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Efficacy of Remdesivir in Obese Versus Non Obese Individuals with Positive COVID-19

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ABSTRACT

OBJECTIVE: The aims and objectives of the study is to evaluate and analyze the effectiveness of anti viral drug, Remdesivir for the treatment of covid-19 patients in two population groups i.eNon-Obese and obese individuals with positive covid-19.

STUDY DESIGN: Randomized, placebo-controlled trial study.

SETTING: THQ Hospital Sambrial and THQ Hospital Wazirabad.

METHODOLOGY: The study is initiated in the outpatient department where the subjects complaining about the respiratory symptoms were further assessed for covid-19 laboratory examination. The patients with positive labs were included in the study. A clinical trial is conducted on three groups, a placebo category comprising of covid-19 patient not treated with remdesivir, obese category and non-obese category with positive covid-19 treated with remdesivir.

RESULTS: A total of 60 patients underwent randomization, with 40 assigned to remdesivir (20 in non obese category while 20 in obese group) and 20 participants to placebo. According to the clinical investigations, individuals who was administered remdesivir in non obese group, improved earlier with (95% confidence interval),while obese individuals recovered lately whereas those who received placebo showed no clinical significance statistically with (95 % confidence interval). Patients who got remdesivir in non obese population were shown to have a higher chance of clinical improvement than those who were in obese and placebo categories.

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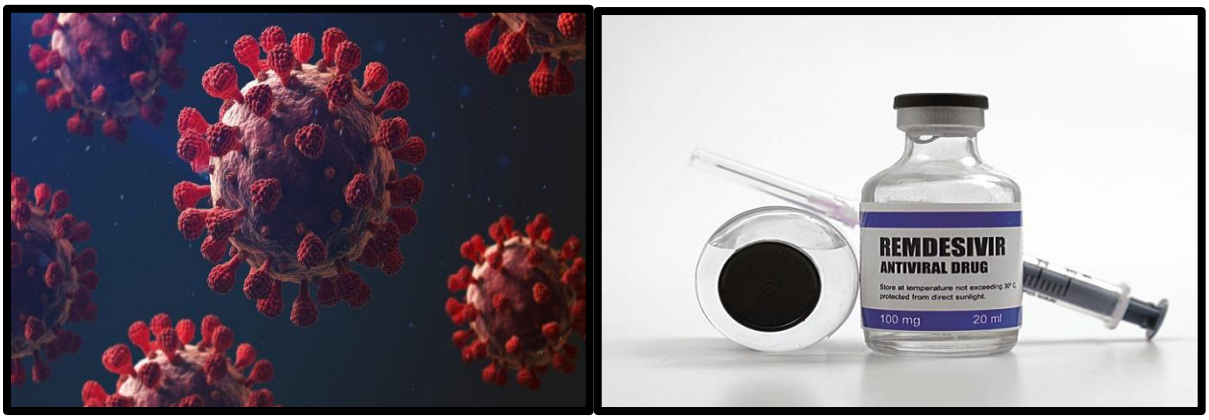
CONCLUSION: In this study, we examine the current evidence for remdesivir's effectiveness against COVID-19 and discuss the comparison between the two population groups and we evaluated the effectiveness of remdesivir in non obese in contrast with obese category. Non obese group showed better improvement than obese group, while control group shows no effect.To confirm these findings, more large-scale, randomised placebo-controlled clinical trials are needed.

INTRODUCTION:

Covid-19 was initially identified in December 2019 as the virus responsible for respiratory disease [1]. Numerous antiviral medications have been tested for Covid-19 treatment, but none have been found to be effective.Dexamethasone has been shown to reduce morbidity (25.7 percent in the usual care group vs. 22.9 percent in the dexamethasone group; P0.001), with the greatest effect observed in patients undergoing invasive mechanical ventilation.



Remdesivir is a nucleotide prodrug that inhibits viral RNA-dependent RNA polymerases, a family of structurally conserved enzymes required for virus replication. It inhibited SARS-CoV-2 replication in human airway epithelial cells in vitro. It is currently being studied in a clinical setting as an interventional treatment with FDA Authorization. Although the precise mechanism of action of this medication is unknown, it appears to work in a variety of ways. Even when nsp12 polymerase is intact, exoribonuclease proofreading can interfere with it. It can also synthesise nucleoside triphosphate NTP, an alternative substrate for the RNA-chain terminator that prevents active triphosphates from entering coronavirus RNA. There appears to be a significant genetic barrier to developing resistance to Remdesivir in coronavirus, indicating that it remains effective in antiviral therapy against these viruses. Remdesivir has been shown to be effective against a variety of coronaviruses, including Alphacoronavirus NL63 and other coronaviruses associated with SARS/MERS[2, 3].

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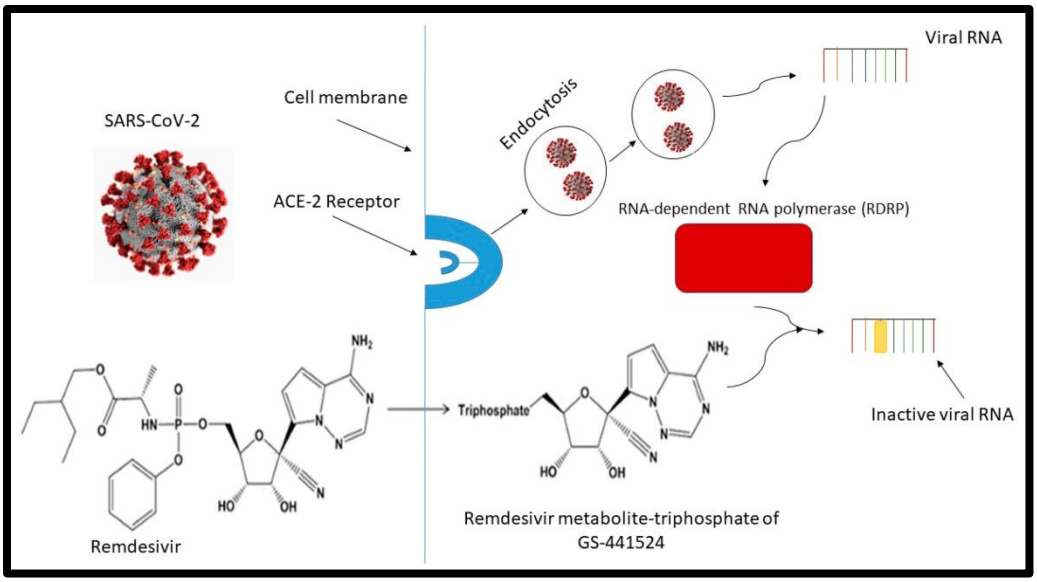

Many sick patients are asymptomatic or have only slight symptoms, and they recover on their own. 3.4 Seniors, as well as those who have hypertension, diabetes, obesity, or heart disease, are more likely to suffer life-threatening illnesses. While the majority of infections are self-limiting, about 15% of infected adults develop severe pneumonia, requiring oxygen therapy, and another 5% develop critical illness, such as hypoxemic respiratory failure, acute respiratory distress syndrome, and multiorgan failure, requiring several weeks of ventilatory support. . At least half of the patients who needed invasive artificial breathing as a result of coronavirus disease (COVID-19) died in hospitals in 2019. 4, 5 in a number of countries, putting a lot of pressure on health-care systems, especially intensive-care units [6,7,9].

LITERATURE SEARCH:[1, 2, 3, 4, 5]

AUTHOR	PATIENT GROUP	OUTCOME	RESULTS
S Antinori et al, Italy1 2020	35 patients over the age of eighteen were referred to the critical care unit with a confirmed COVID-19 infection requiring mechanical ventilation, a SpO2 of 94 percent on room air, or a national early warning score of 418. Antiviral medications must be discontinued, although other treatments, such as hydroxychloroquine, may be continued. Side effects led	Hospitalization status as primary outcome Side effects as secondary outcome	82.3 percent of patients in the infectious illness ward had been discharged by the end of the 28th day, while 5.9 percent had died. 33.3 percent of those in icu were discharged, 44.4 percent died, and 16.7% were still on mechanical ventilation. The most common side effect is hepatotoxicity, which accounts for 42.8 percent of all cases.

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	37% of those who began the intervention to abandon it.		
J Grein et al., 2020	53 people with confirmed COVID-19 infection and a SpO2 of less than 94 percent or who needed oxygen support received at least one dose of remdesivir.	Improvement in oxygen support, hospital discharge and adverse events	The cumulative incidence of improvement at day 28 was 84 percent (95% confidence interval 70 to 99). In 0.56 out of every 100 hospitalizations, someone died (95 percent CI 0.14 to 0.97) Severe adverse events occurred in 23% of the participants.
J Goldman et al., USA 2020	Patients with COVID-19 infection who have a SpO2 below 94 percent or who require supplementary oxygen therapy and have radiographic evidence of pneumonia. 200 individuals received Remdesivir for 5 days and 197 individuals received it for 10 days. Patients who required ventilatory support at the start of the study were not allowed to participate.	Clinical status at day 14 based on an ordinal scale Adverse events as secondary outcomes	Both patient groups showed similar outcomes at day 14 (p=0.14) after adjusting for clinical state. 70% of the subjects in the five-day group reported negative effects, compared to 74% in the 10-day group.
J Beigel et al., 2020	COVID-19 infection in 1063 patients with proven lower respiratory tract involvement 541 people were randomly assigned to remdesivir and 522 to placebo. Other supportive treatments were permitted for the patients.	Time to recovery Serious adverse events	The intervention group had a shorter recovery period (median days 11 vs 15 in the placebo group) 1.32. (95 percent confidence interval: 1.12 to 1.55, p0.001) The intervention group had a mortality rate of 7.1 percent, while the control group had a rate of 11.9 percent (HR 0.70). (95 percent confidence interval: 0.47 to 1.04) 21.1 percent of the intervention group and 27 percent of the placebo group experienced serious side events.
Wang et al., China	237 individuals with COVID-19 pneumonia confirmed by	Clinical improvement	The intervention failed to improve the situation (median 21 days vs.

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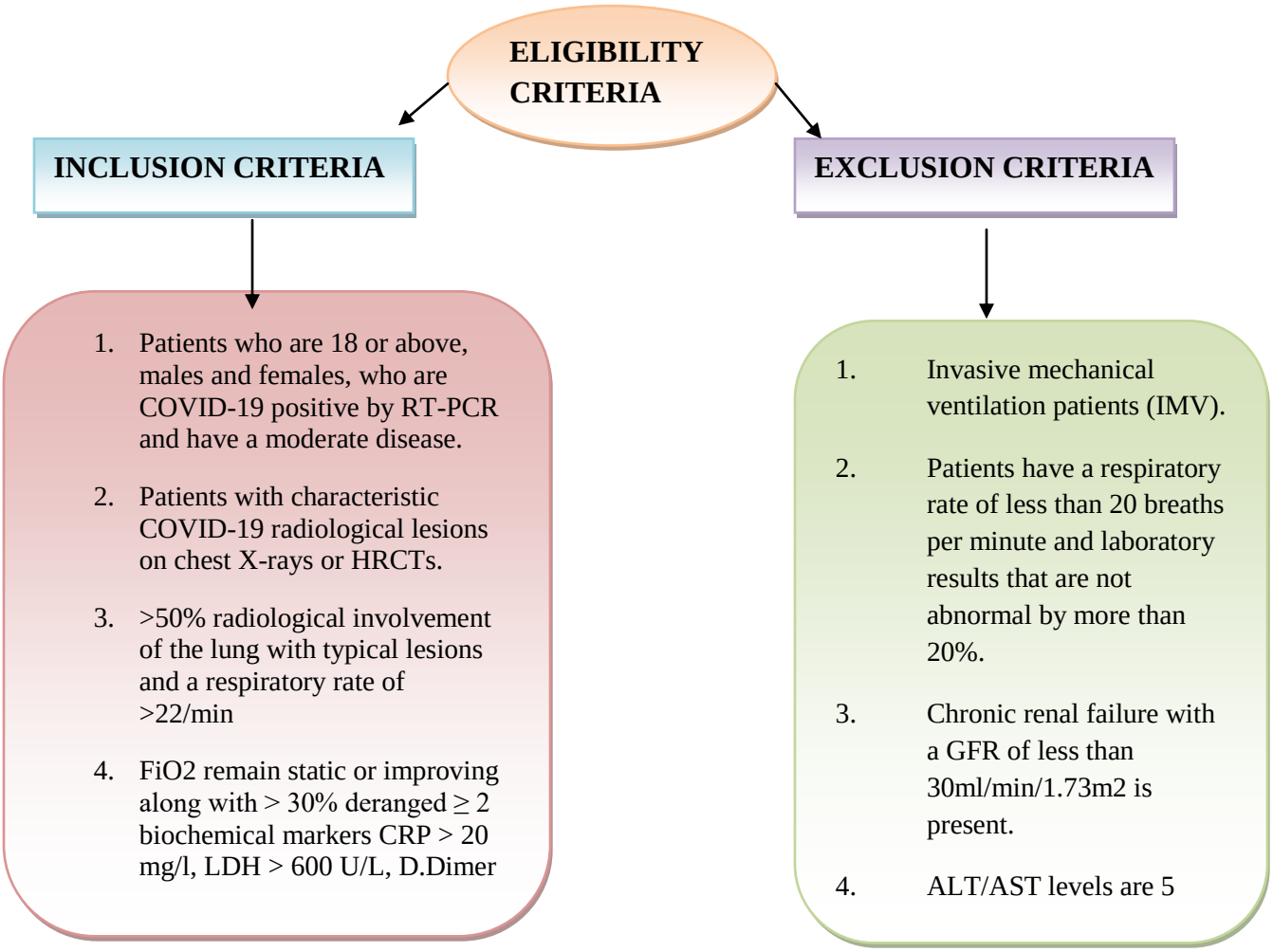
2020	imaging with a SpO2 of 94 percent or PaO2/FiO2 of 300 mm Hg158 were randomly assigned to the intervention group and 79 to the placebo group (2:1 randomization) Patients were allowed to take antiretrovirals, corticosteroids, and interferons at the same time.	Adverse events	23 days in the placebo group) 1.23 HR (95 percent CI 0.87 to 1.75) At the end of 28 days, 14% had compared. A difference of 1.1 percent results in a death rate of 13%. (95 percent CI 8.1 to 10.3) In the intervention group, 66 percent of patients experienced adverse events, compared to 64 percent in the control group.

MATERIAL AND METHODS:

Covid-19 infection was confirmed by polymerase chain reaction in hospitalized patients with mild COVID-19 pneumonia within four days of randomization (defined as any radiographic evidence of lung infiltrates and oxygen saturation greater than 94 percent on room air).



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Remdesivir was randomly assigned to obese and non-obese patients, while supportive treatment was given to placebo group. Randomization was stratified by study site and disease severity at the time of recruitment. Each participant's efficacy, safety, and laboratory performance will be assessed. Safety laboratory tests, blood samples (serum and plasma), and oropharyngeal (OP) swabs will be collected on days 1 (before to infusion), 3, 5, 8, and 11 for research purposes (while hospitalized). OP swabs and blood (only serum) will be taken on Days 15 and 29, as well as safety laboratory tests12, 13, and 14.

Remdesivir 200 mg intravenously was given to obese and non-obese subjects on day 0, followed by four 100 mg doses on days 1-4, or until death or hospital discharge. At the same time supportive treatment to placebo was given. According to the hospital's standard of care, all patients received supportive care. If a hospital has a stated policy or guideline in place, patients may have access to alternative treatment for Covid-19. From day one through day 29 of their hospitalization, patients were assessed daily. The patients' clinical status was evaluated using an international scale[16, 17].

STATISTICAL ANALYSIS:

A stratified log-rank test of time to recovery with remdesivir versus placebo, with disease severity stratification, was used as the primary analysis. For time-to-recovery and time-to-improvement analyses, data for patients who did not recover and data for patients who died were censored at day 29[18, 19].

Predefined subgroups were created in these analyses based on gender, age, the existence of co-existing illnesses, and the illness severity baseline. The primary outcome was originally a comparison of clinical state on an international scale at day 15. The primary outcome was changed to a comparison of time to recovery by day 29 in response to new findings from outside the experiment. This suggests that Covid-19's path may be longer than previously predicted[20].

RESULTS:

A total of 60 patients were included in the trial. 20 participants were categorized under non obese group with the remdesivir treatment and 20 individuals were in obese category, also the placebo group with 20 subjects completed the trial through day 29, recovered, or died. Patients in 3 groups were balanced in disease characteristics. Non- obese group depicts diabetes 29% and hypertension 42% while obese category shows 32% diabetic individuals and 50% individuals were hypertensive. On the other hand, placebo group reported 30% diabetes and 48% hypertension among the patients[6, 8, and 10].

Clinical Characteristics of the Patients at Baseline			
Characteristics	Non-Obese Group	Obese Group	Placebo

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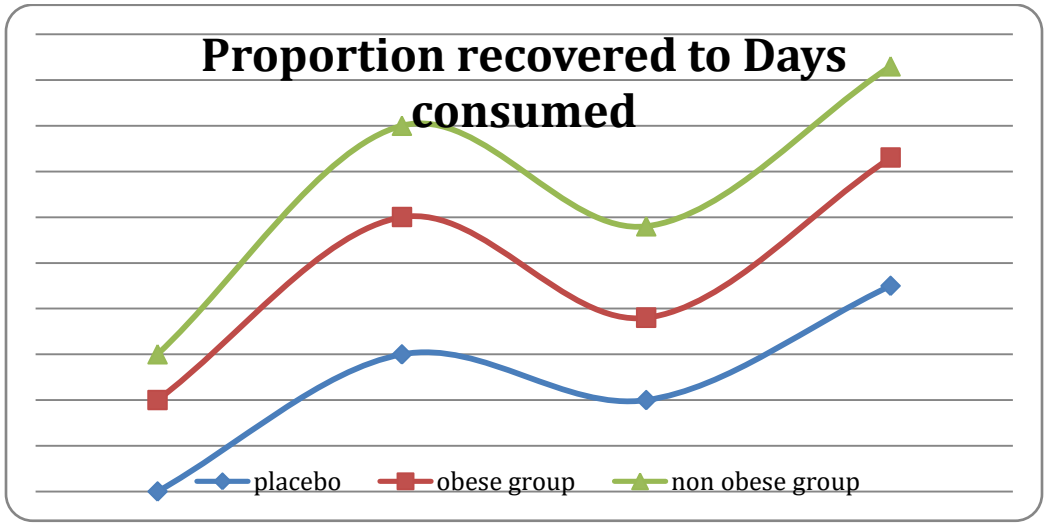
	(Remdesivir)	(Remdesivir)	
Age	18-58	20-62	18-60
Gender (Males)	64%	65%	63%
Gender (Females)	36%	35%	37%
Diabetes	29%	32%	30%
Hypertension	42%	50%	48%
Hospitalized, not requiring oxygen	13%	12%	10%
Hospitalized, requires oxygen	39%	41%	47%
Median time from symptoms onset to randomization(days)	6-12	6-12	7-13

Patients in the remdesivir treatment in non obese individuals improved faster than those placed in the obese category and placebo group with 95% confidence interval, $p < 0.01$ as depicted in the graph below:



The laboratory examinations were performed at the time when covid-19 came positive and after the treatment and recovery of the patients, labs were repeated for analysis and future follow up assessment.

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Laboratory Examinations	Reference Range	Non-Obese before/after	Obese before/after	Placebo before/after
BMI(median)	18.5-24.9	22.2	27.8	24.4
Ferritin level(median)	13-150(mg/ml)	240/180	920/710	310/450
D-Dimer Value(median)	<0.5 (g/l)	0.7/0.6	0.9/0.85	0.8/0.7
CRP level(median)	<5	115.7/90	118.2/102	112.5/96
LDH level(median)	Upto 250 (u/l)	740/450	920/680	730/542

DISCUSSION:

Although several licenced medications have exhibited antiviral activity against SARS in vitro, no antiviral treatment has been proved to be successful in treating individuals infected with this developing virus. Remdesivir, an adenosine prodrug that inhibits all human and animal coronaviruses in vitro, has shown promise in a human trial[20].

At the time of writing, this picture is fast altering as a result of ongoing clinical trials. Although only a few short trials have been published1–3, two larger trials warrant greater attention and inquiry. Despite the fact that Wang et al. were unable to enrol all eligible patients as anticipated at the start of the research due to the outbreak's ending, they were unable to demonstrate any clinical advantage related with remdesivir that was statistically significant. At the time of review and publishing, only the preliminary report for the Beigel et alstudy, the largest to date. Remdesivir was beneficial in patients requiring supplemental oxygen, but was unlikely to be sufficient on its own because of the substantial risk of death associated with its use[19, 21].

CONCLUSION:

There was statistically significant difference in clinical state between the obese and non-obese groups assigned to a course of remdesivir and the placebo group on the 15th day after the treatment began. Patients in either the non-obese or obese groups who received a 5-day course of remdesivir treatment had a statistically significant difference in clinical status and the difference was clinically consequential[20].

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