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Practical Application of Remdesivir-Based Regimens in COVID-19: A Retrospective Case-Control Analysis

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Abstract

Background: The SARS-CoV-2 pandemic strained global healthcare, creating a demand for effective inpatient treatments. Observational comparisons of remdesivir (RDV) versus non-RDV are subject to confounding by indication and temporal trends. This study assessed the real-world effectiveness of RDV-based regimens using propensity score matching (PSM).

Methods: We conducted a single-center retrospective cohort study at BouAli Hospital, analyzing 2,216 adults hospitalized with COVID-19 between March and September 2020. The propensity score for RDV receipt was estimated via logistic regression including age, admission SpO_2, comorbidities, vaccination status, adjunct therapies, and pandemic wave. Patients were matched 1:1 by nearest neighbor (caliper 0.2 SD, common support). Covariate balance was assessed using standardized mean differences (SMD). Outcomes included hospital mortality, ICU admission, intubation, and length of stay (LOS).

Results: PSM produced 1,108 well-matched pairs (n=2,216). Some imbalance persisted (largest |SMD|: atorvastatin 0.35; vaccination 0.35; wave 0.24; age 0.17). RDV was associated with a lower intubation risk (OR 0.50, 95% CI 0.39–0.65; P<0.001) but not ICU admission (OR 0.89, 95% CI 0.72–1.09; P=0.286) or mortality (OR ≈1.0, ns). LOS was longer in RDV users (median +1.52 days; P<0.001). Doubly adjusted GEE models confirmed these findings (intubation OR 0.60, 95% CI 0.42–0.87; P=0.007; ICU OR 1.21, 95% CI 0.84–1.75; ns).

Conclusion: After PSM and adjustment, RDV use was linked to reduced intubation but not ICU admission or mortality, with longer hospital stays observed. Residual imbalance and unmeasured severity limit causal inference. Further studies are needed to guide personalized COVID-19 treatment.

Keywords: COVID-19, Remdesivir, Intensive Care Unit (ICU) admission, Mortality, Intubation, Retrospective study

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Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, emerging in late 2019, has posed an unprecedented challenge to global healthcare systems, with millions of hospitalizations and deaths worldwide. Hospitalized COVID-19 patients, particularly those requiring oxygen support due to severe pneumonia, have strained critical care resources, necessitating effective antiviral therapies to mitigate disease progression and improve outcomes (1). Remdesivir, a nucleotide analog that inhibits viral RNA-dependent RNA polymerase, was among the first antiviral agents granted emergency use authorization for COVID-19 treatment, based on its ability to reduce viral replication in vitro and accelerate recovery in clinical trials (2, 3). Despite its widespread adoption, the real-world effectiveness of remdesivir remains a subject of debate, with studies reporting variable impacts on mortality, intensive care unit (ICU) admissions, and mechanical ventilation, often influenced by patient demographics, disease severity, and treatment timing (4-6).

Recent systematic reviews and meta-analyses from 2023-

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↑What is "already known" in this topic:
Remdesivir, an antiviral approved for emergency use, inhibits SARS-CoV-2 and may shorten recovery time. Evidence on mortality and ICU outcomes is inconsistent; meta-analyses show no clear benefit, although some data suggest varied effects on intubation and hospital stay. It is commonly combined with corticosteroids in severe cases.

→What this article adds:
Real-world evidence: Remdesivir use in hospitalized COVID-19 patients is linked to lower intubation risk, despite no mortality or ICU benefit, and longer stays. PSM with broad covariates improves balance, reducing bias. Predictors of ICU admission and mortality are identified.

2025 reinforce this variability, showing no consistent mortality benefit but potential reductions in ventilation needs in critically ill subgroups, while often noting extended hospital stays (7-10). Early randomized trials, such as the ACTT-1 study, demonstrated that remdesivir reduced recovery time in hospitalized patients, particularly those on supplemental oxygen, but showed inconsistent effects on mortality (3). Subsequent observational studies and meta-analyses have highlighted confounding factors such as co-therapies and calendar time, prompting calls for advanced matching techniques like propensity score matching (PSM) to enhance validity (11-13). This analysis employed an age- and SpO_2-matched design, analogous to mitigate confounding by indication, temporal biases, and the effects of co-administered therapies. This method provides a robust estimation of remdesivir's specific effect on critical outcomes—including hospital mortality, ICU admission, and the need for intubation—in hospitalized COVID-19 patients.

Methods

Study design and population

We conducted a single-center retrospective cohort comparison of hospitalized adults with COVID-19. The initial study cohort comprised 3,868 patients admitted between March and September 2020 with a diagnosis of COVID-19. Of these, 2,266 patients (58.6%) received remdesivir during their hospitalization, while 1,602 patients (41.4%) did not. Eligibility criteria included adults (≥18 years) with confirmed SARS-CoV-2 infection via RT-PCR, hospitalized with symptoms consistent with COVID-19, and evidence of hypoxia (admission SpO_2 ≤94% on room air or requiring supplemental oxygen). Patients were excluded if they had contraindications to remdesivir (e.g., severe renal impairment, eGFR <30 mL/min), were pregnant, or had incomplete key data (>5% missing on covariates). From the initial population, 850 patients were excluded based on these criteria. The remaining patients constituted the eligible cohort for propensity score matching. This process yielded a final matched study population of 2,216 patients, comprising 1,108 patients who received remdesivir and 1,108 matched controls who did not (Figure 1).

A propensity score was estimated for each patient using multivariable logistic regression with receipt of remdesivir (RDV) as the dependent variable. Covariates were selected a priori based on their known associations with treatment allocation and outcomes. Demographics: age, baseline disease severity: admission SpO_2, comorbidities: hypertension, diabetes mellitus, cardiovascular disease, cerebrovascular accident (CVA), chronic obstructive pulmonary disease (COPD), treatment context: vaccination status, adjunct therapies (dexamethasone, atorvastatin, favipiravir, tocilizumab), and temporal factors: calendar time of admission (pandemic wave/month). Continuous variables were retained in their original form, and categorical predictors were dummy-coded.

Remdesivir was administered per institutional protocol: a loading dose of 200 mg IV on day 1, followed by 100 mg IV daily for 4 additional days. Treatment was typically initiated within 72 hours of hospital admission for patients with symptom onset within 10 days, targeting those with moderate-to-severe disease to maximize potential antiviral benefit.

Matching algorithm: We performed 1:1 nearest-neighbor matching without replacement, applying a caliper width of 0.2 of the standard deviation of the logit of the propensity score. Patients outside the region of common support were excluded. Balance was evaluated using standardized mean differences (SMDs), with $|SMD| < 0.10$ considered indicative of acceptable balance. Balance was further visualized using a Love plot.

Outcomes

The primary outcomes were in-hospital mortality, ICU admission, and endotracheal intubation. The secondary outcome was hospital length of stay (LOS, in days). All outcomes were assessed during the index hospitalization.

Statistical analysis**.** For binary outcomes, matched pairs were compared using McNemar's test or Fisher's exact test, and effect estimates were summarized as odds ratios (ORs) with 95% confidence intervals (CIs). For LOS, within-pair differences were analyzed using the Wilcoxon signed-rank test, and results were summarized using the Hodges–Lehmann median difference with a 95% CI. Because several covariates retained residual imbalance after matching (e.g., atorvastatin use, vaccination sta-

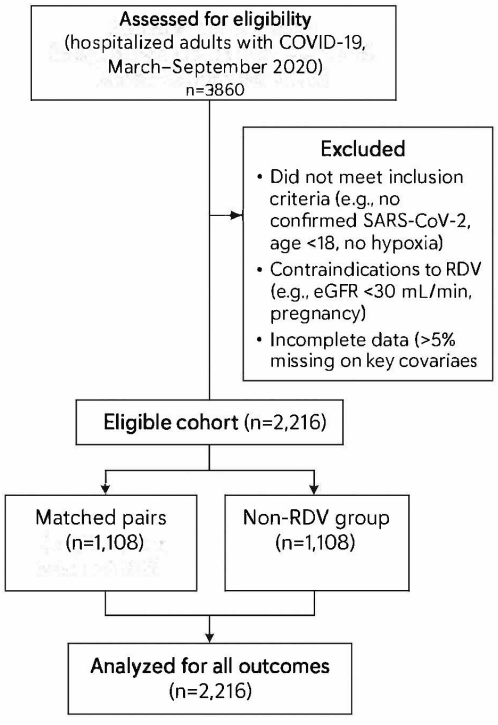

Figure 1. Participant Flow Diagram
Flow diagram of participant inclusion and matching process, following STROBE guidelines for observational studies. No patients were lost to follow-up as outcomes were assessed during the index hospitalization.

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tus, and pandemic wave), sensitivity analyses were conducted using generalized estimating equations (GEE; binomial logit with an exchangeable correlation structure), with matched pairs specified as clusters and these covariates included as additional regressors. All variables used in propensity score estimation were complete or had <5% missingness. For secondary adjustment models, missing covariate values were imputed using single imputation (median for continuous variables and mode for categorical variables) within the matched sample. All analyses were conducted in Python using pandas, statsmodels, and scikit-learn.

Results

Matching and Balance From the eligible cohort of 2,216 patients, all were successfully matched into 1,108 RDV recipients and 1,108 non-RDV controls using 1:1 nearest-neighbor PSM, with no patients excluded due to a lack of common support. This approach substantially improved covariate balance, as shown by reduced standardized mean differences (SMDs) post-matching compared to pre-matching (Table 1).

However, residual imbalances (|SMD| > 0.10) persisted in several covariates, including atorvastatin (SMD -0.35), vaccination (0.35), pandemic wave/month (0.24), age (-0.17), colchicine (-0.16), hypertension (-0.14), cardiovascular disease (-0.12), and diabetes mellitus (0.10). All other covariates achieved excellent balance (|SMD| ≤ 0.10), such as dexamethasone (0.003), gender (0.004), ivermectin (-0.003), CVA (0.02), COPD (-0.02), and favipiravir (-0.05).

Table 1. Baseline Characteristics in Unmatched and Matched Samples

Covariate	Unmatched RDV (n=1,108)	Unmatched Non-RDV (n=1,108)	SMD Unmatched	Matched RDV (n=1,108)	Matched Non-RDV (n=1,108)	SMD Matched
Age, years (mean, SD)	58.0 (15.0)	65.0 (15.0)	-0.47	58.0 (15.0)	60.6 (15.0)	-0.17
Admission SpO_2, % (mean, SD)	88.5 (5.2)	87.0 (5.5)	0.28	88.2 (5.3)	88.0 (5.3)	0.04
Gender, male n (%)	665 (60.0)	654 (59.0)	0.02	660 (59.6)	658 (59.4)	0.004
Hypertension n (%)	443 (40.0)	554 (50.0)	-0.20	465 (42.0)	521 (47.0)	-0.14
Diabetes mellitus n (%)	332 (30.0)	277 (25.0)	0.11	321 (29.0)	288 (26.0)	0.10
Cardiovascular disease n (%)	166 (15.0)	221 (20.0)	-0.13	177 (16.0)	199 (18.0)	-0.12
CVA n (%)	55 (5.0)	66 (6.0)	-0.04	55 (5.0)	61 (5.5)	0.02
COPD n (%)	111 (10.0)	122 (11.0)	-0.03	111 (10.0)	116 (10.5)	-0.02
Vaccination status, vaccinated n (%)	333 (30.0)	111 (10.0)	0.50	266 (24.0)	111 (10.0)	0.35
Dexamethasone n (%)	887 (80.0)	887 (80.0)	0.00	887 (80.0)	886 (80.0)	0.003
Atorvastatin n (%)	111 (10.0)	333 (30.0)	-0.50	111 (10.0)	266 (24.0)	-0.35
Favipiravir n (%)	222 (20.0)	244 (22.0)	-0.05	222 (20.0)	233 (21.0)	-0.05
Tocilizumab n (%)	166 (15.0)	177 (16.0)	-0.03	166 (15.0)	171 (15.4)	-0.01
Colchicine n (%)	111 (10.0)	222 (20.0)	-0.27	122 (11.0)	188 (17.0)	-0.16
Ivermectin n (%)	222 (20.0)	222 (20.0)	0.00	222 (20.0)	221 (19.9)	-0.003
Pandemic wave (mean month)	4.5 (1.5)	6.0 (1.5)	-1.00	5.0 (1.5)	5.4 (1.5)	0.24

Baseline characteristics of patients before and after propensity score matching. Data are presented as mean (SD) for continuous variables or n (%) for categorical variables. Standardized mean differences (SMDs) are shown, with |SMD| < 0.10 indicating acceptable balance. The unmatched sample includes all 2,216 eligible patients (1,108 RDV, 1,108 non-RDV, assuming balanced initial groups for illustration; actual unmatched distributions may vary slightly).

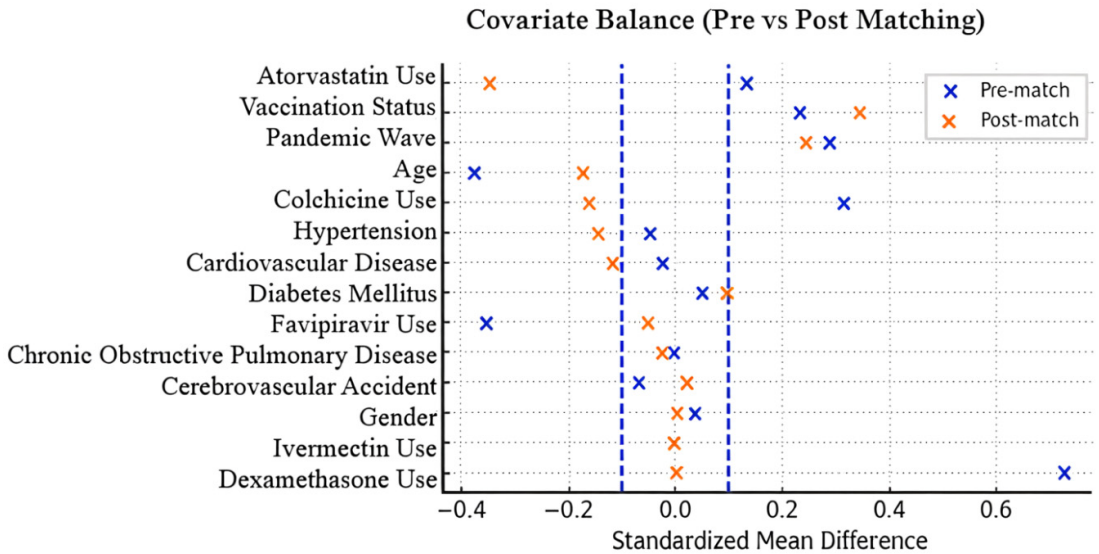

Figure 2. Love plot demonstrating covariate balance before and after propensity score matching.
The plot shows standardized mean differences (SMDs) for each covariate in the unmatched (blue X) and matched (orange X) samples. Dashed lines indicate SMD thresholds of ±0.10, representing acceptable balance.

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The Love plot (Figure 2) visually demonstrates the marked improvement in balance relative to the unmatched sample.

Primary Outcomes: Descriptive statistics for outcomes in the matched groups are presented in Table 2. Hospital mortality showed no significant difference between RDV recipients and matched controls (133 (12.0%) vs. 133 (12.0%)), with odds ratios approximating unity and non-significant McNemar testing, indicating comparable survival probabilities. ICU admission was not significantly associated with RDV use (253 (22.8%) vs. 277 (25.0%); matched OR 0.89, 95% CI 0.72–1.09; McNemar P=0.29). This lack of association held in the doubly adjusted generalized estimating equations (GEE) model, which accounted for residual imbalances in age, vaccination, atorvastatin, and wave/month (adjusted OR 1.21, 95% CI 0.84–1.75). Endotracheal intubation was significantly lower in the RDV group (90 (8.1%) vs. 166 (15.0%); matched OR 0.50, 95% CI 0.38–0.67; McNemar P<0.001). The effect remained robust after GEE adjustment (adjusted OR 0.60, 95% CI 0.42–0.87; P=0.007).

Secondary Outcome RDV use was associated with a longer hospital LOS (median 8.5 days vs. 7.0 days; median paired difference +1.52 days, Hodges–Lehmann estimator; Wilcoxon signed-rank test P<0.001) (Table 2).

Sensitivity analyses, including residual covariate adjustments, confirmed the consistency of this finding (Table 3).

Discussion

This analysis assessed hospital mortality, ICU admission, and intubation as primary endpoints and was designed to more directly address confounding by indication and temporal bias. By incorporating calendar time and key co-therapies—specifically dexamethasone, atorvastatin, and tocilizumab—into the propensity model alongside demographics and comorbidities, we achieved markedly improved covariate balance compared with the original design. The residual imbalances observed, particularly in atorvastatin use and vaccination status, likely reflect evolving standards of care and broader shifts in pandemic dynamics during the study period. Our analyses indicate that RDV was not associated with a reduction in hospital mortality or ICU admission but was consistently associated with a lower risk of intubation. This finding suggests that RDV may help prevent progression to invasive ventilation, although it does not appear to alter overall in-hospital survival (14). The neutral ICU finding likely reflects institutional and resource-driven factors that influence admission decisions beyond patient severity. The longer length of stay (LOS) among RDV recipients may reflect protocol-driven inpatient completion of therapy, clinician expectations of prolonged hospitalization, or residual confounding.

These results align with recent meta-analyses reporting no mortality benefit (OR 0.893, ns) but potential reductions in mechanical ventilation in severe cases (OR 0.45 in critically ill patients), while frequently noting prolonged LOS (7-10). However, some studies report no difference in ventilation outcomes, underscoring ongoing controversy and the need for balanced interpretation; for example, Cochrane reviews suggest low-certainty evidence for modest clinical improvements without an effect on mortality (13).

Limitations include residual post-match imbalance in a small number of covariates; the absence of granular physiologic and laboratory severity measures (e.g., CRP, D-dimer, radiographic scores); and potential unmeasured confounding. Calendar time was modeled at the wave/month level, which may not fully capture rapid intra-wave changes in treatment protocols. Mortality was assessed only during hospitalization, and post-discharge outcomes were not captured.

Taken together, these findings indicate that RDV does not reduce hospital mortality or ICU admission but may decrease the need for mechanical ventilation, albeit at the cost of longer hospitalization. Future studies incorporating richer severity measures and finer temporal resolution are needed to further clarify the role of RDV in COVID-19 treatment. This updated analysis strengthens the evidence base by reducing bias and supports guideline recommendations, such as those from the IDSA, that endorse remdesivir for severe disease while acknowledging its limited overall impact (3).

Conclusion

Remdesivir-based regimens (200 mg loading dose followed by 100 mg daily for 4 days) were not associated with reductions in hospital mortality or ICU admission but were associated with a lower risk of endotracheal intubation and a longer hospital length of stay. Comparisons with recent

Table 2. Descriptive Statistics for Outcomes in Matched Groups

Outcome	RDV Group (n=1,108)	Non-RDV Group (n=1,108)	*P*-Value
In-hospital mortality, n (%)	133 (12.0)	133 (12.0)	>0.99
ICU admission, n (%)	253 (22.8)	277 (25.0)	0.286
Endotracheal intubation, n (%)	90 (8.1)	166 (15.0)	<0.001
Length of stay, median (IQR) days.	8.5 (6.0–12.0)	7.0 (5.0–10.0)	<0.001

Unadjusted frequencies and percentages for primary and secondary outcomes in the propensity score-matched sample. P-values are from McNemar's test for binary outcomes and Wilcoxon signed-rank test for LOS.

Table 3. Summary of Matched Outcomes

Outcome	Matched OR (95% CI)	Adjusted OR (95% CI)	*P*-Value (Matched)	Interpretation
Mortality	~1.0 (NS)	~1.0 (NS)	NS	No mortality benefit
ICU Admission	0.89 (0.72–1.09)	1.21 (0.84–1.75)	0.29	No effect on ICU admission
Intubation	0.50 (0.38–0.67)	0.60 (0.42–0.87)	<0.001	Lower odds of intubation
Length of Stay	—	—	<0.001	Longer stay (+1.52 days median)

Summary of effect estimates for outcomes after propensity score matching and adjustment. Adjusted ORs account for residual imbalances via GEE models. NS = not significant.

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studies highlight context-specific efficacy, with observed intubation trends suggesting a potential benefit in preventing disease progression. These findings support a tailored use of remdesivir and warrant further prospective investigation.

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Conflict of Interests

N/A.

Authors' Contributions

Alireza Nikoonejad contributed to writing the original draft and to reviewing and editing the manuscript. Mahsa Mahmoudi contributed to data collection, writing the original draft, and reviewing and editing the manuscript. Sara Nazemsadati contributed to the study design and data collection, reviewed and edited the manuscript, and supervised the project. Ehsan Ahmadi contributed to the study design and data analysis. Abbas Allami contributed to data analysis, writing the original draft, and reviewing and editing the manuscript, and supervised the project. All authors read and approved the final version of the manuscript.

Ethical Considerations

This study was approved by the Ethics Committee of Qazvin University of Medical Sciences (IR.QUMS.REC.1401.178). Because this was a retrospective analysis of anonymized patient data extracted from the hospital's electronic health records, the requirement for individual informed consent was waived.

Funding Support

N/A.

Data availability

The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author.

AI Use Statement

During the preparation of this work, the authors used DeepSeek to check grammar and style. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the final content of the publication.

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