Original Article

Comparison of Clinical Improvement with VS without Remdesivir Treatment in Hospitalized Patients with COVID-19

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ABSTRACT

Objective: To determine the role of remdesivir administered for treatment of hospitalized coronavirus disease 2019 (COVID-19) in terms of rapid clinical improvements.

Study Design: Retrospective comparative study

Place and Duration of Study: This study was conducted at the Department of Pulmonology and Covid-19 department, Recep Tayyip Erdogan Hospital Muzaffargarh from April 2020 to December 2021.

Materials and Methods: A total of 923 patients were enrolled in study. Clinical outcomes like hospital stay, ICU stay, mechanical ventilation time, discharge from hospital and duration of death after admission and mortality rate of patients treated with remdesivir and who were treated without remdesivir was taken from hospital record. Data was analyzed by using SPSS version 24.

Results: The mean length of stay of remdesivir patients was 8.19±5.71 days with 95% C.I (7.68-8.70) and non-remdesivir patients was 6.07±5.66 days with 95% C.I (5.54-6.60), and the difference was statistically significant, (p=0.000). The most common diagnosed complication in remdesivir patients was diabetes mellitus 7.6% and the second most common complication was sepsis 6.0%. Among total 14.8% of remdesivir patients needed to admit in ICU versus 14.9% with (p=0.980). Distribution of mortality was 39.5% of remdesivir patients versus non-remdesivir 26.3%.

Conclusion: Remdesivir is associated with poor clinical outcomes, mean hospital stay, ICU stay and death rate is higher in patients treated with remdesivir, as compared to those treated without remdesivir. Final outcome regarding discharge of patients is also better in without remdesivir group.

Key Words: Clinical outcomes, COVID-19, Death, Hospitalization, Remdesivir

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INTRODUCTION

Novel coronavirus, severe acute respiratory syndrome, was first identified in December 2019 as the cause of a respiratory disease designated coronavirus disease 2019, or Covid-19. Many therapeutic agents have been evaluated for the treatment of Covid-19, but no antiviral agents have proved to be efficacious[1].

median incubation period of 5.1 days and a basic reproduction number of 2.24–3.58[2,3]. The ongoing pandemic of severe acute respiratory syndrome coronavirus infections has led to more than 262,736,568cases and 5,229,500 deaths globally as of Nov, 2021[4,5]. Due to severity and expected high CFR of the pneumonia caused by SARS-CoV-19, it is important to find an effective drug treatment because supportive care and oxygen supplementation is not always enough[6].

Remdesivir, an inhibitor of the viral RNA-dependent, RNA polymerase was identified early as a promising therapeutic candidate for Covid-19treatment. Remdesivir is a monophosphoramidate pro drug of an adenosine analogue that has a broad antiviral spectrum including filo-viruses, paramyxo-viruses, pneumo-viruses, and corona viruses [7,8].

In a trial conducted in 2020 by WHO showed that remdesivir, hydroxychloroquine, lopinavir, and interferon regimens had little or no effect on hospitalized patients with Covid-19, as indicated by overall mortality, initiation of ventilation, and duration of hospital stay. The UK-based RECOVERY (Randomized Evaluation of COVID-19 Therapy) trial

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showed that dexamethasone administration compared with placebo led to a significant reduction in mortality rate (22.9% vs 25.7%)[9]. Trials examining the benefit of different corticosteroids were stopped early after the results of RECOVERY led to corticosteroids being considered the standard of care. Whether there is additional benefit from using both remdesivir and corticosteroids requires further evaluation[10].

MATERIALS AND METHODS

It is a retrospective cohort study conducted at Department of Pulmonology and Covid-19 department, Recep Tayyip Erdogan Hospital Muzaffargarh. Non probability consecutive sampling type of sampling technique was used. Study was carried out after ethical approval from hospital ethical board. The inclusion criteria for this study was as follows; Patients with COVID 19 pneumonia with severe clinical status on day 1, Patients who received other medical standard care according to institutional guidelines, Patients with previously chronic lung disease like COPD, asthma and ILD evaluated on history and medical records, Both genders, 18 years to 80 years of age. The exclusion criteria was as follows; Patients who required ICU admission or mechanical ventilation on day 1, patients with COVID 19 pneumonia with mild to moderate disease, patients with ALT levels >5 times.

Previous data of COVID 19 patients from April 2020 to December 2021 was evaluated according to inclusion and exclusion criteria. Demographic variables like age, gender, BMI and previous clinical status like diabetes mellitus, hypertension, ischemic heart disease, asthma and chronic obstructive pulmonary disease was recorded on Performa. On day of presentation clinical severity of each patient was noted. Two groups were made for remdesivir and non-remdesivir. Every patient was followed for the primary and secondary outcome like length of hospital stay, ICU admission, recovery; complications of disease and death were recorded.

Data was analysed by SPSS 24. Quantitative variables like age BMI, length of hospital stay, was statistically analysed in mean and standard deviation. Qualitative variables like gender, presence of comorbidity, clinical severity on admission, event of ICU admission, complications of disease and mortality was analysed in percentage and frequency. Chi-square test was applied to check the significance. Length Of hospital stay, ICU admission, recovery, complications of disease and death was analysed in mean and standard deviation and independent t test was applied to check its significance. P value $\leq$0.05 was taken as significant.

RESULTS

Over the study period, 923 patients were admitted in Recep Tayyip Erdogan Hospital Muzaffargarh in Covid-19 ward. Out of these, 486 (52.7%) treated with remdesivir and 437 (47.3%) treated without remdesivir. The mean age of the remdesivir patients was greater than non-remdesivir patients and the majority of both the groups between 51-60 years. The mean CRP in non-remdesivir patients was greater than that of remdesivir patients, (p=0.040), but the same median was to be found. Most of patients of remdesivir and non-remdesivir patients were non-smokers, 464 (95.5%) and 404 (92.4%), respectively. Further, it was seen that very severe clinical stage of disease, 185 (38.1%), was statistically more common in remdesivir patients and least common, 115 (26.3%), in non-remdesivir patients.(Table. I).

Table No.1: Demographic characteristics of the patients

Variable	Hospital Treatment Remdesivir		P-value
	Yes, N (%)	No, N (%)	
Gender			
Male	268 (55.1)	264 (60.4)	0.106
Female	218 (44.9)	173 (39.6)	
Age			
Mean±S.D	56.63±13.25	54.37±16.77	0.023
<30 years	12 (2.5)	41 (9.4)	0.000
30-40 years	44 (9.1)	58 (13.3)	
41-50 years	80 (16.5)	74 (16.9)	
51-60 years	146 (30.0)	88 (20.1)	
61-70 years	129 (26.5)	88 (20.1)	
71-80 years	60 (12.3)	71 (16.2)	
>80 years	15 (3.1)	17 (3.9)	
CRP on admission			
Mean±S.D	37.41±46.17	44.10±52.91	0.040
Median± I.Q.R	32.00±51	32.00±64	
Smoking status			
Current smoker	5 (1.0)	13 (3.0)	0.069
Ex-smoker	17 (3.5)	20 (4.6)	
Non smoker	464 (95.5)	404 (92.4)	
Comorbidity			
Asthma	10 (2.1)	8 (1.8)	0.016
COPD	7 (1.4)	16 (3.7)	
Clinical stage of disease			
Severe	238 (49.0)	201 (46.0)	0.000
Very Severe	185 (38.1)*	115 (26.3)*	
P≤0.05 considered as significant, * standardized residual>1.96			

The mean length of stay of remdesivir patients was 8.19±5.71 days with 95% C.I (7.68-8.70) and non-remdesivir patients was 6.07±5.66 days with 95% C.I (5.54-6.60), and the difference was statistically significant, (p=0.000).(Figure. I). The most common diagnosed complication in remdesivir patients was diabetes mellitus 37 (7.6%) and the second most common complication was sepsis 29 (6.0%). Only 72 (14.8%) of remdesivir patients needed to admit in ICU

versus 65 (14.9%) with (p=0.980). Distribution of ICU stay was shown in figure. 2. 192 (39.5%) of remdesivir patients died versus non-remdesivir 115 (26.3%) (Table. 2).

Table No.2: Outcome representation of the patients

Outcome	Hospital Treatment Remdesivir		P-value
	Yes, N (%)	No, N (%)	
Length of hospital stay			
Mean±S.D	8.19±5.71	6.07±5.66	0.000
95% C.I	7.68 to 8.70	5.54 to 6.60	---
Median±I.Q.R	7.00±5.00	4.00±5.00	---
ICU admission			
Yes	72 (14.8)	65 (14.9)	0.980
No	414 (85.2)	372 (85.1)	
Length of ICU stay			
Mean±S.D	9.27±6.38	8.34±6.41	0.403
95% C.I	7.75 to 10.79	6.74 to 9.94	---
Median ± I.Q.R	7.50±9.00	7.00±9.00	---
Final outcome			
Death	192 (39.5)*	115 (26.3)	0.000
Discharge at room air	244 (50.2)	267 (61.1)	

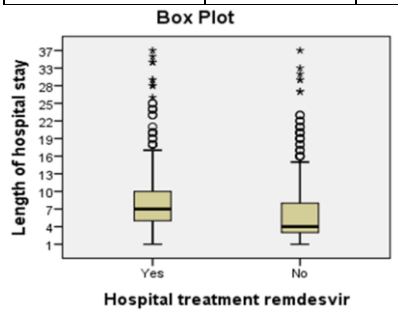

Figure No.1: Hospital treatment remdesvir with length of hospital stay.

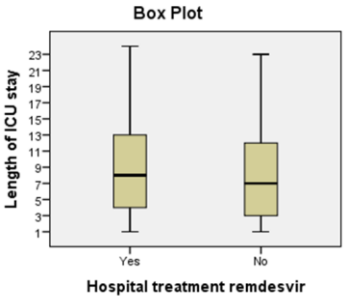

Figure No.2: Hospital treatment remdesvir with length of ICU stay.

DISCUSSION

In this comparative study 923 patients were admitted in COVID-19 ward in 1st 2days. Mean age of the remdesivir patients was greater than non-remdesivir patients and the majority of both the groups between 51-60 years. Male gender is dominant in our study. The mean CRP in non-remdesivir patients was greater than that of remdesivir patients, (p=0.040).

A study was conducted by Abd-Elsalam et al[11] in 2022 on 200 patients, remdesivir was given in 100 patients and 100 were treated without remdesivir. Mean hospital stay was higher in remdesivir group 12.37 ± 8.96 as compare to without remdesivir 16.72 ± 5.78, but mortality was found higher in remdesivir group 9% vs 7% respectively. It was reported in this study that mean CRP level is also associated with mortality. A study was conducted by Garibaldi et al[12] on 2483 COVID-19 patients, among them 342 patients were treated with remdesivir having median age of 60 years (IQR-46-69 years) and 55.3% were male. Mortality rate was 7.7% with 22 days duration.

In our study most common comorbidities were smoking, COPD. A study was conducted by Mozaffari et al[13] and observed similar findings as Diabetes, COPD, Obesity, cardiovascular disease, renal disease are common co morbidities. This study also favors use of remdesivir in COVID-19 patients as use of remdesvir improves the clinical outcomes and enhances the hospital stay. Another study by Wang et al[14] hastening recovery and reduction in mortality rate was observed but at day 29 there was not a significant improvement noted.

In our study Distribution of ICU stay was prolonged in remdesivir group. Among total 39.5% of remdesivir patients died versus non-remdesivir 26.3%. Further, 6.4% and 4.6% of remdesivir and non-remdesivir patient improved and discharged to home, respectively. In a study by Consortium et al[15] on benefits of remdesivir in mortality and recovery time and reported that a positive role in both outcomes. Another study by Kaka et al[16] showed positive role of remdesivir in mortality rate reduction and duration of death enhancement when compared with treatment without remdesivir patients.

Another randomized trial was conducted by Olender et al[17] and found 62% decrease in death rate within 14 days when compared with standard of care, 74.4% of remdesivir patients recovered within 14 days and in non remdesivir group 59% patients recovered and death rate was 7.6% and 12.5% respectively. A study by Elsawah et al[18] also reported similar findings that in patients with HFO requirements at baseline remdesivir reduced the risk of mortality at 14 days but at 28 days its role in mortality reduction and recovery benefits is not well documented.

In our study we used remdesivir for 10 days and at the end of study 50.2% patients discharged at room air mortality was 39.5%. A study was conducted by Goldman et al[19] on 397 patients in 2020 and reported that 52% patients were discharged from hospital and mortality was 11% with 10 days treatment. Another

similar study was conducted by Spinner et al[20] on 584 patients and compared standard care treatment with remdesivir for 5 day and 10 days, at 28 day of admission death was observed in 2% of patients in patients with 10 days treatment plan.

A study by Terks et al[21] was completed in 2022 on 137 patients data form hospital record, remdesivir was given for 5 to 10 days and observed improvement in clinical outcomes in 75.9% patients and mortality was observed in 24.1% of patients. Mortality was higher in severe/critically diseased patients 34.8% than moderately ill patients 5.9%.

CONCLUSION

Remdesivir is associated with poor clinical outcomes, mean hospital stay, ICU stay and death rate is higher in patients treated with remdesivir, as compared to those treated without remdesivir. Final outcome regarding discharge of patients is also better in without remdesivir group.

Author's Contribution:

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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