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REAL WORD EFFECTIVENESS OF REMDESIVIR IN THE MANAGEMENT OF HOSPITALIZED COVID-19 PATIENTS: A RETROSPECTIVE COHORT STUDY

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Abstract

Background: Covid-19, caused by SARS-CoV-2, has led to severe cases requiring prolonged hospital stays and intensive care, particularly for patients with moderate to severe disease. Remdesivir, an antiviral agent, has shown potential in improving outcomes for hospitalized Covid-19 patients, but results have varied.

AIM: This study evaluates the efficacy of Remdesivir in reducing hospital length of stay, need for ventilatory support, and mortality rates compared to standard care in age- and gender-matched patients.

Methods: This retrospective cohort study was conducted at the Department of Pulmonary Medicine, Sukh Sagar Medical College, Jabalpur, from October 2020 to December 2021. The study included 2200 PCR-confirmed Covid-19 patients, divided equally into Remdesivir (n = 1100) and Standard Care groups (n = 1100). Participants were matched by age and gender. Data on clinical characteristics and outcomes, including length of hospital stay, need for ventilator support, and discharge status, were collected from hospital records.

Results: Patients in the Remdesivir group had a significantly shorter hospital stay (mean 9.8 days vs. 14.5 days; $p < 0.001$) and a reduced need for ventilator support (8.6% vs. 14.5%; $p < 0.01$) compared to the Standard Care group. The discharge rate was higher in the Remdesivir group (93.2% vs. 89.1%; $p = 0.001$), with a lower mortality rate (6.8% vs. 10.9%). The Relative Risk (RR) for ventilator need was 0.58, with a Number Needed to Treat (NNT) of 17, and for mortality, the RR was 0.63 with an NNT of 24.

Conclusion: The findings suggest that Remdesivir treatment in hospitalized Covid-19 patients with moderate to severe disease may reduce hospital stay, ventilator requirements, and mortality rates, thus supporting its efficacy as part of inpatient Covid-19 management strategies. Further studies are recommended to corroborate these outcomes across diverse populations.

Keywords: Covid-19, Remdesivir, retrospective cohort study, hospital length of stay, ventilator support, mortality, SARS-CoV-2, antiviral therapy

Introduction

The Covid-19 pandemic, caused by the SARS-CoV-2 virus, has become one of the most significant public health crises in recent history[1–3]. Since the first case was identified in Wuhan, China, in December 2019, the disease has spread globally, resulting in millions of infections and deaths[1–3]. The spectrum of Covid-19 severity ranges from asymptomatic and mild cases to severe, life-threatening illness. Moderate and severe cases are particularly concerning due to their association with significant morbidity, high healthcare burden, and, in severe cases, mortality[3]. With limited treatment options early in the pandemic, clinicians faced substantial challenges in managing patients with moderate and severe forms of the disease[4,5]. Remdesivir, an antiviral drug initially developed for treating hepatitis C and later investigated for Ebola, emerged as a potential therapeutic agent against SARS-CoV-2 due to its mechanism of action and initial promising results in preclinical studies[6].

Remdesivir is a nucleotide analog prodrug that inhibits viral RNA-dependent RNA polymerase, a critical enzyme for SARS-CoV-2 replication[7]. Early in vitro studies demonstrated the drug's potential to reduce viral replication in infected cells[7]. The antiviral properties of Remdesivir against SARS-CoV-2 led to its widespread use and emergency authorization by regulatory agencies like the U.S. Food and Drug Administration (FDA) and the World Health Organization (WHO) for treating moderate and severe Covid-19 cases[8]. Despite its rapid authorization, the clinical efficacy of Remdesivir has been met with varying degrees of success, with several studies presenting conflicting results regarding its impact on clinical outcomes, mortality rates, and length of hospital stay[9].

In moderate Covid-19, patients often exhibit symptoms that may progress to severe disease without timely intervention. In severe cases, patients typically experience respiratory distress, hypoxemia, and other systemic complications that can lead to multi-organ failure and require intensive care support. Given the progressive nature of Covid-19, timely and effective antiviral treatment could be essential in preventing escalation to critical illness[10]. Observational data and randomized clinical trials have suggested that Remdesivir may offer benefits in reducing the time to clinical improvement, particularly in hospitalized patients with oxygen requirements[11]. However, recent evidence highlights the need for more detailed assessments to understand fully whether Remdesivir contributes to a reduced mortality rate or significantly shorter hospital stays in moderate and severe cases[12].

The current study examines the efficacy of Remdesivir in hospitalized patients with moderate and severe Covid-19 at Sukh Sagar Medical College, Jabalpur. The study's primary objective is to evaluate the effectiveness of Remdesivir in managing moderate and severe Covid-19 cases by analyzing its impact on clinical outcomes, including mortality rates, hospital length of stay, and progression of disease severity.

Material and Methods:

♦ **Study Design:** This retrospective cohort study was conducted to evaluate the efficacy of Remdesivir in hospitalized patients with moderate and severe Covid-19, focusing on patient outcomes in a single-center setting.

♦ **Study Settings:** Department of Pulmonary Medicine at Sukh Sagar Medical College, Jabalpur.

♦ **Ethical Clearance**: The study underwent a comprehensive ethical review to ensure adherence to medical and ethical standards. The protocol, data collection forms, and informed consent documents were rigorously scrutinized by the Institute's Ethical Committee.

♦ **Study Duration**: The total duration of the present study was 15 months: from October 2020 to December 2021. Patients admitted to study institute and fulfilling the selection criteria were included in the present study.

♦ **Primary Outcomes:** The primary outcome was to assess the impact of Remdesivir on mortality rates among moderate and severe Covid-19 patients. Mortality was evaluated at discharge and through hospital records for the duration of hospitalization.

♦ **Secondary Outcomes**: Secondary outcomes included length of hospital stay and disease progression.

♦ **Dependent Variables:** The primary dependent variable was patient survival status. Secondary dependent variables included length of hospital stay and any noted clinical improvement or deterioration during hospitalization.

♦ **Independent Variables:** Independent variables included patient demographics (age, sex), clinical severity of Covid-19 at admission, and administration of Remdesivir.

♦ **Confounding Variables**: Potential confounding variables identified included comorbidities, baseline oxygen requirements, and other concurrent treatments, which were accounted for during analysis to assess their impact on the primary and secondary outcomes. To reduce the impact of cofounding variables, we matched the age (± 3years), gender and smoking status of those who received remdesivir and standard care.

♦ **Definition of the Intervention:** Remdesivir was administered as the primary antiviral intervention for Covid-19 management in moderate and severe cases as per the study protocol, with dosage and administration guided by standard institutional treatment protocols and patient-specific requirements.

♦ **Study Universe:** The study universe comprised all Covid-19 patients admitted to the Sukh Sagar Medical College and associated hospital, Jabalpur, during the designated study period.

♦ **Study Participants:** Participants for the present study included hospitalized Covid-19 patients who met the eligibility criteria for moderate or severe disease as defined by clinical guidelines. Eligible participants were those who were PCR-confirmed Covid-19 cases, aged over 18 years, and classified as having moderate or severe Covid-19. Patients who met these criteria were considered for inclusion in the study.

Inclusion Criteria

i.PCR-confirmed Covid-19 patients
ii.Patients with moderate to severe Covid-19
iii.Age > 18 years
iv.Patients with complete medical records including clear mention of the outcome.

Exclusion Criteria

i.Patients with mild Covid-19
ii.Patients in a coma or on ventilator support at admission
iii.Patients who received other antiviral drugs for Covid-19 management

♦ **Study Groups:** Participants were categorized into two groups based on treatment with Remdesivir. The intervention group received Remdesivir as part of their Covid-19 management, while the control group received standard care without Remdesivir.

♦ **Allocation to Groups**: Participants were allocated to treatment groups based on a mutual discussion between the clinical team and the patients (or their representatives) about the available treatments, including the benefits and limitations of Remdesivir. Following these discussions, patients opted into the treatment group that best aligned with their preferences and clinical recommendations, ensuring informed participation in the study.

♦ **Sample Size:** The records of all Covid-19 patients admitted to hospital during the designated period were retrieved. From this study universe those who fulfilled the selection criteria were selected. Following this approach a total of 2200 patients; 1100 who received remdesivir and 1100 who received only standard care were shortlisted and included in the present study.

♦ **Sampling Methodology:** Participants were selected using non-probability convenience sampling, where eligible patients admitted to the hospital during the study period were included in the present study. Participants were recruited from the pool of Covid-19 patients admitted to the Department of

Pulmonary Medicine at Sukh Sagar Medical College, Jabalpur. Double screening was conducted to identify those meeting the moderate and severe disease criteria. Two consultants from the department individually screened the medical records. Any conflict in categorising the record was resolved by the senior consultant.

♦ **Obtaining Informed Consent**: Not required as this was a retrospective study. The institute Ethical Committee gave the permission to review the medical records of the patients.

♦ **Data Collection Tool**: The data collection form for this study was developed in several stages. Initially, a draft was prepared based on the study objectives, outlining the variables of interest, including demographic data, clinical parameters, and treatment details. After the initial draft, feedback was sought from clinical experts to ensure the form comprehensively captured relevant data. The revised form was then pilot-tested on a small sample to assess usability, clarity, and completeness.

♦ **Data Sources:** All the data were obtained from hospital medical records, which included patient demographics, clinical status at admission, treatment records, and clinical outcomes. All records were systematically reviewed to ensure accuracy and completeness.

♦ **Data Collection Procedure**: Data were collected from hospital records, covering demographic details, clinical characteristics, and the treatment specifics, including Remdesivir administration where applicable. Data on primary outcomes, such as mortality and length of hospital stay, were recorded from discharge summaries, while secondary outcomes, including disease progression, were documented from follow-up records within the hospital stay period. All data points were systematically logged into a structured form, ensuring each variable was accurately recorded for subsequent analysis.

♦ **Data Quality Assurance:** Double data retrieval and entry methodology was employed to collect the data for the study. Two independent teams consisting of pulmonary consultants and data managers were employed to collect data. Data quality was rigorously monitored by the study supervisor, who conducted regular audits of the data collection forms to ensure completeness and accuracy. Random checks were performed on a subset of collected data to verify consistency with the source records.

♦ **Statistical Analysis:** Data from paper-based data collection forms were initially entered into MS Excel and subsequently imported into Stata software version 17.0 for analysis. Descriptive statistics were used to summarize demographic characteristics, clinical parameters, and treatment outcomes. Comparative analyses were conducted to evaluate the differences in outcomes between study groups.

♦ **Funding:** There was no external funding for this study; all expenses were borne by the study institute. The Principal Investigator covered the costs associated with data collection.

♦ **Conflict of Interest:** The authors of this study declare no conflict of interest in the design, implementation, or interpretation of the study findings. All data collection, analysis, and reporting were conducted objectively, with the sole intention of contributing to evidence-based practices in the management of Covid-19 with Remdesivir. No personal or financial interests influenced any aspect of the study, ensuring unbiased research outcomes.

Results: The study included 2200 participants, equally divided into the Remdesivir group (n = 1100) and the Standard Care group (n = 1100), with participants matched on age and gender. Both groups had a similar mean age of 55 years (SD ± 14) and a matching distribution of males, comprising 66% of each group. Smoking prevalence was also consistent across both groups, with 25% of participants identified as smokers in each group. The presence of fever, headache, and cough was similarly distributed, with no statistically significant differences between groups. Both groups had a mean oxygen saturation of approximately 88%, with mean respiratory rates around 22 breaths per minute. Overall, the baseline characteristics indicate a well-matched study population, ensuring that any observed differences in clinical outcomes can more confidently be attributed to the effects of Remdesivir rather than baseline variations.

Table 1: Baseline Clinical and Laboratory Characteristics of the Study Groups

Characteristic	Remdesivir Group (n = 1100)	Standard Care Group (n = 1100)	p-value
Age (years), mean ± SD	55 ± 14	55 ± 14	1.00
Male, n (%)	726 (66%)	726 (66%)	1.00
Smoking, n (%)	270 (25%)	270 (25%)	1.00
Diabetes Mellitus (DM), n (%)	430 (39%)	425 (38%)	0.876
Hypertension (HTN), n (%)	365 (33%)	370 (34%)	0.812
Fever, n (%)	883 (80%)	871 (79%)	0.665
Headache, n (%)	709 (64%)	700 (64%)	0.891
Cough, n (%)	785 (71%)	790 (72%)	0.923
Temperature (°C), mean ± SD	37.96 ± 0.65	38.01 ± 0.68	0.502
Respiratory Rate (bpm), mean ± SD	22.3 ± 4.4	22.1 ± 4.5	0.622
Oxygen Saturation (%), mean ± SD	88.0 ± 11.0	88.5 ± 10.8	0.753
Hemoglobin (g/dL), mean ± SD	12.2 ± 2.1	12.3 ± 2.0	0.701
Platelets (10^3/mm^3), median (IQR)	220 (180–300)	225 (185–305)	0.841
WBC (10^3/mm^3), mean ± SD	5.8 ± 4.6	5.7 ± 4.5	0.912
Total Bilirubin (mg/dL), mean ± SD	0.80 ± 0.37	0.81 ± 0.35	0.915
Albumin (g/dL), mean ± SD	3.98 ± 0.55	3.96 ± 0.52	0.846
ALT (U/L), median (IQR)	33.5 (18.0–51.0)	32.0 (19.0–50.0)	0.682
AST (U/L), median (IQR)	28.0 (20.0–53.5)	27.0 (21.0–52.0)	0.760
INR, mean ± SD	1.10 ± 0.21	1.11 ± 0.20	0.889
Creatinine (mg/dL), mean ± SD	0.92 ± 0.22	0.91 ± 0.20	0.812
C-reactive Protein (mg/dL), median (IQR)	15.0 (5.0–55.0)	14.5 (6.0–54.0)	0.793
D-dimer (mg/L), median (IQR)	0.78 (0.5–11.0)	0.77 (0.4–10.5)	0.865
Ferritin (ng/mL), median (IQR)	210 (115–365)	205 (120–360)	0.921

Table 2: Clinical Outcomes of the Study Groups

Clinical Outcome	Remdesivir Group (n = 1100)	Standard Care Group (n = 1100)	P-value
Length of Hospital Stay (days)			
Mean ± SD	9.8 ± 6.2	14.5 ± 7.8	**<0.001**
Median (IQR)	8 (6–12)	13 (10–17)	
Need for Ventilator, n (%)	95 (8.6%)	160 (14.5%)	**<0.01**
Discharged Alive, n (%)	1025 (93.2%)	980 (89.1%)	0.001
Mortality, n (%)	75 (6.8%)	120 (10.9%)	

The length of hospital stay was significantly shorter in the Remdesivir group, with a mean of 9.8 days (SD ± 6.2) compared to 14.5 days (SD ± 7.8) in the Standard Care group ($p < 0.001$). The median stay was also notably reduced, with Remdesivir patients experiencing a median stay of 8 days (IQR 6–12) compared to 13 days (IQR 10–17) for the Standard Care group. The need for ventilator support was lower in the Remdesivir group, where 8.6% of patients (n = 95) required ventilation, in contrast to 14.5% (n = 160) in the Standard Care group ($p < 0.01$). The mortality rate was consequently lower in

the Remdesivir group, with 6.8% (n = 75) of patients, versus 10.9% (n = 120) in the Standard Care group.

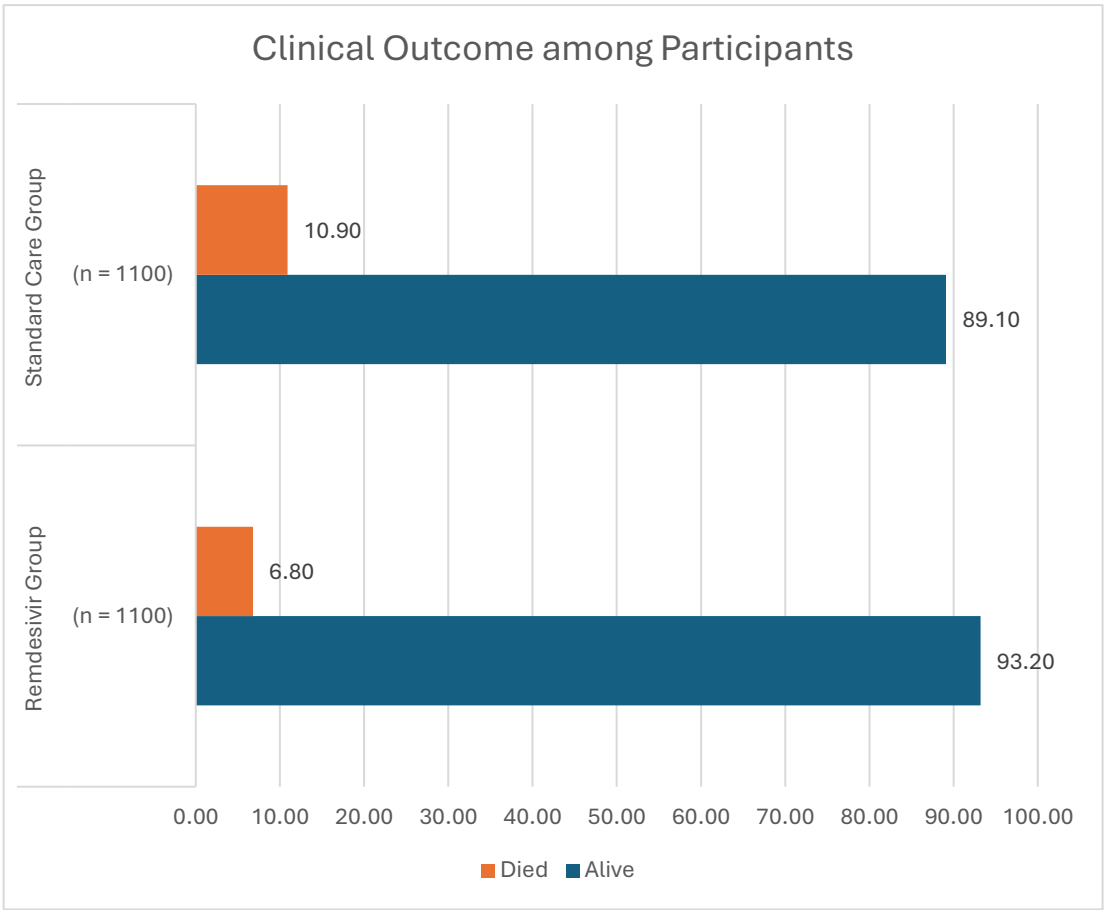

Table 3: Relative Risk and Number Needed to Treat

Outcome	Relative Risk (RR)	Number Needed to Treat (NNT)
Need for Ventilator	0.58 (95% CI 0.51 – 0.74)	17
Mortality	0.63 0.58 (95% CI 0.56 – 0.71)	24

For the outcome of Need for Ventilator, the Relative Risk for the Remdesivir group was calculated at 0.58, suggesting that patients treated with Remdesivir had a 42% lower risk of requiring ventilator support compared to those receiving standard care. The Number Needed to Treat (NNT) was 17, meaning that 17 patients would need to be treated with Remdesivir to prevent one additional patient from requiring ventilator support. For Mortality, the Relative Risk for the Remdesivir group was 0.63, indicating a 37% reduction in the risk of death compared to the Standard Care group. The NNT for mortality was 24, implying that 24 patients would need to receive Remdesivir to prevent one additional death. These findings underscore the efficacy of Remdesivir in improving critical outcomes for Covid-19 patients, specifically in lowering both ventilator dependency and mortality rates among those hospitalized with moderate to severe disease.

Discussion

The findings of this study contribute to the ongoing discussion about the role of Remdesivir in managing hospitalized COVID-19 patients, specifically its impact on hospital stay duration, need for ventilatory support, and mortality. Our discussion will focus on these aspects, incorporating insights

from recent systematic reviews and randomized controlled trials (RCTs) for a more comprehensive understanding.

The study observed that patients receiving Remdesivir had a significantly shorter hospital stay than those on standard care. This aligns with findings from multiple systematic reviews and meta-analyses, which have reported moderate reductions in hospital stay with Remdesivir treatment[13]. For instance, a systematic review by Angamo et al. (2021) found that Remdesivir significantly reduced the length of hospital stay by up to four days in moderate to severe COVID-19 cases[14]. Similarly, a Canadian trial under the Solidarity trial umbrella showed that patients receiving Remdesivir had a shorter hospital stay and higher discharge rates, highlighting its role in expediting recovery for hospitalized patients[15]. However, contrasting results have emerged, particularly in the WHO Solidarity Trial, which did not find a substantial reduction in hospital stay duration with Remdesivir use, suggesting the need for further investigation in varied healthcare settings[15]. These discrepancies may reflect differences in healthcare resources, patient demographics, or disease severity at the time of hospital admission.

Our study showed a reduction in the need for ventilator support among patients treated with Remdesivir, an effect supported by various systematic reviews and meta-analyses[13,16]. According to a meta-analysis by Ryoo et al. (2023), Remdesivir treatment correlated with a decreased likelihood of requiring invasive mechanical ventilation, particularly for patients not on mechanical ventilation at baseline[17]. This study calculated a relative risk (RR) of 0.74, indicating a 26% reduction in ventilator requirements for the Remdesivir group[17]. Conversely, the Solidarity Trial reported less favorable outcomes for ventilatory support, showing little to no impact from Remdesivir on the need for mechanical ventilation[15]. This discrepancy may highlight the importance of patient selection criteria, as evidence suggests that Remdesivir benefits are more pronounced in non-ventilated patients or those requiring only low-flow oxygen at baseline[18].

In terms of mortality, our findings indicate a reduced mortality rate among patients receiving Remdesivir compared to those on standard care. This outcome aligns with systematic reviews like those by Patnaik et al. (2023), which demonstrated a non-significant trend towards lower mortality in patients receiving Remdesivir, particularly those with moderate disease severity[19]. However, the Solidarity Trial found no significant mortality benefit for Remdesivir, especially among patients requiring advanced respiratory support[15]. This discrepancy could be due to variations in study design, patient populations, and disease severity levels across trials. The Cochrane review also suggests that while Remdesivir may not significantly impact overall mortality, it shows promise in reducing early-stage mortality in patients needing supplemental oxygen but not mechanical ventilation[18].

Conclusion

While this study supports the efficacy of Remdesivir in reducing hospital stay, ventilator dependency, and mortality among hospitalized COVID-19 patients, these findings echo mixed results from larger trials and meta-analyses. The variations in outcomes across studies underscore the importance of patient selection criteria and indicate that Remdesivir may be most beneficial in early-stage, moderate to severe COVID-19. Future research should aim to clarify the specific contexts in which Remdesivir offers the greatest therapeutic advantage.

Strengths

1. Large Sample Size: This study included 2,200 participants, providing a substantial sample size to assess the effectiveness of Remdesivir, which enhances the statistical power and reliability of the findings.
2. Matched Groups: By matching participants on age and gender, the study minimized potential confounding variables that could influence outcomes, making the comparisons between the Remdesivir and standard care groups more robust.

3. Real-World Setting: Conducted in a clinical setting during the COVID-19 pandemic, this study reflects real-world conditions, which enhances the applicability of the results to similar healthcare environments.
4. Comprehensive Outcome Measures: The study evaluated multiple relevant outcomes, including hospital stay length, need for ventilator support, and mortality, providing a holistic view of Remdesivir's potential benefits in managing moderate to severe COVID-19 cases.

Limitations

1. Single-Center Design: The study was conducted at one institution, which may limit the generalizability of the findings to other healthcare settings with different patient demographics, resources, and treatment protocols.
2. Retrospective Design: As a retrospective cohort study, there is a risk of selection bias and reliance on existing records, which might lead to incomplete or inconsistently recorded data, potentially affecting the accuracy of the findings.
3. Lack of Randomization: Without random assignment, there may be unmeasured confounding factors that could influence the outcomes, even with age and gender matching.
4. No Long-Term Follow-Up: The study focused on in-hospital outcomes without examining longer-term effects, which limits understanding of Remdesivir's impact on post-discharge recovery or long-term mortality.

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