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ORIGINAL ARTICLE

EFFECT OF REMDESIVIR TREATMENT ON CLINICAL OUTCOME IN HOSPITALIZED PATIENTS WITH COVID-19 IN KIRKUK CITY

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ABSTRACT

Background: One of the greatest pandemic illnesses of the century, Coronavirus Disease 2019 (COVID-19), is an infectious disease brought on by the SARS-CoV-2 virus, which causes severe acute respiratory syndrome. Currently, Remdesivir (RDV) is thought to be the only antiviral medication that has received complete approval for treating COVID-19 in hospitalized patients who are 12 years of age or older. The objective of the study was to evaluate RDV's effectiveness in reducing death and length of stay in patients admitted with Covid-19.

Materials & methods: This prospective cohort study was conducted among 341 hospitalized COVID-19 patients admitted to the isolation units at Azadi Teaching Hospital and Rizgari Hospital in Kirkuk City between February and August 2021. Participants were divided into two groups: the remdesivir group comprising 120 patients who received remdesivir plus standard treatment, and the control group consisting of 221 patients who received standard management without remdesivir. All patients were followed until discharge, ICU admission, or death, and clinical outcomes were compared between the two groups.

Results: After initiation of RDV there were significant reduction in deaths among RDV group in comparison to control group (p=0.0001). there was significant lower mean time to discharge from hospital among RDV group (15 days) in comparison to control group (17 days) (p=0.0001).

Conclusions: Receiving RDV plus standard regimen is effective in reducing mortality and duration of hospitalization among patient with COVID-19 in comparison to standard regimen without RDV.

KEY WORDS: Antiviral Agents, COVID-19, Hospital Mortality, Length of Stay, Remdesivir, SARS-CoV-2

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INTRODUCTION

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the etiological agent of Coronavirus Disease 2019 (COVID-19), emerged in China in late 2019 and rapidly escalated into a global pandemic.[1-3] Declared a public health emergency by the World Health Organization (WHO) on January 30, 2020, and a pandemic on March 11, 2020, COVID-19 has infected approximately 190 million individuals worldwide, causing over 4 million deaths as of mid-July, 2021.[4]

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Remdesivir (RDV), a nucleoside analog targeting viral RNA-dependent RNA polymerase (RdRp), emerged as a leading therapeutic candidate during the pandemic.[5] Approved by the U.S. Food and Drug Administration (FDA) for hospitalized patients aged ≥12 years (≥40 kg), its authorization relied on the Adaptive COVID-19 Treatment Trial (ACTT-1), which demonstrated reduced recovery times.[6,7] However, conflicting evidence from the WHO Solidarity trial questioned its mortality benefits, fueling debates over its efficacy.[8,9]

SARS-CoV-2 transmission occurs via respiratory droplets (within 1.8 m), aerosolized particles (over 1.8 m), and fomite contact.[10] RDV's antiviral activity, validated in preclinical models, inhibits viral RNA synthesis, improving pulmonary function and reducing viral loads.[3] Early compassionate use in the U.S. showed clinical improvement, though guidelines from Milan, Italy, restrict its use to hospitalized patients with oxygen saturation <94% on room air, discouraging routine administration in milder cases.[11,12]

Despite accumulating evidence, critical knowledge gaps persist regarding remdesivir's effectiveness across diverse clinical and demographic contexts. Geographic and regional variations in healthcare infrastructure, patient demographics, and viral variants further complicate the generalizability of existing evidence. While data from low- and middle-income regions, including Iraq, remain sparse, Kirkuk City, a multiethnic urban center in northern Iraq, experienced significant pandemic-related high prevalence and morbidity during successive waves of SARS-CoV-2 transmission. The present study addresses these gaps with aimed to evaluate the efficacy and safety of Remdesivir (RDV) in improving clinical outcomes for hospitalized COVID-19 patients in Kirkuk City, Iraq.

MATERIALS AND METHODS

This prospective cohort study examined the clinical outcomes associated with remdesivir therapy in hospitalized patients with COVID-19 in Kirkuk City, Iraq. The study was conducted between February 1 and August 31, 2021, at two tertiary care centers: Alshifaa 14 Hospital and Azadi Teaching Hospital. A total of 341 adult patients (≥18 years) with confirmed SARS-CoV2 infection, diagnosed by reverse transcription–polymerase chain reaction (RT-PCR), were enrolled.

Patients were assigned to treatment groups according to existing hospital protocols rather than randomization. The remdesivir group included 120 patients who received intravenous remdesivir in addition to standard care, while the control group consisted of 221 patients who received standard care alone. Remdesivir was administered as a 200-mg intravenous loading dose on the first day, followed by 100 mg daily for four consecutive days. Standard care comprised dexamethasone, azithromycin, paracetamol, vitamin D supplementation, and bronchodilator inhalers when clinically indicated. Treatment allocation was determined by drug availability and the treating physician's clinical judgment.

Inclusion criteria were an oxygen saturation level below 94% while receiving supplemental oxygen, evidence of significant pulmonary involvement on chest imaging, and a positive RT-PCR test obtained within 14 days of symptom onset. Patients were excluded if they were pregnant, had hepatic dysfunction with transaminase levels exceeding five times the upper limit of normal, severe renal impairment (creatinine clearance <30 mL/min), or RT-PCR positivity beyond 14 days. Written informed consent was obtained from all participants after a full explanation of the study objectives and procedures.

Data were collected using a standardized case report form capturing demographic characteristics, underlying comorbidities, vital signs, clinical symptoms, and laboratory findings. Laboratory assessments included complete blood count, D-dimer, ferritin, C-reactive protein, lactate dehydrogenase, and renal function tests. Radiologic evaluation consisted of chest X-ray or computed tomography scans, as clinically indicated.

Primary outcomes included in-hospital mortality, length of hospital stay, intensive care unit admission, and the development of complications such as septic shock, acute kidney injury, multiorgan dysfunction syndrome, and thromboembolic events. Adverse drug reactions were actively monitored throughout the treatment period and during hospitalization.

The study protocol was approved by the Research Ethics Committee of the College of Medicine, Kirkuk University (Approval No. 26, dated January 18, 2023), and all procedures were conducted in accordance with the principles of the Declaration of Helsinki. Statistical analyses were performed using SPSS version 24.0. Continuous variables were summarized as means with standard deviations or medians with interquartile ranges, depending on data distribution, and compared using independent-sample t-tests or Mann–Whitney U tests. Categorical variables were expressed as frequencies and percentages and analyzed using chi-square or Fisher's exact tests, as appropriate. A two-sided p-value <0.05 was considered statistically significant.

RESULTS

A total of 341 hospitalized patients with laboratory-confirmed COVID-19 were included in this analysis, comprising 120 patients in the remdesivir group and 221 patients in the control group. Baseline demographic and clinical characteristics were comparable between groups. The remdesivir group had a mean age of 65.54 ± 12.54 years with 50.83% female participants, while the control group had a mean age of 66.37 ± 18.14 years with 37.55% female participants. No statistically significant differences were observed in age, sex distribution, or prevalence of underlying comorbidities including cardiovascular disease, diabetes mellitus, respiratory disorders, or renal disease (all $p > 0.05$) (Table 1).

Clinical presentation revealed similar frequencies of fever and cough between groups. However, patients receiving remdesivir demonstrated significantly lower oxygen saturation (median 84% versus 87%, $p = 0.033$) and lower PaO2/FiO2 ratio (median 116 versus 188, $p = 0.032$) at admission compared to controls, indicating greater baseline disease severity. Consistent with this observation, the remdesivir group included a higher proportion of patients classified as having severe disease (25.8% versus 8.6%, $p < 0.001$) (Table 2).

Initial laboratory parameters were largely comparable between groups. Notably, the remdesivir group exhibited significantly elevated baseline levels of ferritin (median 1723 versus 740.1 ng/ml, $p < 0.001$) and

D-dimer (median 1.9 versus 0.7 ng/ml, p < 0.001), reflecting heightened inflammatory and thrombotic activity at presentation (Table 3).

Table 1: COVID-19 patients' charactseristics upon admission to Alshifaa 14 hospital & Azadi Teaching Hospital

Variable;	RDV N (%) N=120	Non-RDV (control) N (%) N=221	p-value
Age$^{\beta}$	65.54 ± 12.54	66.37 ± 18.14	0.685
Sex			
Male	59 (49.16%)	138 (62.44%)	0.370
Female	61 (50.83%)	83 (37.55%)	
Cardiovascular			
Yes	76 (63.33%)	102 (46.15 %)	0.665
No	44 (36.66%)	119 (53.8%)	
Diabetes			
Yes	36 (30%)	55 (24.88%)	0.308
No	84 (70.0)	166 (75.11)	
Respiratory problem			
Yes	11 (9.16 %)	26 (11.76%)	0.888
No	109 (90.83)	195 (88.23)	
Renal Problem			
Yes	6(5%)	20 (9.04%)	0.898
No	114 (95%)	201 (90.95)	

βMean (SD), P value, *<0.05, **<0.001

Regarding clinical outcomes, patients treated with remdesivir experienced significantly fewer in-hospital complications overall (p < 0.001), including lower rates of nosocomial infection, septic shock, and thromboembolic events (Figure 1) and (Table 4).

Table 2: Displays the percentage frequency and intensity of primary symptoms experienced by COVID-19 participants during hospital visits.

Variable	RDV N (%) N=120	Control (Non-RDV) N (%) N=221	p-value
Fever			
Yes	101 (84.16)	186 (84.16)	0.900
No	19 (15.8)	35 (15.82)	
Cough			
Yes	65 (54.16)	132 (59.72)	0.089
No	55 (45.83)	89 (40.27)	
Shortness of breath			
Yes	91 (75.583)	186 (84.16)	0.066
No	29 (24.16)	35 (15.82)	
(Systolic) BP^ mmHg	136 (116-152)	137 (122-154)	0.437
(Diastolic) BP^ mmHg	78 (74-81)	78 (71-88.5)	0.247
Pulse rate^ b/min	102 (84-112.5)	104 (94-114.5)	0.333
Respiratory Rate^ /min	34 (27-37)	33 (26-37)	0.147
Oxygen Saturation^ %	84 (76-90)	87 (75-92)	0.033*
the(PaO2/FiO2) Ratio^	116 (73.9-243.5)	188 (105.3-267.3)	0.032*
Clinical Severity			
Moderate	10 (8.3)	24 (10.9)	<0.001**
Severe	3 (25.8)	19 (8.6)	
Critical	79 (65.8)	178 (80.54)	
Utilizing Non-Invasive Ventilation			
Yes	46 (37.3)	86 (37.9)	0.973
No	74 (62.7)	135 (61.1)	
Days from the start of symptoms to the end of treatment. β	7.55 ± 4.55	7.9 ± 3.83	0.8

^ Median (IQR), β Mean (SD), P value: *<0.05, **<0.001

Table 3: Standard laboratory parameters

Variable	RDV group	Non-RDV (control)	p-value
	Median (IQR)	Median (IQR)	
Hemoglobin (mg/dl)	13.8 (11.7-14.3)	13.6 (11.6-14.7)	0.931
White blood cells (x10^9/L)	14.7 (9.8-16.7)	13.1 (7.6-16.5)	0.872
Neutrophils (%)	85.3 (85-91.9)	84.4 (81.3-91.4)	0.819
Lymphocytes (%)	7.1 (5.0-12.6)	8.0 (7.5-12.9)	0.914
Platelet (x10^9/L)	281 (108.5-297.5)	213 (141-361)	0.237
Creatinine (mg/dl)	1.1 (0.9-1.2)	1.0 (0.9-1.8)	0.069
CRP level (mg/L)	1381.7 (56.7-186.8)	139.7 (78.1-210.8)	0.601
Ferritin level (ng/ml)	1723 (616.9-1885.7)	740.1 (403.7-1176.5)	<0.001
LDH (U/L)	413.6 (347.3-581.2)	531.5 (463.8-771)	0.762
D-dimer level (ng/ml)	1.9 (0.8-6.9)	0.7 (0.5-1.8)	<0.001

(CRP) C-reactive protein, (LDH) Lactate dehydrogenase

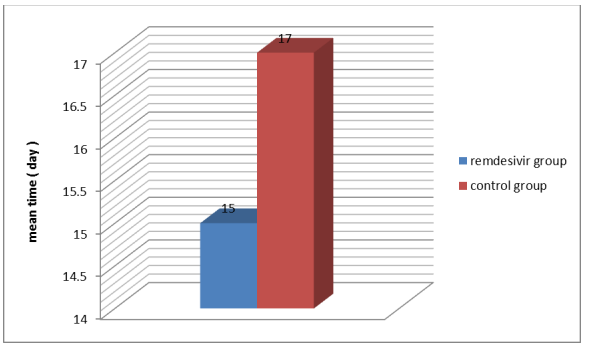

Figure 1: Mean time to discharge from hospital among treatment and CG

The median duration of hospitalization was shorter in the remdesivir group (15 days; IQR 11.5–19.5) compared to the control group (17 days; IQR 13.3–23.4, $p < 0.05$). Hospital mortality was significantly lower among remdesivir recipients (42.5% versus 57.5%, $p = 0.006$). Adverse reactions were infrequent and comparable between groups, with only two patients (1.6%) in the remdesivir group developing hypersensitivity reactions during infusion (Table 5).

DISCUSSION

The optimal management of COVID-19 remains critical to reducing morbidity and mortality. While the ACTT-1 trial demonstrated accelerated clinical recovery with remdesivir (RDV), the WHO Solidarity trial reported no mortality benefit, fueling ongoing debate.[13, 14] The present study evaluated 341 hospitalized COVID-19 patients in Kirkuk City , with 120 receiving RDV and 221 serving as controls (CG). The mean age of participants was in the mid-60s, consistent with U.S. data highlighting higher susceptibility among older adults.[10] A male predominance was observed, contrasting with Chinese studies reporting equal gender distribution.[15]

Comorbidities, particularly obesity, hypertension, and diabetes, were prevalent, aligning with global trends.[16] Biomarker analysis revealed elevated baseline D-dimer and ferritin levels, both of which significantly decreased post-RDV initiation compared to the CG, supporting their role as prognostic indicators.[13, 17] However, CRP levels remained unchanged, diverging from studies reporting RDV-associated CRP reductions.[18] Cardiovascular disease (52%)

Table 4: RDV-using COVID-19 patient outcomes.

	RDV n(%) n=120	Non-RDV n(%) n=221	p-value
In-hospital complications			<0.0001**
Cardiac Abnormalities	31 (25.8)	66 (29.9)	
Nosocomial Infection	22 (18.3)	64 (29.0)	
CNS Abnormalities	5 (4.1)	21 (9.5)	
Septic Shock	8 (6.6)	55 (24.8)	
MODS	19 (15.8)	52 (23.5)	
AKI	13 (10.8)	25 (11.3)	
Thromboembolism	0	11 (4.9)	
DIC	2 (1.6)	12 (5.4)	
Length of hospital stay ^ (days)	15 (11.5-19.5)	17 (13.3 -23.4)	<0.05
Mortality			
Alive	69 (57.5)	94 (42.5)	<0.001
Dead	51 (42.5)	127 (57.5)	

^ Median (IQR), βdoes not add up to 100.

Table 5: summary of adverse reactions in RDV & CGs

Adverse reactions	No. patients in RDV group (%)	No. patients in CG (%)
Hypersensitivity	2 (1.6 %)	0
Increased ALT&AST	2 (1.6 %)	4 (1.8 %)
Increased S.creatinin	3 (2.5 %)	6 (2.7 %)
Upper GIT bleeding	2 (1.6 %)	4 (1.8 %)
Myocardial infarction	1 (0.8%)	2 (0.9%)

was the most common comorbidity, followed by diabetes (26.6%), respiratory conditions (10.8%), and renal disease (7.6%), consistent with prior research.[19] Fever (84%) and dyspnea (81.2%) were the predominant symptoms, differing from studies where cough predominated.[18, 20]

The RDV administration correlated with fewer in-hospital complications, shorter hospitalization (15 vs. 17 days), and reduced mortality compared to the CG. These findings align with meta-analyses underscoring RDV's efficacy in mitigating disease severity.[21] However, conflicting data exist, including trials showing no mortality benefit and prolonged hospitalization durations.[13, 19] Mortality reduction in this cohort parallels retrospective studies,[22] but contrasts with the Solidarity trial.[13]

The RDV was well-tolerated, with only two cases of hypersensitivity and no significant hepatic or renal toxicity, consistent with its established safety profile.[23] Limitations include non-randomized allocation, potential confounding from concomitant therapies (anticoagulants, steroids), and the observational design, which precludes isolating RDV-specific effects. Despite these constraints, this study provides valuable regional insights into RDV's real-world outcomes. Further randomized controlled trials are warranted to clarify RDV's role in COVID-19 management, particularly regarding timing of initiation and long-term outcomes. As therapeutic options for severe COVID-19 remain limited, identifying optimal treatment strategies remains a global priority.

CONCLUSION

The study's finding exposed the efficacy of RDV in treating hospitalized patients with COVID-19 infection, and it was superior to standard (non remdisivir) treatment in reducing hospital complication, length of hospital stay and mortality. it ascert that remdisivir is safe and effective, in addition to other medications, in the treatment of SARS-CoV-2 infected individuals.

Ethical approval statements and consent to participation: The research was conducted in conformity with the ethical standards outlined in the Declaration of Helsinki, and signed informed permission was acquired from each patient. The information, protocol, and permission form were evaluated and approved by the Research Ethics Committee of the College of Medicine, Kirkuk University, under document number 26 on January 18, 2023.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	AMJ, AKA
Acquisition, Analysis or Interpretation of Data:	AMJ, AKA
Manuscript Writing & Approval:	AMJ, AKA

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.