DOI: 10.1002/hsr2.1676

RESEARCH LETTER

Health Science Reports Open Access WILEY

The effect of remdesivir on mortality and the outcome of patients with COVID-19 in intensive care unit: A case–control study

1 | INTRODUCTION

In 2002, severe acute respiratory syndrome (SARS) first appeared in China. It quickly spread worldwide within 3 months, resulting in the first pandemic of the twenty-first century with a 10% mortality rate.[1] Several unexplained signs and symptoms of acute and chronic pulmonary pneumonia were recorded in Wuhan, China, in late December 2019.[2] Chinese health professionals acted quickly to contain the epidemic and started etiological research.

The World Health Organization designated this new virus as a novel coronavirus-2019 for a time in 2020.[3] One of several single-stranded RNA viruses in a vast family is the severe acute respiratory syndrome coronavirus (SARS-CoV) virus.[4] Lower respiratory symptoms are brought on by the coronavirus, which has been isolated from cats, dogs, and most recently, bats.[5] Also, this newly discovered virus can be spread by nasal drops, close contact, urine, and feces.[6]

Almost 70% of patients experience refractory fevers and shortness of breath, whereas 30% show indications of recovery after 1 week, and 20%–30% of patients require mechanical ventilation.[7] These patients have significant lung damage in the form of pathological findings. Perhaps the virus directly invaded the patient's lungs or immunopathological consequences caused significant lung damage; many of its pathological characteristics have not yet been recognized.[8]

There is a wide range of SARS-CoV-2 infection symptoms.[9] In severe situations, it can be linked to pneumonia and serious and life-threatening complications, such as acute respiratory distress syndrome, failure, involvement of numerous organs, and ultimately death.[10] The patient may not exhibit any symptoms and may be asymptomatic.[11] Those who are older and who have respiratory or cardiovascular illnesses appear to be more likely to be involved and experience serious repercussions.[12] Supportive care, invasive and noninvasive oxygen therapy, and off-label medications such as antivirals and antiparasitic drugs as well as steroidal anti-inflammatory pharmaceuticals are the current treatments available in the lack of a proven viable cure.[13]

Numerous medications have been discovered so far to treat the coronavirus, but none of them have yet demonstrated efficacy. Remdesivir is one of these medicines that is frequently used.[14] The adenosine analog monophosphoramidite prodrug in question has a variety of antiviral effects, including activity against filoviruses, paramyxoviruses, pneumoviruses, and coronaviruses.[15] Middle East respiratory syndrome (MERS) and SARS-CoV are both inhibited by the viral RNA polymerase inhibitor Remdesivir.[16] This medication is regarded as one of the most promising ones for treating coronavirus in a lab setting.[17] In preliminary nonhuman investigations, this medication also decreased virus counts and lessened lung damage 12 h after vaccination.[18]

Remdesivir was well tolerated but less effective than several monoclonal antibodies in studies for the treatment of Ebola virus disease. In some nations, this medication has recently been utilized to treat coronavirus disease 2019 (COVID-19) patients.[19] It has been effective in critically ill COVID-19 patients, according to numerous research. Remdesivir's clinical and antiviral impact on COVID-19, however, remains unclear. Considering this, the purpose of this study was to determine the impact of the medicine remdesivir on COVID-19 patient death rates.

2 | MATERIALS AND METHODS

It is a case–control study. The studied population of patients with COVID-19 hospitalized in Shohada-e-Ashayer Hospital of Khorramabad who met the inclusion criteria was selected. The study group was divided into two control groups and remdesivir group. In the remdesivir group, in addition to receiving standard treatment (dexamethasone + azithromycin + naproxen + vitamin D + salbutamol), remdesivir (treatment for 5 days with a dose of 200 mg on the first day and a single dose of 100 mg on the following days) was also given. They did then, to collect information, a form designed by the researcher was used, and 70 cases of hospitalized patients with COVID-19 were selected in the first half of 2019, and the following factors were measured with the information available in the case of these patients:

- Determining the frequency distribution of underlying characteristics (age, gender, type of underlying disease).

- Determining the effect of medicine on the mortality of patients.
- Determining the effect of medication on hospitalization rates.
- Determining the effect of medication on the rate of hospitalization in intensive care unit (ICU).
- Determining the effect of the drug on mechanical ventilation.
- The severity of the disease was defined as death or hospitalization in ICU or hospitalization in the ward, and the recovery status was defined as discharge or death from the hospital, and after collecting the data, the factors and variables mentioned above were investigated, and analyzed.

Inclusion criteria: age over 18 years, severe pulmonary involvement, oxygen saturation less than 94% while receiving oxygen support, positive polymerase chain reaction (PCR) test.

Exclusion criteria: renal failure, creatinine clearance below 30 cc/min, liver enzyme above five times normal.

Considering that this study is a case–control study, there was no need to determine the sample size using statistical methods. In this study, out of a total of 70 patients, 35 patients were in the control group and 35 patients were in the remdesivir group.

A researcher-made questionnaire including demographic characteristics, clinical results, and laboratory findings.

After collecting the data and entering them into the SPSS-21 statistical software, the proportions and the appropriate central and dispersion indices are presented in the form of tables and graphs. To assess the normality of the distributions of measured variables and select appropriate statistical tests, we conducted Kolmogorov–Smirnov tests. For nominal variables, we applied χ^2 parametric statistical analysis, while for quantitative variables, given their non-normal distribution, we utilized Mann–Whitney nonparametric statistical analysis. These choices were made to ensure the suitability of the statistical tests for our data set, and we acknowledge the importance of explicitly mentioning these decisions in our statistical analysis section for clarity and transparency.

Multiple logistic regression was used to correlate independent variables with the recovery rate of patients and the results were reported at a significance level of 5%.

Also, two scoring systems, Sofa Score and APACHE II Score, were used to predict the mortality rate in the studied patients with COVID-19 in the intensive care unit.

This plan is in the Ethics Committee of Lorestan University of Medical Sciences and with IR Ethics ID. LUMS. REC. 1400.013 was approved.

This work was in line with the STROBE criteria.

3 | RESULTS

After the initial evaluation during one-half year (from the beginning of April to the end of September 2019), 70 patients were included in the study due to meeting the entry criteria, and 20 patients were excluded from the study due to not meeting the entry criteria. Out of 70 eligible patients, 35 patients were in the remdesivir group (receiving remdesivir plus standard regimen) and 35 patients were in the control group (receiving standard regimen).

In the control group, there were 22 men (62.86%) and 13 women (37.14%) with an average age of 66.37 ± 18.14, of which 28 (80%) had a history of drug use, four (11.43%) had a history of smoking or other addictions, and 30 people (85.71%) had an underlying disease. In the remdesivir group, 17 men (48.57%) and 18 women (51.43%) with an average age of 65.54 ± 12.54, of which 28 (80%) had a history of drug use, three (8.57%) had a history of smoking and other addictions, and 28 people (80%) had an underlying disease that statistically did not have a significant difference between the demographic and clinical parameters in the remdesivir and control groups ($p > 0.05$).

3.1 | Comparison of underlying diseases in COVID-19 patients in the control and remdesivir groups

In the control group, out of a total of 35 patients, 16 people (45.71%) had cardiovascular diseases, nine people (25.71%) had diabetes, four people (11.43%) had respiratory problems, and three people (8.57%) renal, and in the remdesivir group, out of 35 patients, 22 (62.86%) had cardiovascular diseases, 14 (40%) had diabetes, four (11.43%) had respiratory diseases, and one (2.86%) had kidney disease, and there was no statistically significant difference between the two control and remdesivir groups ($p > 0.05$).

3.2 | Prevalence of primary symptoms in COVID-19 patients in the control group and remdesivir

In the control group, the highest frequency related to shortness of breath, fever and chills, cough, weakness and lethargy, myalgia, loss of appetite, and nausea and vomiting, respectively, and in the remdesivir group, the highest frequency related to shortness of breath, weakness and lethargy, cough. It was fever and chills, myalgia, nausea, and vomiting.

There was a statistically significant difference between the two variables of weakness and lethargy and respiratory distress in the control and remdesivir groups ($p < 0.05$). However, in terms of other variables, there was no significant difference between the two control and remdesivir groups, as well as the number of days between the onset of symptoms and treatment ($p > 0.05$).

3.3 | Comparison of the average clinical indicators of the studied patients with COVID-19 in the control group and remdesivir at the time of arrival

In the control group, the average body temperature was 37.18 ± 0.49, the average heart rate was 87.59 ± 15.06, the average respiration rate was 87.37 ± 3.2, the average systolic blood pressure was 119.06 ± 28.95, the average blood pressure diastolic 74.31 ± 16.96 and average blood oxygen level 81.53 ± 11.88 and in remdesivir

group average body temperature 37.09 ± 0.57, average heart rate 86.33 ± 12.86, average respiratory rate 34 ± 3.98 20.20, the average systolic blood pressure was 123.40 ± 19.73, the average diastolic blood pressure was 76.48 ± 17.46, and the average blood oxygen level was 85.94 ± 8.60, which statistically, there was no significant difference between the two groups. ($p > 0.05$).

3.4 | Information predicting disease progression in the control and remdesivir groups at baseline

By comparing the information predicting the progress of the disease, including international normalized ratio (INR), lactate dehydrogenase (LDH), Troponin C, creatine kinase, and C-reactive protein (CRP), in the control group and remdesivir in the baseline state, it showed that there was a statistically significant difference in the erythrocyte sedimentation rate (ESR) factor between the two control and remdesivir groups ($p < 0.05$) while in other variables this difference was not significant ($p < 0.05$) (Table 1).

3.5 | Comparison of the average laboratory indices of the studied patients with COVID-19 in the control and remdesivir groups at the time of admission and at the time of discharge

There was a statistically significant difference in the magnesium variable at the beginning of the study ($p < 0.05$), although there was no significant difference at the end of the study. In the examination of other laboratory data, there was no significant difference between the average changes of the two control and remdesivir groups ($p > 0.05$) (Table 2).

TABLE 1 The percentage frequency of primary symptoms in COVID-19 patients when visiting the hospital.

Initial symptoms when visiting the hospital		Control	Remdesivir	*p* Value
Dyspnea	Yes, N(%)	22 (62.86)	21 (60)	0.81
	No, N(%)	13 (37.14)	14 (40)	
Fever and shivering	Yes, N(%)	13 (37.14)	13 (37.14)	>0.99
	No, N(%)	22 (62.86)	22 (62.86)	
Cough	Yes, N(%)	13 (37.15)	16 (45.71)	0.47
	No, N(%)	22 (62.86)	19 (54.28)	
Weakness & lethargy	Yes, N(%)	9 (25.71)	17 (48.57)	0.048
	No, N(%)	26 (74.28)	18 (51.43)	
Myalgia	Yes, N(%)	8 (22.86)	9 (25.71)	0.78
	No, N(%)	27 (77.14)	26 (74.28)	
Anorexia	Yes, N(%)	3 (8.57)	4 (11.43)	0.7
	No, N(%)	32 (91.43)	31 (88.57)	
PONV	Yes, N(%)	3 (8.57)	8 (22.86)	0.1
	No, N(%)	32 (91.43)	27 (77.14)	
Diarrhea	Yes, N(%)	2 (5.71)	3 (8.57)	0.64
	No, N(%)	33 (94.28)	32 (91.43)	
Headache	Yes, N(%)	2 (5.71)	2 (5.71)	>0.99
	No, N(%)	33 (94.28)	33 (94.28)	
Sore throat	Yes, N(%)	1 (2.85)	2 (5.71)	0.55
	No, N(%)	34 (97.14)	33 (94.28)	
ARDS	Yes, N(%)	0 (0)	4 (11.43)	0.04
	No, N(%)	35 (100)	31 (88.57)	
Number of days between onset of symptoms and treatment	Mean ± Std	7.45 ± 4.45	8.04 ± 3.93	0.7

Abbreviations: ARDS, acute respiratory distress syndrome; COVID-19, coronavirus disease 2019; ESR, erythrocyte sedimentation rate; PONV, postoperative nausea and vomiting.

TABLE 2 Factors predicting disease progression in the control and remdesivir groups at baseline.

Clinical indicators and laboratory results	Control (mean ± Std)	remdesivir (mean ± Std)	Mann–Whitney *p* Value	Kolmogorov–Smirnov *p* Value
INR	1.2 ± 0.37	1.07 ± 0.14	0.08	0.03
LDH (U/L)	870.44 ± 269.34	743.36 ± 281.62	0.09	0.02
Troponin C (ng/mL)	0.05 ± 0.02	0.05 ± 00	0.9	0.04
CPK (U/L)	129.28 ± 90.90	184.06 ± 140.56	0.1	0.01
CRP	+2.07 ± 0.73	+1.83 ± 0.94	0.47	0.03
ESR (mm/h)	36.58 ± 27.46	54.89 ± 31.02	0.03	0.02

Abbreviations: CPK, creatine kinase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; INR, international normalized ratio; LDH, lactate dehydrogenase.

3.6 | Comparison of the average length of stay in the hospital, ICU, recovery time, and mechanical ventilation in patients with COVID-19 according to the control and remdesivir groups

In the control group, the average length of hospital stay was 12.97 ± 9.65, the average length of ICU stay was 11.05 ± 9.1, the average duration of mechanical ventilation was 4.62 ± 5.24, and the average recovery time was 18. 0.2 ± 1, and in the remdesivir group, the average duration of hospitalization was 16.11 ± 11.52, the average duration of hospitalization in ICU was 14.03 ± 11.55, the average duration of mechanical ventilation was 7.03 ± 8.92, and the average duration of recovery was 0.43 ± 1.65 days, and there was no statistically significant difference between the control and remdesivir groups ($p > 0.05$) (Table 3).

3.7 | Comparing the prediction of the mortality rate of the studied patients with COVID-19 based on Sofa score in the control group and remdesivir in the baseline state

In the control group, 23 people (65.71%) had a mortality of less than 33%, six people (17.14%) had a mortality of 50%, and six people (17.14%) had a mortality above 95%, and in remdesivir group, 27 people (14/77%) mortality was less than 33%, four people (11.43%) had 50% mortality, and four people (11.43%) had mortality above 95%. Also, the mean SOFA score in the control group was 8.37 ± 3.18 and in the remdesivir group was 8.31 ± 2.50, and there was no statistically significant difference between the two control and remdesivir groups ($p > 0.05$).

3.8 | Comparison of prediction of mortality rate of studied patients with COVID-19 based on APACHE II score in control group and remdesivir in a baseline condition

In the control group, 23 people (65.71%) had a mortality of less than 20%, 10 people (28.57%) had a mortality between 20% and 40%, and two people (5.71%) had mortality between 40% and 60%, and in the intervention group 24 people (68.57%) had mortality less than 20%, 10 people (28.57%) had mortality between 20% and 40%, and one person (2.86%) had mortality between 40% and 60%.

Also, the average Apache-2 score was 13.31 ± 6.29 in the control group and 12.14 ± 5.94 in the remdesivir group. There was no statistically significant difference ($p > 0.05$).

The rate of recovery and mortality in the studied patients with COVID-19 in the control group and remdesivir, in the control group, five patients (14.28%) were discharged from a total of 35 patients and 30 patients (85.71%) died, and in the remdesivir group, out of a total of 35, four patients (4.4%) were discharged and 31 patients (34.06%) died. Statistically, there was no significant difference between the two control and remdesivir groups in terms of recovery and mortality ($p > 0.05$).

4 | DISCUSSION

In the current study, out of 70 eligible patients, 35 patients were included in the intervention group and 35 patients were included in the control group following the initial evaluation within a half year.

Similar to our analysis, the most prevalent underlying disorders in Lee et al. study were cardiovascular diseases. In the study by Long et al.,[19] high blood pressure had the highest percentage of patients with COVID-19 (49%) followed by liver disorders (17%), and lung diseases (1.15%) was in last place.[17]

According to Talebi et al., among all patients who had been referred, shortness of breath was the most prevalent symptom (72.5%), followed by cough (61.8%) and fever (48.9%) and individuals who recovered had much more cough symptoms.[20]

Cough was the most prevalent symptom in Long's study (66%)[19] and in Chen's study, fever (81.7%) and cough (36.5%) were the two most prevalent symptoms in COVID-19 patients.[17,21]

According to the study by Jalali Farahani et al., who evaluated clinical, biochemical, and radiographic data in old and nonelderly patients with Covid-19, all patients, elderly, and nonelderly, had higher levels of neutrophils, ESR, aspartate transaminase, LDH, and CRP.[22]

Stoeckle et al. did a retrospective cohort analysis on 55 individuals who were hospitalized because of COVID-19. Patients who advanced to intubation or death within 14 days had significantly greater levels of

TABLE 3 Comparison of the average laboratory indicators of the studied patients with COVID-19 in the control and remdesivir groups at the time of arrival and at the time of discharge.

Variables	Group	End, *p* Value	End (mean ± Std)	Start, *p* Value	Start (mean ± Std)	Kolmogorov–Smirnov *p* Value
WBC ($\times 10^3$/Ul)	Control	0.95	11.84 ± 9.86	0.23	12.31 ± 13.97	0.02
	Remdesivir		11.99 ± 7.45		9.11 ± 5.49	
Lamphocyte (%)	Control	0.08	5.18 ± 4.84	0.64	11.53 ± 8.25	0.01
	Remdesivir		7.81 ± 5.92		12.50 ± 8.64	
Hb (g/dL)	Control	0.44	11.70 ± 2.62	0.45	13.93 ± 2.45	0.03
	Remdesivir		11.23 ± 1.94		13.49 ± 2.16	
Platelet ($\times 10^3$)	Control	0.21	102.62 ± 95.39	0.99	193.88 ± 101.09	0.01
	Remdesivir		131.19 ± 69.23		194.06 ± 96.66	
Creatinine (mg/dL)	Control	0.56	1.57 ± 1.05	0.61	1.14 ± 0.46	0.04
	Remdesivir		1.40 ± 1.14		1.08 ± 0.46	
Urea (mg/dL)	Control	0.17	126.54 ± 89.31	0.23	50.96 ± 32.16	0.02
	Remdesivir		93.85 ± 74.03		50.38 ± 24.58	
Total Bilirobin (mg/dL)	Control	0.22	5.27 ± 5.57	0.61	0.92 ± 0.49	0.04
	Remdesivir		2.75 ± 2.85		0.83 ± 0.31	
Sodium(meq/L)	Control	0.9	141.68 ± 9.31	0.13	140.03 ± 5.88	0.03
	Remdesivir		141.41 ± 5.94		138.03 ± 4.51	
Potassium (meq/L)	Control	0.9	4.5 ± 0.77	0.07	3.90 ± 0.5	0.04
	Remdesivir		4.53 ± 0.89		4.12 ± 0.46	
Calcium (mg/dL)	Control	0.38	8.06 ± 1.44	0.15	8.50 ± 0.92	0.02
	Remdesivir		7.60 ± 1.05		8.20 ± 0.63	
Phosphor(mg/dL)	Control	0.71	3.78 ± 1.01	0.20	2.73 ± 0.52	0.04
	Remdesivir		3.43 ± 1.95		3.12 ± 0.91	
Magnesium (mg/dL)	Control	0.82	2.16 ± 0.55	0.01	1.98 ± 0.44	0.03
	Remdesivir		2.27 ± 0.71		1.71 ± 0.30	
AST (U/L)	Control	0.93	57.4 ± 66.06	0.43	49.07 ± 29.15	0.03
	Remdesivir		55.08 ± 36.77		43.90 ± 21.31	
ALT (U/L)	Control	0.88	68.25 ± 46.72	0.24	40.8 ± 26.31	0.01
	Remdesivir		73.28 ± 60.19		33.66 ± 19.58	
ALP (U/L)	Control	0.96	235.33 ± 113.62	0.68	214.6 ± 106.83	0.02
	Remdesivir		231.38 ± 129.63		203.07 ± 109.47	

Abbreviations: ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase.

CRP, D-dimer, and lactate dehydrogenase than patients who remained stable. Those who did not require intubation during the trial period had significantly lower CRP levels following remdesivir treatment.[23]

The risk of hospital discharge was 33% greater for the remdesivir-treated group than for the control group in Chen-Yang et al. study from 2020.[17] The average hospital stay for the 76 patients in Lee et al. study from 2020 was 10.09 days (11.6–8.6), and a total of 14 (18.4%) of the patients who got remdesivir died.[24] They were admitted to the ICU, where they spent an average of 9.29 days (ranging from 5.6 to 13.0). The remdesivir group demonstrated a considerably shorter average period of hospitalization (10 days) than the control group (16 days) based on the findings of Abd-Elsalam et al.[13] In this study, contrary to the results of our study, remdesivir had a positive effect on reducing the length of hospital stay.

In contrast to the findings of the current study, Oksuz et al. found that patients treated with remdesivir and those who were

transferred from the ward to the ICU experienced an average hospital stay of 17.3 days grew more.[9]

The average duration of mechanical breathing for patients in the study by Lee et al.[8] among 76 patients receiving remdesivir was 9.42 days (10.8–0.8), which is longer than the average seen in the intervention group of our study. Hospitalization in the intensive care unit (242 patients (20.7%) for the group receiving remdesivir compared to 234 patients (19.1%) in the control group) and the use of mechanical ventilation (69 patients (5.9%) for the intervention group compared with 45 patients (3.8%) for the intervention group) were both registered in the study by Ohl et al.[10,25] In the study by Abd-Elsalam et al.,[13] 11 patients (11%) in the remdesivir group and eight patients (8%), in comparison, required mechanical ventilation.

In the study by Grein et al., 30 of the 53 patients (or 57%) who were undergoing mechanical ventilation at the beginning of the study were extubated after a 10-day course of remdesivir therapy.[12]

Remdesivir medication had no positive impact on mortality in Egyptian patients with COVID-19, much like in Abd-Elsalam et al.[13] Our findings supported the Solidarity Treatment trial's findings, which indicated that remdesivir had no mortality benefit.

In the Grein et al. research, the death rate was 5% (1 of 19) for patients not undergoing invasive ventilation while it was 18% (6 of 34) for patients receiving remdesivir treatment.[12]

In agreement with our study, Lee et al. stated that there was no statistically significant difference in in-hospital mortality between the groups receiving remdesivir and the control group as one of the findings of their investigation.[8,26]

The meta-analysis by Yokoyama et al., which included four randomized controlled trials, revealed that the rate of clinical improvement in the remdesivir-treated group was noticeably higher than the rate in the group receiving conventional therapy.[11] The conclusions from our investigation were not supported by the findings of this study.

Numerous well-conducted randomized controlled trials (RCTs) have consistently demonstrated favorable outcomes associated with the utilization of Remdesivir in COVID-19 patients.

Chokkalingam et al.'s retrospective cohort study,[27] encompassing a substantial cohort of 24,856 individuals diagnosed with COVID-19, stands as a robust testament to the tangible reduction in inpatient mortality linked to remdesivir treatment. Leveraging health insurance claims and hospital chargemaster data lends authenticity to the study's real-world implications. The notable 17% decline in inpatient mortality observed among COVID-19 patients treated with remdesivir resonates harmoniously with findings drawn from randomized clinical trials. This concurrence reaffirms the tangible clinical advantages conferred by remdesivir administration in ameliorating patient outcomes.

In a parallel vein, Gupte et al.'s investigation[28] yields invaluable real-world insights into the safety and clinical repercussions of remdesivir intervention for COVID-19 patients in the Indian context. The retrospective analysis of an active surveillance database orchestrated by the authors shines a clarifying light on multifaceted dimensions of remdesivir's efficacy and safety profile. Within their study, remdesivir emerges as largely well tolerated, with manageable adverse events. Moreover, the report highlights a noteworthy clinical amelioration rate of 84%, thereby reinforcing the constructive influence of remdesivir on patient trajectories. By juxtaposing our study's findings against the backdrop of Gupte et al.'s research, the significance of real-world data in substantiating treatment effectiveness becomes strikingly evident. While our study imparts unique insights tailored to a specific patient subset, it is imperative to contextualize it within the broader spectrum of investigations such as Gupte et al.'s, which collectively contribute to the ongoing evolution of comprehension regarding the role of remdesivir in managing COVID-19.

By interweaving the insights of Chokkalingam et al. and Gupte et al. with our findings, we cultivate a more comprehensive and nuanced understanding of the intricate interplay between remdesivir treatment, clinical outcomes, and patient safety. These studies collectively serve as pivotal pillars shaping the narrative around remdesivir's contribution to the multifaceted landscape of COVID-19 management.

In light of the two recent clinical studies[29,30] comparing the efficacy of different antiviral agents in the treatment of hospitalized COVID-19 patients, it becomes evident that remdesivir may not necessarily offer superior benefits compared with other therapeutic options such as monoclonal antibodies, specifically casirivimab and imdevimab. The study by Hegazy et al.[29] found that casirivimab and imdevimab, an antibodies combination, resulted in better outcomes in terms of lower disease progression and improved multiorgan function compared with remdesivir and favipiravir. Additionally, the study by Hegazy et al. reported that casirivimab and imdevimab achieved lower mortality rates than remdesivir and favipiravir in hospitalized COVID-19 patients.[29,30] These findings underscore the potential advantages of monoclonal antibodies like casirivimab and imdevimab over remdesivir in the management of COVID-19 patients, suggesting that remdesivir may not always be the most effective treatment option in all cases. These studies may prompt a reconsideration of treatment protocols for COVID-19 patients and emphasize the importance of tailored therapeutic approaches based on the specific clinical condition of each patient.

5 | CONCLUSION

The study's outcomes unveiled that Remdesivir exhibited no noteworthy statistical disparity in patient mortality rates, hospital admissions, ICU admissions, or mechanical ventilation occurrences within the intervention group as opposed to the control group. The current study's findings do not substantiate the efficacy of this drug as a compelling treatment option for Covid-19 patients. However, it is important to emphasize that randomized controlled trials are imperative to definitively ascertain the safety and efficacy of remdesivir, alongside other investigational agents, in the therapeutic approach to individuals afflicted with SARS-CoV-2 infection.

KEYWORDS

coronavirus, Covid-19, ICU, mortality rate, remdesivir, SARS-CoV-2

AUTHOR CONTRIBUTIONS

Mehran Amirizadeh: Conceptualization; data curation; resources; software. **Ali Kharazmkia**: Formal analysis; funding acquisition; supervision; validation. **Kobra Sharifi abdoli**: Funding acquisition; investigation; validation; visualization. **Hadi Hayati abbarik**: Methodology; project administration; writing—original draft; writing—review & editing. **Ghasem Azimi**: Formal analysis; funding acquisition; supervision; validation.

ACKNOWLEDGMENTS

The authors extend our thanks to the clinical research development center of Shahid Rahimi Hospital affiliated with Lorestan University of Medical Sciences, for their kind support.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

ETHICS STATEMENT

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

TRANSPARENCY STATEMENT

The lead author Ali Kharazmkia, Ghasem Azimi affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Mehran Amirizadeh[1]
Ali Kharazmkia[1,2]
Kobra Sharifi abdoli[3]
Hadi Hayati abbarik[4]
Ghasem Azimi[5]

[1]*Department of Clinical Pharmacy, School of Pharmacy, Lorestan University of Medical Sciences, Khorramabad, Iran*
[2]*Clinical Research Development Center, Shahid Rahimi Hospital, Lorestan University of Medical Sciences, Khorramabad, Iran*
[3]*Student Research Committee, School of Pharmacy, Lorestan University of Medical Sciences, Khorramabad, Iran*
[4]*Department of Pharmacoeconomics and Management, School of Pharmacy, Lorestan University of Medical Sciences, Khorramabad, Iran*
[5]*Department of Internal Medicine, School of Medicine, Shahed University, Tehran, Iran*

Correspondence
Ali Kharazmkia, Assistant Professor of Clinical Pharmacy, Lorestan University of Medical Sciences, Khorramabad 6813833946, Iran.
Email: kharazmkia@lums.ac.ir

Ghasem Azimi, Associate Professor of Pulmonary Diseases, Shahed University, Tehran, Iran.
Email: md.ghasemazimi@gmail.com

ORCID

Ali Kharazmkia http://orcid.org/0000-0001-9081-8065
Ghasem Azimi http://orcid.org/0000-0002-1657-7352

REFERENCES

1. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020;579(7798):270-273.
2. World Health Organization. Coronavirus disease 2019 (COVID-19): situation report 73. 2020. https://www.who.int/
3. Walker PJ, Siddell SG, Lefkowitz EJ, et al. Changes to virus taxonomy and the Statutes ratified by the International Committee on Taxonomy of Viruses. 2020.
4. Wu A, Peng Y, Huang B, et al. Genome composition and divergence of the novel coronavirus (2019-Ncov) originating in China. *Cell Host Microbe*. 2020;27(3):325-328.
5. Viner RM, Ward JL, Hudson LD, et al. Systematic review of reviews of symptoms and signs of COVID-19 in children and adolescents. *Arch Dis Child*. 2021;106:802-807.
6. Rodriguez-Guerra M, Jadhav P, Vittorio TJ, et al. Current treatment in COVID-19 disease: a rapid review. *Drugs Context*. 2021;10:1-8.
7. Mehta PharmD, MPH M, Shyh GI, et al. A review of remdesivir for COVID-19: data to date. *Cardiol Rev*. 2020;28(Issue 6):332-334.
8. Lee S, Santarelli A, Caine K, Schritter S, Dietrich T, Ashurst J. Remdesivir for the treatment of severe COVID-19: a community hospital's experience. *J Osteopath Med*. 2020;120(12):926-933.
9. Oksuz E, Malhan S, Gonen MS, et al. Cost-Effectiveness analysis of remdesivir treatment in COVID-19 patients requiring low-flow oxygen therapy: payer perspective in Turkey. *Adv Ther*. 2021;38:4935-4948.
10. Ohl ME, Miller DR, Lund BC, et al. Association of remdesivir treatment with survival and length of hospital stay among US veterans hospitalized with COVID-19. *JAMA Network Open*. 2021;4(7):e2114741.
11. Yokoyama Y, Briasoulis A, Takagi H, Kuno T. Effect of remdesivir on patients with COVID-19: A network meta-analysis of randomized control trials. *Virus Res*. 2020;288:198137.
12. Grein J, Ohmagari N, Shin D, et al. Compassionate use of remdesivir for patients with severe Covid-19. *N Engl J Med*. 2020;382(24):2327-2336.
13. Abd-Elsalam SH, Ashraf Ahmed O, Mansour N, et al. Remdesivir efficacy in COVID-19 treatment: a randomized controlled trial. *Am J Trop Med Hyg*. 2021;106(3):886-890.
14. Padilla R, Arquiette J, Mai Y, Singh G, Galang K, Liang E. Clinical outcomes of COVID-19 patients treated with convalescent plasma or remdesivir alone and in combination at a community hospital in California's central valley. *J Pharm Pharm Sci*. 2021;24:210-219.

15. Poliseno M, Gallo C, Cibelli DC, et al. Efficacy and safety of remdesivir over two waves of the Sars-CoV-2 pandemic. *Antibiotics*. 2021;10:1477.
16. Paranjape N, Husain M, Priestley J, Koonjah Y, Watts C, Havlik J. Early use of remdesivir in patients hospitalized with COVID-19 improves clinical outcomes a retrospective observational study. *Infect Dis Clin Pract*. 2021;29:e282-e286.
17. Chen J, Qi T, Liua L et al. Clinical progression of patients with COVID-19 in shanghai, China. *J Infect*. 2020;80:e1-e6.
18. Sheikhi F, Mirkazehi Z, Azarkish F, et al. Clinical and demographic characteristics of patients with COVID -19 in iranshahr hospitals, southeastern Iran in 2020. *J Marine Med. Spring*. 2021;3(Issue 1):46-52.
19. Long L, Xu L, Xiao X, et al. Epidemiological and clinical characteristics of patients with coronavirus disease -2019 in shiyan city China. *Front Cell Infect Microbiol*. 2020;10:284.
20. Talebi S, Nematshahi M, Tajabadi A. Comparison of clinical and epidemiological characteristics of deceased and recovered patients with COVID -19 in Sabzevar. *J Mil Med*. 2020;22(6):509-516.
21. Antinori S, Cossu MV, Ridolfo AL, et al. Compassionate remdesivir treatment of severe Covid-19 pneumonia in intensive care unit (ICU) and Non-ICU patients: clinical outcome and differences in post-treatment hospitalisation status. *Pharmacol Res*. 2020;158:104899.
22. Jalali Farahani A, Swann J, Razi S, et al. Comparison of clinical, laboratory and radiological findings in Iranian elderly and Non-Elderly patients with COVID-19. *J Marine Med*. 2021;2(Issue 4): 216-225.
23. Stoeckle K, Witting B, Kapadia S, An A, Marks K. Elevated inflammatory markers are associated with poor outcomes in COVID-19 patients treated with remdesivir. *J Med Virol*. 2022;94:384-387.
24. van Laar SA, de Boer MGJ, Gombert-Handoko KB, Guchelaar HJ, Zwaveling J. Liver and kidney function in patients with Covid-19 treated with remdesivir. *Br J Clin Pharmacol*. 2021;87(11):4450-4454.
25. Rezagholizadeh A, Khiali S, Sarbakhsh P, Entezari-Maleki T. Remdesivir for treatment of COVID-19; an updated systematic review and meta-analysis. *Eur J Pharmacol*. 2021;897:173926.
26. Spinner CD, Gottlieb RL, Criner GJ, et al. GS-US-540-5774 Investigators Effect of remdesivir vs standard care on clinical status at 11 days in patients with moderate COVID-19: a randomized clinical trial. *JAMA*. 2020;324(11):1048.
27. Chokkalingam AP, Hayden J, Goldman JD, et al. Association of remdesivir treatment with mortality among hospitalized adults with COVID-19 in the United States. *JAMA Network Open*. 2022;5(12): e2244505.
28. Gupte V, Hegde R, Sawant S, et al. Safety and clinical outcomes of remdesivir in hospitalised COVID-19 patients: a retrospective analysis of active surveillance database. *BMC Infect Dis*. 2022;22(1):1.
29. Hegazy SK, Tharwat S, Hassan AH. Study to compare the effect of casirivimab and imdevimab, remdesivir, and favipiravir on progression and multi-organ function of hospitalized COVID-19 patients. *Open Med*. 2023;18(1):20230768.
30. Hegazy SK, Tharwat S, Hassan AH. Clinical study to compare the efficacy and safety of casirivimab & imdevimab, remdesivir, and favipravir in hospitalized COVID-19 patients. *J Clin Virol Plus*. 2023;3(2):100151.

How to cite this article: Amirizadeh M, Kharazmkia A, Sharifi abdoli K, Hayati abbarik H, Azimi G. The effect of remdesivir on mortality and the outcome of patients with COVID-19 in intensive care unit: a case–control study. *Health Sci Rep*. 2023;6:e1676. doi:10.1002/hsr2.1676