Original Research Article

A study of the effect of Remdesivir therapy on mortality in patients suffering from respiratory COVID infection

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Abstract

Background: Mortality due to SARS-CoV-2 infection (COVID-19) is on the rise worldwide, including India. Out of the many drugs being repurposed for the treatment of SARS-CoV-2 infection (COVID-19), a broad-spectrum anti-viral drug Remdesivir has also been tried for compassionate use in severe COVID-19. Recently available randomized clinical trials have shown some promising results; however, data is limited for its effectiveness in the treatment of COVID-19. **Aims and objectives:** To study the effect of Remdesivir therapy on mortality in patients suffering from respiratory COVID-19 infection. **Materials and methods:** The case records of patients admitted to the District Covid Hospital Located at the Super speciality Hospital of Jayaragya Groups of Hospitals Gwalior, MP were studied retrospectively. These patients were admitted during the period of 8th September to 7th Oct 2020.The cases were divided into Group A (n=52; cases of Covid 19 respiratory infection who received Remdesivir therapy along with standard care) and Group B (n=344, cases of Covid 19 respiratory infection who received standard care but noRemdesivir). The outcome was measured in terms of mortality. **Results:** COVID-19 was more prevalent in those with age between 61-70 years (36.54%) with mean age of 57.90±8.12 years, also COVID-19 was more prevalent in males (75%). The mean duration of hospital stay was significantly more for moderate patients (14.38±5.95 days) than severe patients (12.86±7.47 days) with a p-value of 0.021. Out of 52 patients in Group A, the majority were discharged (71.15%). Mortality was reported in 15 (28.85%) patients. The mortality rates in patients receiving Remdesivir were 28.85%. We also compared this with mortality rates in patients who did not received Remdesivir which was 18.60% (p=0.142). There was no significant difference between Group A and Group B.**Conclusion:** Despite its efficacy in improving the clinical outcome, we recorded high mortality with Remdesivir, suggesting a need for several other treatment modalities along with Remdesivir. There was no difference in outcome according to severity grade at presentation.

Keywords: Mortality, anti-viral drugs, COVID-19, pneumonia.

Introduction

The current pandemic of SARS-CoV-2 infection is characterized by progressively severe pneumonia and ARDS leading to increasing in-hospital mortality. This poses challenges to the medical community to assess rapidly any possibly effective treatment option for the management of COVID-19 infections[1].Due to the expected high case fatality rate and severity of pneumonia caused by COVID-19, there is a need for effective drug treatment in addition to available supportive care and oxygen supplementation[2].Remdesivir is a nucleoside pro-drug that acts by inhibiting viral RNA transcription. In-vitro trial and a few small human trials have show its effectiveness against coronavirus and SARS-CoV-2 and be safely used as a compassionate basis in managing COVID-19 infections [3,4].Though recently available randomized clinical trials have shown some promising results;however, data is limited for its effectiveness of Remdesivirin the treatment of COVID-19. Hence, through this observational analysis, we tried to study the effects of Remdesivir therapy on mortality in patients suffering from respiratory COVID infection.

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Materials and methods

The case records of patients admitted to the District Covid Hospital Located at the Super speciality Hospital of Jayaragya Groups of Hospitals Gwalior, MP were studied retrospectively. These patients were admitted during the period of 8th September to 7th Oct 2020. Eligible patients were men and non-pregnant women with COVID-19 who were aged at least 18 years and were RT-PCR positive for SARS-CoV-2 and had pneumonia confirmed by chest imaging or had an oxygen saturation of 94%.Exclusion criteria included pregnancy or breastfeeding; hepatic cirrhosis; alanine aminotransferase or aspartate aminotransferase more than five times the upper limit of normal; known severe renal impairment (estimated glomerular filtration rate <30 ml/min per 1·73 m^2) or receipt of continuous renal replacement therapy, hemodialysis, or peritoneal dialysis; the possibility of transfer to a non-study hospital within 72 h; and enrolment into an investigational treatment study for COVID-19 in the 30 days before screening.The cases were divided in to two groups;Group A:Cases of Covid 19 respiratory infection who received Remdesivir therapy along with standard care (n=52), Group B: Cases of Covid 19 respiratory infection who received standard care but no Remdesivir (n=344). The outcome was measured in terms of mortality.All the data were analyzed using IBM SPSS ver. 20 software. Cross tabulation and frequency distribution were used to prepare the tables. Quantitative data were expressed as mean and standard deviation, whereas categorical data were expressed as a percentage. ANOVA was used to compare the means, whereas the

chi-square test was used to compare the percentage. The level of significance was assessed at 5%.

Results

COVID-19 was more prevalent in those with age between 61-70 years (36.54%) followed by 51-60 years (19.23%) with mean age of 57.90±8.12 years, also COVID-19 was more prevalent in males (75%).

Table 1: Showing age distribution

Age group	Frequency	Percentage
<40	8	15.38
41-50	7	13.46
51-60	10	19.23
61-70	19	36.54
>70	8	15.38
Total	52	100

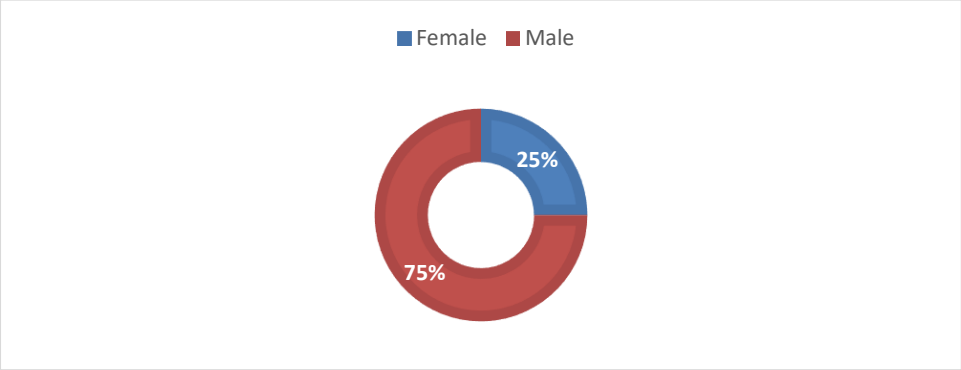

Fig 1: Showing gender distribution in present study cohort

Table 2: Comparing the mean duration of hospital stay with case severity

Case severity	Mean duration (days)	Standard deviation	P-value
Moderate	14.38	5.96	0.021
Severe	12.86	7.47	
Total	13.55	6.871	

The mean duration of hospital stay was significantly more for moderate patients (14.38±5.95 days) than severe patients (12.86±7.47 days) with a p-value of 0.021.

Table 3: Showing Mortality rates with Remdesivir in the treatment of Covid 19 (n=52)

Outcome	Frequency	Percentage
Discharged	37	71.15
Expired	15	28.85
Grand Total	52	100.00

Out of 52 patients in Group A enrolled in the study, the majority were discharged (71.15%). The mortality was reported in 15 (28.85%) patients. The mortality rates in Group A was 28.85%.

Table 4: Association of Outcome with case severity in Group A (n=52)

Outcome	Case severity		Total	P-value
	Moderate	Severe		
Discharged	23 (62.16)	14 (37.84)	37 (100)	0.445
Expired	3 (20)	12 (80)	15 (100)	
Grand Total	26 (50)	26 (50)	52 (100.00)	

Out of 15 patients who expired, most were severe patients (80%), whereas 20% had the moderate disease.

A total 344 patients did not receive remdesivir, of that 64 died. The mortality rate among those who did not receivedremdesivir was 18.60%.

Table 5: Comparison of mortality between Group A and Group B

Remdesivir received	Outcome		Mortality rate (%)	P value
	Survived	Expired		
Yes (n=52)	37	15	28.84	0.142
No (n=344)	280	64	18.60	
Total	317	79		

Discussion

Before repurposing, Remdesivir was the drug for treating patients with Ebola virus infection[5].After the outbreak in 2020, remdesivir was included in the international clinical trial list conducted by the World Health Organization (WHO) to look for an effective treatment for COVID-19[6].Remdesivir is a broad-spectrum antiviral drug that is being used for the treatment of the Ebola virus. Several in vitro studies have shown activity against SARS-Cov-2. Several phase II and phase III randomized clinical trials have also demonstrated the efficacy of parenteral Remdesivir in patients with mild-to-moderate and severe COVID-19[7].In the present study, we evaluated Remdesivir therapy's effects on mortality in patients suffering from respiratory COVID infection. We found that the mean duration of hospital stay was significantly more for moderate patients than in severe patients.We found that out of 52 patients enrolled in the study, the majority were discharged. The mortality was reported in 28.85% of patients. However, those who expired, the majority were severe cases.However this difference was not statistically significant. Beigel et al., investigating the role of Remdesivir, reported that mortality rates estimated by Kaplan–Meier analysis was 6.7% with Remdesivir and 11.9% with placebo by day 15.[8]Olender et al., in an interim data from SIMPLE-severe and a concurrent retrospective cohort study, reported significantly reduced mortality by Remdesivir compared to standard of care (7.6% vs. 12.5% respectively p<0.001)[9].However, a recent NIH clinical trial had not reported any significant survival benefit with Remdesivir than the control group. The Remdesivir group had a mortality rate of 8.0% compared to 11.6% for the placebo group (p = 0.059)[10]. In another randomized, double-blind, placebo-controlled, multicentre phase III trial from China reported similar mortality at day 28 (14% in the Remdesivir group and 13% in the placebo group)[11].The present study had few limitations; small sample size and lack of randomization are a few of them; there is a need for a large randomized clinical trial to provide strength to present study findings.

Conclusion

Given high mortality in the present study despite the use of Remdesivir, treatment with an antiviral drug alone like Remdesivir is not likely to be sufficient for COVID-19 patients. There is a need for additional treatment strategies along with the Remdesivir in improving the mortality related outcome. Several randomized clinical trials are currently ongoing evaluating Remdesivir in combination with several modifiers of the immune response. This highlights various therapeutic approaches, including novel antivirals, modifiers of the immune response or other intrinsic pathways, and combination approaches are needed to continue to improve outcomes in patients with Covid-19.

Conflict of Interest: Nil
Source of support:Nil

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