Original Article

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Safety of Remdesivir in Covid Patients with Acute or Chronic Kidney Disease

Haseeb Nasir[1], Khalid Mehmood Raja[2], Shahzeb Satti[3], Ahmed Tanveer[4] , Roshaan Tahir[5], Maryam Zafar[6]

[1]Resident Medicine, General Medicine, Pak Emirates Military Hospital Rawalpindi

[2]Dept. of Nephrology Pak Emirates Military Hospital Rawalpindi, [3]Dept. of Pulmonology, Pak Emirates Military Hospital Rawalpindi, [4]Medical Officer, Imtiaz Surgical Hospital, Lahore, [5]Resident, General Medicine Pak Emirates Military Hospital Rawalpindi

[6]Resident Radiology, CMH Rawalpindi

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Address of Correspondent

Dr. Haseeb Nasir

Resident Medicine, General Medicine, Pak Emirates Military Hospital Rawalpindi

haseebnasir2807@gmail.com

ABSTRACT

Objective: The aim was to assess the safety of Remdesivir in Patients with Acute and Chronic Kidney Disease

Methodology: Quasi-experimental study was conducted at the Pak Emirates Military Hospital Rawalpindi from March 2021 to April 2022. A sample was collected through a non-random sampling method, recruiting those who were diagnosed with pneumonia caused by the COVID-19 virus. A total of 56 patients with acute or chronic kidney disease were the participants of our study. The inclusion criterion was patient with positive COVID PCR 7-10 days prior to the commencement of the study. Patients admitted to the hospital nephrology ward with any stage of AKI were also considered for inclusion in the study. However, patients under the age of 18 and those who refused to participate were excluded.

Results: The serum creatinine value were 125.15 ± 8.61 u/L and 126.44 ± 5.72 micromoles/L before and after Remdesivir use respectively. The serum ALT changed from 34.55 ± 2.69 u/L to 33.26 ± 1.85 u/L while Serum AST changed from 54.69 ± 4.04 u/L to 55.42 ± 3.09 u/L in patients with renal diseases when treated with Remdesivir for COVID-19.

Conclusion: This study concluded that Remdesivir had no statistically significant effect on serum creatinine, AST and ALT. It also showed that these values showed and above normal pattern from baseline before and after the administration of Remdesivir when given in participants of the study undergoing COVID treatment with AKI or CKD.

Keywords: Covid–19, Kidney disease, Remdesivir, Therapeutic drugs.

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Introduction

Since its first hit on Pakistan in February 2020, COVID has taken our country by storm, taking many lives and leaving hundreds in its effect.[1] Till date Pakistan has seen **1,531,581** infections and **30,382** coronavirus-related deaths due to this pandemic.[2] According to Reuter's research on daily pandemic statistics around the world, currently Pakistan is reporting **87** new infections on average each day.[3] However these statistics gets disturbing for patients that have Co-morbidities. According to researchers, dialysis patients and kidney transplant recipients are a high-risk population with unusual clinical characteristics that pose a challenge. CKD, on the other hand, has recently been shown to be a major risk factor for mortality in patients with COVID-19 pneumonia, and has a significant correlation between mortality rate and amount of dysfunction.[4]

Many treatment regimens have been introduced for COVID since its discovery; however, because of its changing forms no drug was considered the final treatment option. In the earlier peaks of the pandemic, medical professionals were persuaded that Corticosteroids were the only drugs that could treat the symptoms of this Virus.[5] On the other hand, as the virus changed, so did the research, and the FDA approved several different medications, such as Remdesivir, Tocilizumab, and Favipiravir. However, it was seen that majority of these antivirals had little or no

effect on the changing morphology of Virus, but Remdesivir was the only drug that showed promising results. Food and Drug Regulatory Authority (FDA) has also approved the use of Remdesivir for everyday use in COVID patients under proper monitoring, similarly, other effective drugs like paxlovid and molnupiravir have been authorized to be used in emergencies by the FDA.

Remdesivir, is an antiviral medication with wide antiviral activity that effects the ability of virus to replicate. It acts nucleoside analog by inhibiting the RNA dependent Polymerase required for Corona Virus replication.[6] Unfortunately, the benefits of this drug cannot be put into use in patients with renal diseases as Remdesivir is eliminated through the kidneys and is not recommended for patients with a glomerular filtration rate (GFR) of less than 29-30 mL/min or those on Dialysis.[7] However, it was also seen that if administered within 48 hours after the onset of symptoms, this drug, Remdesivir, has the potential to help dialysis patients recover more quickly with no adverse effects.[8] Other antiviral drugs such as molnupiravir which doesn't have these side effects are currently unavailable in Pakistan.[9]

Keeping in light the effect of this antiviral regimen on kidney functions, our study aimed to evaluate the safety of antiviral drug Remdesivir in patients with acute and chronic kidney and renal disease. This will help with provision of evidence-based data for the use of this drug in such patients without causing any side effects and will also provide clinicians with a basic research strategy to focus on while studying the effects of antiviral therapy in such patients.

Methodology

Our study was a prospective cohort study, conducted at Pak Emirates Military Hospital Rawalpindi after approval from institute's ethical committee from March 2021 to April 2022.

To collect data, we started our research by recruiting 80 patients who were diagnosed with pneumonia caused by COVID-19 virus. Among these 80, 12 didn't meet the inclusion criteria while 7 patients didn't consent for participation, and while 5 patients died prior to the end of their treatment regimen. Patients admitted to the hospital nephrology ward with any stage of AKI were also considered for inclusion in the study. All patients who had viral pneumonia on a chest HRCT scan, or who had an O2, or mechanical ventilation need of less than 94% on room air, are also included in the study.

Chronic Kidney Disease was defined as patients with irreversible loss of renal function requiring dialysis for >3 months. AKI was defined as per clinical practice guidelines (2012) by Kidney Disease Improving Global Outcomes (KDIGO). Patients with all stages of AKI admitted to the hospital unit till were included. Patients under the age of 18 and those who refused to give their consent to participate were, however, omitted from the study.

Primary outcome was studying the safety of remdesivir by evaluating clinical and laboratory parameters in these patients. Preoperative presence of other co-morbidities was recorded and Baseline Serum creatinine, ALT and AST and GFR was also recorded. Secondary outcomes like duration of hospital stay, mortality was also recorded.

The treatment protocol provided at our unit to these patients was to treat every patient who had severe COVID-19 i.e. those who required oxygen provision were treated with intravenous (I/V) remdesivir 200mg on day 1, followed by 100 mg daily for four consecutive days. This therapy could be extended up to 10 days if indicated as per ruling of treating physician.

The patients were daily monitored for their baselines, and other medical information needed for the recovery and data Clinical and Laboratory findings were taken before the administration of the drug and at 3,5th and 7th Day of drug administration. The baseline lab tests were recorded at these days along with the need to mechanically ventilate the patient during their management.

Data was analyzed using SPSS V20. Both quantitative and qualitative variables were recorded. Qualitative variables like gender and co morbidities were recorded as frequencies and percentages. Meanwhile quantitative variables like age, baseline and Post Remdesivir administration Serum Creatinine, ALT and AST were recorded as Means and S.D and Median value. Kolmogorov-Smirnov test for normality of data was used to assess normality, P value was less than 0.05 which met the assumption was not met and the non-parametric (Wilcoxon Signed Ranks) tests were used to compare mean difference between pre and post remdesivir values.

Results

A total of 56 patients with acute or chronic kidney disease were the participants of our study. Among which the mean age was 50.46 ± 9.34 years and lowest and highest values were 33 to 69 years respectively. Diabetes and Hypertension were the most common co-morbidities,

comprising about 34.1 and 29.1% of the cases respectively. (Table I)

Forty-seven patients (83.9%) received Remdesivir for 4 days and the remaining 9(16.1%) had to extend the use for Remdesivir for more than 4 days up to 10 days. (Table I)

Serum Creatinine, AST and ALT all increased from baseline values after the administration of Remdesivir, with their respective P Value. (Table II)

Table I: Baseline Demographics of the Participants.

Parameters		Baseline Values
Age (Years)		50.46 ± 9.34
Gender	Male	41(73.2%)
	Female	15(26.8%)
Days of Hospitalization median (IQR)		9(6-12)
Co-Morbidities	Diabetes	34.1%
	Hypertension	29.1%
	Heart Failure	Nil
	Cirrhosis	7.4%

Table II: Comparisons of Laboratory Investigations before and After Remdesivir Use.

	Before Drug Administration	After Drug administration	P Value
Serum Creatinine	125.14 ± 8.61	126.44 ± 5.72	0.907
Serum ALT	34.55 ± 2.69	33.26 ± 1.85	0.001
Serum AST	54.69 ± 4.04	55.42 ± 3.09	0.34

Discussion

Management of COVID-19 has not yet fully established but antiviral drugs like Remdesivir have shown promising results. However, this pandemic has known to be prevalent among patients with co morbid, and not all drugs are safe in such conditions. [3,7]

Many studies on non-human subjects have shown Remdesivir to cause adverse effects on the renal functions.[10] Thus in patients with Renal Diseases this drug can do more harm than good. Not many clinical trials have been conducted on this topic addressing the effect of such antiviral drugs on renal system and in the studies conducted however, the adverse effects of the drugs on kidney was rarely noticed because the dose accumulated in a 5-10 day course is very low. [7-9]

Our research aimed to evaluate the safety of antiviral drug-Remdesivir use in patients with acute and chronic renal disease. The mean age of our participants were 50.46 ± 9.34 with a male predilection, this is in accordance with a previous study in which there was a prevalence of male patients with a mean age of 50.1 ± 12.2 years.[11] It is possible that the male predominance can be attributed to the fact that higher testosterone levels in men may lead to kidney dysfunction[12]. In Addition, estrogen, which is greater in women until menopause, may not protect the kidneys of men.[13] In general, men are more likely to maintain unhealthy lifestyles, which can contribute to renal failure.[14] Although in contrast another study showed female predominance which was related to the fact that dialysis dispensaries accommodate more to women due to their insurance provision in that country this research was conducted.[9]

Our study showed that mean laboratory test showed an increasing pattern before and after the administration of our antiviral regimen. Creatinine levels were deranged for the patients who participated in our study before the administration of Remdesivir and it showed similar readings after administration of Remdesivir in our study which is in contrast with a study conducted by Wang S et al which stated that Creatinine reduced from baseline (20.9%)to last day of remdesivir treatment(20.5%) with a P value < .0001. [15]

ALT and AST also showed no effects after drug administration. Our study showed comparable results to another study conducted by Thakare S et al noted that there was no significant elevation of ALT levels due to remdesivir therapy; neither did any patient required discontinuation of the antiviral therapy.[16] However in contrast. An earlier study found that although aminotransferase (AST) was elevated at T1 (+1.5%), it was reduced in T2 (-15.78%). There was a 25 percent increase in ALT (alanine transaminase) at both T1 and T2 (P =.004 and P.137, respectively).

Limitations: There were no definitive endpoints in our trial, thus there was no comparison with other treatment modalities or long-term effects of Remdesivir. Additionally, our study only included a small sample of patients who were treated at a single facility. These were the limitations of our research. Because of this, the conclusions that can be drawn from this study are somewhat restricted. As a result, we advocate for more advanced research to be conducted in this area so that we can overcome all these constraints and foster therapeutic innovations that have a greater impact in clinical settings.

Conclusion

This study concluded that Remdesivir had a no statistically significant effect on Serum Creatinine. AST and ALT. It

also showed that these values remained increased from baseline before and after the administration of Remdesivir when used in Patients undergoing COVID treatment with Acute or chronic Renal Diseases.

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