although the study was underpowered, no significant difference in efficacy was observed between treatment groups. REDPINE demonstrated that remdesivir is safe in patients with COVID-19 and severe kidney impairment.

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Keywords. SARS-CoV-2; COVID-19; remdesivir; kidney impairment.

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Conclusions. Although the study was underpowered, no significant difference in efficacy was observed between treatment groups. REDPINE demonstrated that remdesivir is safe in patients with COVID-19 and severe kidney impairment.

RESEARCH Open Access

Propensity score matched analysis for the safety and effectiveness of remdesivir in COVID-19 patients with renal impairment

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Abstract

Backgrounds Remdesivir (RDV) is an antiviral agent approved for the treatment of coronavirus disease 2019 (COVID-19); however, is not recommended for patients with renal impairment. Due to limitations associated with prospective clinical trials, real-world data on the safety and efficacy of RDV in patients with renal impairment are necessary.

Methods Propensity score-matched (PSM) retrospective analysis was conducted between March 2020 and September 2022 in COVID-19 patients with an eGFR < 30 mL/min in four Korean hospitals. The RDV treatment group was matched to the untreated control group. The safety and clinical outcomes in patients who received RDV were analyzed.

Results A total of 564 patients were enrolled; 229 patients received RDV either for treatment or prophylaxis. On day 5, no difference in nephrotoxicity was observed between the two groups, and liver enzyme levels were within the normal range. In multivariate analysis for new dialysis, RDV treatment was not a risk factor for new dialysis. Among the 564 patients, 417 were indicated for a 5-day course of RDV treatment and 211 patients were treated with RDV. After PSM, no differences in the clinical outcomes were observed between the two groups.

Conclusion RDV use in COVID-19 patients with renal impairment did not result in significant nephrotoxicity or hepatotoxicity.

Keywords Remdesivir, COVID-19, Renal insufficiency, Propensity Score, Safety

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Conclusion

In conclusion, the use of RDV for COVID-19 in patients with renal impairment was confirmed to be safe. Furthermore, RDV was not significantly associated with hepatotoxicity or renal toxicity. In patients with severe conditions, such as pneumonia and oxygen requirement, the administration of RDV did not seem to significantly improve mortality; therefore, better-designed studies are necessary.

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RESEARCH ARTICLE

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Safety and effectiveness of remdesivir in hospitalized patients with COVID-19 and severe renal impairment: experience at a large medical center

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ABSTRACT

Background: Literature on the safety of remdesivir in hospitalized COVID-19 patients with severe renal impairment is limited. We aimed to investigate the safety and effectiveness of remdesivir in this population.

Methods: We conducted a retrospective cohort study of adult hospitalized COVID-19 patients who received remdesivir between April 2022 and October 2022. Outcomes were compared between estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2 and ≥30 mL/min/1.73 m^2 groups. The primary safety outcomes were acute kidney injury (AKI) and bradycardia, while the primary effectiveness outcomes included mortality in COVID-19-dedicated wards and hospital mortality. Secondary outcomes included laboratory changes, disease progression, and recovery time.

Results: A total of 1,343 patients were recruited, with 307 (22.9%) in the eGFR <30 group and 1,036 (77.1%) in the eGFR ≥30 group. Patients with an eGFR <30 had higher risks of AKI (adjusted hazard ratio [aHR] 2.92, 95% CI 1.93–4.44) and hospital mortality (aHR 1.47, 95% CI 1.06–2.05) but had comparable risks of bradycardia (aHR 1.15, 95% CI 0.85–1.56) and mortality in dedicated wards (aHR 1.43, 95% CI 0.90–2.28) than patients with an eGFR ≥30. Risk of disease progression was higher in the eGFR <30 group (adjusted odds ratio 1.62, 95% CI 1.16–2.26). No difference between the two groups in laboratory changes and recovery time.

Conclusions: Hospitalized COVID-19 patients receiving remdesivir with severe renal impairment had an increased risk of AKI, hospital mortality, and COVID-19 disease progression compared to patients without severe renal impairment.

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