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Original Article

Treatment Outcomes of Remdesivir in COVID-19 Patients

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ABSTRACT

Objective: To evaluate effectiveness of Remdesivir in COVID-19 patients in terms of length of hospital stay, duration of oxygen dependency, and mortality.

Study Design: Quasi-experimental study.

Place and Duration of Study: Department of Medicine, Combined Military Hospital, Bahawalpur Pakistan, from Nov 2021 to Apr 2022.

Methodology: We included 170 patients diagnosed with COVID-19 and recorded their clinical characteristics in addition to outcomes related towards oxygen dependence, death, and hospital stay duration on a self-designed data collection tool which was administered by the researchers. The data was analyzed, and statistical correlations were determined.

Results: Our total sample size of 170 patients, comprised of 91(53.5%) males and 79(46.5%) females with an average age of 53.95±14.09 years. We noted mild disease to be present in 17.6 % of patients, moderate in 65.9 %, and severe in 16.5 % while 65 (38.2%) patients were oxygen-dependent at the time of admission. Fever was the most frequent complaint experienced by 84.7% of patients. Remdesivir was administered to 90(52.9%) patients, among which 65 recovered early with a hospital stay of less than a week while 20(23.3%) patients had prolonged stay due to oxygen dependency, other complications (10, 11.1%) or comorbidities (11, 12.2 %) respectively (p-value=0.000) while the rate of mortality was also significantly reduced in patients who received Remdesivir (4.44 %) compared to those who did not (17.5 %) (p-value<0.001).

Conclusion: Remdesivir significantly decreased the duration of hospital stay, oxygen dependency, and rate of mortality without causing any adverse effects.

Keywords: COVID-19, Remdesivir, SARS-CoV-2, Safety, Treatment outcome.

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INTRODUCTION

In December 2019, Wuhan reported a case of atypical pneumonia, which eventually spread all over the world and became the COVID-19 pandemics.[1] The World Health Organization (WHO) classified it as an outbreak in January, 2020, and later, a pandemic, by which time COVID-19 had spread across 210 countries with relatively higher mortalities reported from Algeria (15%) and Belgium (13.95%), whereas mortalities in Qatar (0.17%) and Singapore (0.2%) were low.[2] Pakistan reported its first case of SARS-COV-2, a coronavirus with an enveloped single-stranded RNA virus with spike glycoproteins, in Karachi, on 26 February 2020.[3] Transmission occurred via respiratory droplets with clinical manifestations ranging from asymptomatic presentations to severe complications, such as, multi-organ failure.[4] To mitigate COVID-19 spread, social distancing and personal protective equipment were advised with symptomatic treatment encompassing inflammation control, oxygen therapy, and fluid management while potential therapies were also studied, including plasma antibodies, Remdesivir, Chloroquine, and corticosteroids.[5] Remdesivir, a broad-spectrum intravenous antiviral consisting of an adenosine analogue nucleotide prodrug with antiviral activity, stops the early termination of RNA synthesis by interacting with the viral RNA-dependent RNA polymerase to halt viral replication,[6] due to which the Food and Drug Administration (FDA) granted emergency use approval on May 1, 2020.[7] Anticoagulants are advised for hospitalized patients while antibiotics should be reserved for those with confirmed secondary bacterial infections, as they offer no benefit in disease management.[8] As of February 2021, a meta-analysis of ten clinical trials found that Remdesivir administration was linked to a notable increase in rescue and a decrease in the requirement for mechanical breathing,[9] however, the WHO SOLIDARITY trial revealed that Remdesivir had no statistically substantial impact on death rates.[10] Thus,

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we planned to assess the effectiveness of Remdesivir in terms of mortality, oxygen requirement, and hospital admission duration in managing moderate to severe COVID-19 cases.

METHODOLOGY

After taking approval from Institutional Review Board at Combined Military Hospital (CMH), Bahawalpur, Pakistan, via letter EC-10-2021, our study was begun and lasted for a duration of six months from November 2021 to April 2022. A sample size of n=97 was estimated by taking confidence interval of 95% and 6.7% mortality in patients treated with Remdesivir,[11] however, to increase the strength of our study, we enrolled a total of 170 patients through non-probability consecutive sampling technique.

Inclusion Criteria: Patients of either gender, admitted to a hospital with symptoms, High-Resolution Computed Tomography (HRCT) findings, positive Polymerase Chain Reaction (PCR) test for COVID-19 through nasopharyngeal sampling and requiring immediate hospitalization were included.

Exclusion Criteria: Patients with alanine transaminase (ALT) or aspartate transaminase (AST) > 5 times the upper limit of normal, assessed glomerular filtration rate (eGFR) < 30 ml/min (including patients receiving hemodialysis or hemofiltration), chronic liver disease, malignancy or allergy to Remdesivir were excluded.

Demographic information, the severity of the illness, and comorbidities, including history of hypertension, diabetes mellitus, asthma, chronic obstructive pulmonary disease (COPD), tuberculosis, hepatitis, chronic liver disease, and chronic kidney disease, were noted. Laboratory tests for serum ferritin, D-dimer, lactate dehydrogenase, C-reactive protein, liver function tests, renal function tests, and complete blood count (CBC) were done. Severity of illness was categorized into mild, moderate and severe depending upon the HRCT severity scoring and oxygen saturation at room air where mild disease meant patient had HRCT chest with a severity score of less than 10/25 and oxygen saturation ≥94% on room air, moderate disease indicated Oxygen saturation <94% but >90% and HRCT chest with infiltrates and severity score of 11-18/25 while severe disease meant SpO2 ≤ 90% on room air and HRCT chest with infiltrates and severity score of greater than 18/25.[8] All patients received paracetamol, steroids, oxygen inhalation, anti-coagulation and mechanical ventilation as per protocol while patients with symptomatic mild to moderate disease, with positive RT PCR and normal Liver Function Tests (LFTs), were given Remdesivir as 200 mg single dose on Day 1 then 100 mg daily for next 4 days. The drug's dosage, duration, and results were noted, as well as the span of hospital stays, complications, and patient mortality. We conducted statistical analysis using Statistical Package for the Social Sciences (SPSS) where the mean and standard deviation were used to display quantitative data, whereas frequency and percentage were used to present qualitative data. To compare the quantitative results between the treatment and control groups, the Chi-square test was performed where a *p*-value of ≤0.05 was taken as statistically significant.

RESULTS

In final analysis, there were 91(53.5%) males and 79(46.5%) females with mean age being 53.95±14.09 years, ranging from 22 to 85 years. At presentation, 30(17.6%) patients had mild disease, 112(65.9%) had moderate disease and 28(16.5%) had severe disease while 65(38.2%) patients were reliant on oxygen at the time of admission. Fever was the most frequent presenting complaint (84.7%) patients followed by cough (61.7%), shortness of breath (38.9%), gastrointestinal symptoms (10%) and neurological symptoms (1.7%) as shown in Table-I.

Table-I: Clinical Characteristics of COVID-19 patients, (n=170)

Gender	n (%)
Male	91(53.5%)
Female	79(46.5 %)
Clinical Presentation	n(%)
Fever	144(84.7 %)
Shortness of breath	66(38.9%)
Cough	105(61.7%)
Gastrointestinal symptoms	17(10.0%)
CNS symptoms	3(1.7%)
Radiological Classification	n(%)
Mild <10%	30(17.6%)
Moderate10-18%	112(65.9%)
Severe>18%	28(16.5%)
Oxygen Dependent at Admission	n(%)
Yes	65(38.2%)
No	105(61.8%)
Duration of Hospitalization	n(%)
Less than 1 week	99(58.2%)
More than 1 week	71(41.8%)

No co-morbidities were reported by 72(42.3%) patients, 39(22.9%) had diabetes mellitus, 25(14.7%) had hypertension, 5(2.94%) had cerebrovascular disease, 6(3.5%) patients had chronic kidney disease, 2(1.17%) patients had ischemic heart disease, 7(4.1%)

people had COPD, and the remaining 13(7.64%) patients had more than one co-morbidity. Among 170 patients, Remdesivir was given to 90(52.9%) patients, among these 90 patients, 65 patients recovered early and stayed at hospital for less than a week while 20(23.3%) patients had prolonged stay due to oxygen dependency and other complications (10, 11.1%) or comorbidities (11, 12.2%) respectively (*p*-value <0.001) as shown in Figure-2. The rate of mortality was significantly less in patients who received Remdesivir (4.44%) compared to those who did not (17.5%) (*p*-value<0.001) as shown in Table-II.

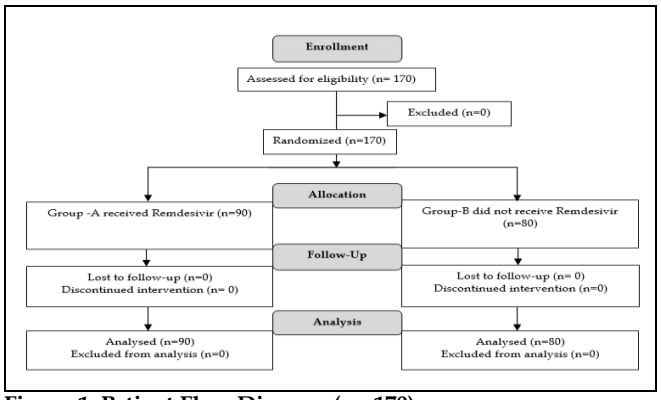

Figure-1: Patient Flow Diagram (n= 170)

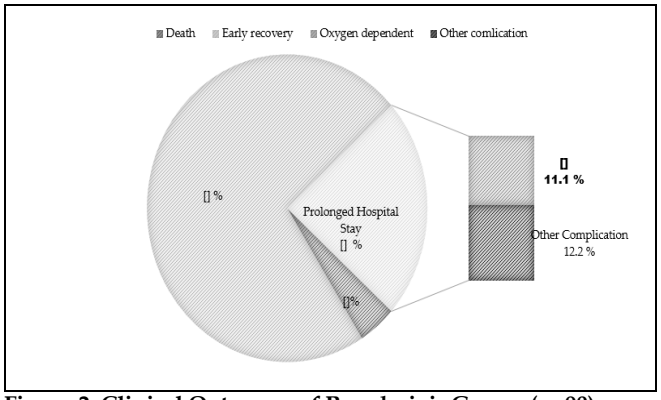

Figure-2: Clinical Outcomes of Remdesivir Group, (n=90)

cases, resulting in more than 30,000 fatalities (4) with significant detrimental influence on the country's healthcare system. Since the emergence of this disease, treatment protocols have been changing, with an absence of global consensus. In our study, 91(53.5%) patients were males similar to previous research, where one study reported 66% male distribution while another reported 60%,[12,13] however, more females (83.7%) presented with moderate to severe disease compared to males (81.9 %) in our study, although this difference was statistically not significant. We noted 11 female deaths compared to 3 male ones, in contrast to other studies, which reported that males had more severe disease when they were first diagnosed, and they died twice as often as females did with bilateral lung involvement present along with moderate to severe disease, consistent with other studies.[14-16] The most prevalent comorbid ailment in our cohort was diabetes mellitus, similar to another study which documented diabetes (29.69%) and hypertension (20.33%) as the most frequent comorbidities.[17] Length of hospital stay in our study was significantly less among patients who were administered Remdesivir, where 65 recovered early and stayed at hospital for less than a week (*p*-value=0.000), comparable to the findings of another study, where 43(27%) patients were cleared in less than seven days, 109(68.5%) patients in 7–14 days, and 7 patients in 15–21 days (13), thus, span of hospital stay in treatment group was considerably shorter than the control group. In our study, twenty patients (23.3%) had prolonged stay due to oxygen dependency while mortality was significantly less in patients who received Remdesivir (4.44%) compared to those who did not (17.5 %) (*p*-value=0.000) which was similar to the results from another study where remdesivir treatment was linked to a substantial improvement in low flow oxygen support from days one to fourteen and the 28-day recovery,[9] but a different meta-analysis of eleven

Table-II: Comparison of Outcomes Between Both Groups (n=170)

Remdesivir	Outcome					*p*-value
	Prolong Hospital due to Complication/Comorbidities	Prolong O2 Therapy	Early Recovery	Death	Total	
Given	11(25.0%)	10(38.5%)	65(75.6%)	4(28.6%)	90(52.9%)	< 0.001
Not Given	33(75.0%)	16(61.5%)	21(24.4%)	10(71.4%)	80(47.1%)	
Total	44	26	86	14	170	

DISCUSSION

Since the start of the coronavirus disease-2019 (COVID-19) pandemic in late December 2019, Pakistan has recorded over 1.5 million laboratory-confirmed trials,[18] found clinical improvement and varying death rates among individuals who received remdesivir while a randomized, double-blind, placebo-controlled, multicenter study including ten hospitals in Hubei, China, found no correlation between Remdesivir use

and difference in the time to clinical improvement as patients with a sign duration of 10 days or less who received remdesivir had a statistically quicker time to clinical improvement than those who received placebo, albeit this difference was not statistically significant with adverse events recorded in 102(66%) of 155 patients taking remdesivir versus 50(64%) of 78 patients taking a placebo,[19] unlike our study where no serious adverse effect of remdesivir were noted.

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LIMITATIONS OF STUDY

The most important limitation encountered was the constrained sample size as this study was carried out in a single health care facility. A larger sample size involving multiple centers would have given richer data on the effect of Remdesivir on COVID-19 patients.

CONCLUSION

The use of Remdesivir significantly decreased duration of hospital stay, oxygen dependency and rate of mortality with no severe adverse effects noted.

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Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

HI & SWA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

AR & MFUR: Conception, data analysis, drafting the manuscript, approval of the final version to be published.

MF & UI & HAS: Data acquisition, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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