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COMPARISON AND DRUG UTILISATION STUDY OF CORTICOSTEROID (METHYLPREDNISOLONE) WITH REMDESIVIR V/S REMDESIVIR IN COVID-19 PATIENTS

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Abstract:

Due to the 2019 pandemic caused because to the coronavirus disease (Covid-19) has led to the investigation of different drugs for their efficacy and therapeutic benefits for people suffering from the Covid-19 illness because of its high prevalence, easy spreading of the virus mortality rates due to severe respiratory viral infection. Many pre-existing medications have been known to provide a rapid and effective response due to their known effects, characteristics, and the dose to be used.

Objective: *To show the advantageous effect of using combination therapy of Corticosteroid (Methylprednisolone) with Remdesivir as opposed to using monotherapy of Remdesivir in the treatment of Covid-19 patients.*

Methods: *The retrospective observational study was carried out for six months in the Medical Records Department. A total of 150 patients affected with Covid-19 were admitted to the Hospital. The patients were organized into two different groups, with 100 patients in Group-1 (Corticosteroid, i.e. Methylprednisolone with Remdesivir) and 50 patients in Group-2 (Remdesivir). The patients were administered with desired doses of drugs, and the following data was collected in the patient data collection form. The patient's demographic information, hemodynamic parameters, laboratory values, symptoms, and conditions were collected.*

Results: *Patients treated with a combination of Corticosteroid (Methylprednisolone) with Remdesivir showed a high frequency of efficacy and more significant therapeutic outcome when compared to Remdesivir as monotherapy. The results can potentially assess the severity of COVID-19 from the hemodynamic parameters and biomarkers.*

From this, we can conclude that when the patient is given the combination therapy of the Corticosteroid (Methylprednisolone) with Remdesivir, there is a significant improvement in the patient's health. They are more hemodynamically stable, and their cough and SOB are also treated as opposed to the Group-2 patients who have been administered Remdesivir as a monotherapy.

Conclusion: *Our study found a significant and influential therapeutic outcome from using Corticosteroid (Methylprednisolone) when given in with the Antiviral drug Remdesivir as opposed to the monotherapy of Remdesivir.*

Keywords: *Covid-19, Corticosteroid, Methylprednisolone, Remdesivir, Pandemic, and Coronavirus.*

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INTRODUCTION:

In late 2019, a novel coronavirus (CV) called SARSCov2 emerged as a highly contagious virus that can cross the species barrier and spread efficiently from human to human. CVs are a family of viruses that can cause respiratory or gastrointestinal diseases, ranging from the common cold to more severe illnesses like MERS-CoV and SARS-CoV. The term "corona" refers to the crown-like appearance of the virus, characterized by protein spikes surrounding its genetic material. CVs are zoonotic, meaning they can be transmitted between animals and humans, and experts believe this particular strain likely originated in bats or pangolins. The first human transmission occurred in Wuhan, China, and the virus has since spread predominantly through person-to-person contact, causing diseases in both animals and humans. SARS-CoV is a strain of the coronavirus family, and there was a widespread outbreak of SARS during 2002-2003. The new strain of coronavirus, SARS-CoV-2, is the cause of the disease known as COVID-19. Coronaviruses are tiny enveloped RNA viruses that infect animals and humans. SARS-CoV-2 has 19 encoded proteins, including four main structural proteins: spike (S), membrane (M), envelope (E), and nucleocapsid (N). The virus enters cells through endocytosis, using the spike protein to bind to known receptors such as ACE-2. The binding process involves the ectodomain, consisting of the S1 and S2 subunits, leading to host cell binding and fusion. Cleavage of the spike protein is crucial for fusion, and various proteases like TMPRSS-2 and cathepsins play a role in this process. Once inside the host cell, the virus replicates its genome using the replicase complex. SARS-CoV-2 can spread directly from cell to cell, avoiding detection by the immune system. The virus employs various mechanisms to evade immune responses, including suppressing host gene expression, inhibiting cytokine pathways, and downregulating antigen unveiling by cells.

Etiology: Since late December 2019, the outbreak of Covid-19, caused by the SARSCov2 virus, has had devastating effects globally. It has resulted in millions of confirmed cases and over 5.3 million deaths worldwide. The virus quickly spread, leading the World Health Organization to declare it a global pandemic in March 2020. Covid-19 stands out from previous respiratory illnesses like MERS and SARS due to its high transmission rate, severe post-recovery effects, frequent mutations, and uncontrolled viral effects.

Symptoms: The clinical manifestations of Covid-19 extend beyond respiratory symptoms, affecting various organs such as the brain, hematological system, liver, kidneys, and endocrine system. Initially, there was a lack of emergency treatments and a shortage of life-saving drugs due to limited understanding of the virus. However, scientists and industries worked together to repurpose existing drugs and develop vaccines quickly. Common symptoms include fever, cough, dyspnea, loss of smell, myalgia's, fatigue, headache, gastrointestinal and respiratory problems. Covid-19 can also lead to complications in the kidneys and the nervous system, including stroke, seizures, and meningitis. The disease's impact on clotting processes has been observed, with abnormal clotting and coagulopathy contributing to severe cases. Overall, symptoms may vary among individuals, and they typically appear within two to fourteen days after infection.

Risk factors: The risk factors for contracting Covid-19 include the level of spread in the patient's surroundings, which is generally low for most of the population. However, older adults are at a higher risk of illness, as are individuals with certain health conditions. These conditions include heart conditions, kidney diseases, chronic obstructive pulmonary disease (COPD), obesity, and type 2 diabetes. These factors can increase the susceptibility and severity of the illness in individuals exposed to the virus.

Diagnosis: To diagnose Covid-19, a diagnostic testing kit has been developed and is available in clinical testing labs. The most reliable test is the Reverse Transcription Polymerase Chain Reaction (RT-PCR) test. The availability of testing may vary by country. The Centers for Disease Control and Prevention (CDC) recommends that individuals who may have had contact with a suspected Covid-19 case and develop fever and respiratory symptoms should contact a healthcare professional for guidance.The diagnostic testing procedure involves collecting upper respiratory tract specimens using a nasopharyngeal swab, and if a productive cough is present, a sputum sample may be collected. Imaging techniques such as chest X-rays and CT scans can provide valuable information, although they are not specific to Covid-19 and can be similar to other respiratory infections. Lung ultrasound has also shown promise as a diagnostic tool. However, viral testing remains the best method for diagnosing Covid-19.Additionally, myocardial injury can impact the severity and mortality of Covid-19 patients. Assessing cardiac injury biomarkers, such as cardiac troponin I and

aspartate aminotransferase levels, in combination with advanced age, can help identify patients at higher risk and guide appropriate therapeutic interventions.

Treatment: In treating Covid-19, there are two main approaches: mitigating the effects of the infection on an individual and preventing the spread of the virus within the host. These approaches involve drug repurposing and drug development.Drug repurposing involves identifying existing drugs that could be beneficial for treating Covid-19. This strategy focuses on approved or investigational medicines with relevant preclinical or safety information. It allows for a faster response than developing new drugs specifically for Covid-19. On the other hand, drug development involves identifying or developing a compound that targets the specific needs of treating Covid-19. However, this process can be time-consuming and costly, with a higher risk of failure. Evidence for treatment approaches mostly comes from observational studies, which compare groups of patients who received treatment with those who did not to assess its potential effects. Although these studies can be conducted quickly, they may be subject to confounding factors. Randomized controlled trials (RCTs) are considered the gold standard for evaluating treatment effects. Patients are prospectively and randomly assigned to receive the treatment or be in the control group. Both observational studies and RCTs play crucial roles in providing valuable information for a rapid response to the Covid-19 crisis.

A) Corticosteroids:

The World Health Organization (WHO) guidance for managing Covid-19 advises against routinely administering systemic glucocorticoids (GCs). The use of GCs for Covid-19 pneumonia has been debated due to the lack of conclusive clinical evidence and potential adverse drug reactions (ADRs). However, GCs are known for suppressing cytokine levels and pro-inflammatory gene expression, effectively mitigating the inflammatory storm. They can reduce serous exudate at the site of inflammation, alleviate tissue edema and injury, and relieve symptoms of inflammation. Pathological observations in Covid-19 patients have shown severe lung serous exudate, which correlates with decreased serum albumin levels in critical patients. Based on these findings, GCs could be beneficial in acute cases of Covid-19. Methylprednisolone (MP), a synthetic glucocorticoid, is commonly prescribed for its anti-inflammatory and immunosuppressive properties. It is administered at low doses for chronic illnesses and high doses during acute flares. MP, derived from hydrocortisone and prednisolone, exhibits a higher affinity to glucocorticoid receptors (GCRs) than mineralocorticoid receptors.Synthetic glucocorticoids, including MP, have pleiotropic effects, meaning they exhibit actions beyond their intended purpose. They are prescribed for their anti-inflammatory properties and immunomodulatory effects.

1) Pharmacodynamics

Methylprednisolone (MP) exerts its effects by binding to glucocorticoid receptors (GRs), blocking pro-inflammatory signals, and promoting anti-inflammatory signals. Although it also binds to mineralocorticoid receptors, its affinity for them is lower. When MP binds to GRs, it causes changes in gene expression.GRs are primarily located in the cytoplasm, forming complexes with various proteins. MP enters cells and binds to GRs, leading to the activation of the MP-GR complex. This complex can induce non-genomic changes in the cytoplasm or translocate to the nucleus to regulate the transcriptional activity of target genes. One of the main anti-inflammatory actions of glucocorticoids is increasing the synthesis and function of Annexin A. This protein represses phospholipase A2, inhibiting eicosanoid production and leukocyte inflammatory events. Glucocorticoids also suppress prostaglandins and leukotrienes, the two primary sources of inflammation. In some instances of high disease activity, the activation of membrane-bound GR expression occurs. Methylprednisolone administration causes a negative feedback effect by inducing apoptosis. It also inhibits calcium and sodium uptake, decreasing ATP usage and immunosuppression.The MP-GR complex blocks the promoter sites of pre-inflammatory genes promotes anti-inflammatory gene products, and inhibits the production of inflammatory cytokines. It also suppresses cyclooxygenase, responsible for prostaglandin production during tissue damage.It is used to reduce inflammation and treat conditions such as arthritis, skin disorders, blood disorders, eye conditions, kidney disorders, thyroid disorders, intestinal disorders, asthma, and severe allergies. It can be administered orally or through injection into different tissues or veins.

2) Pharmacokinetics

Corticosteroids undergo enzymatic alterations in the body, which decrease their physiological activity and increase water solubility for urinary excretion. Metabolism primarily occurs in the liver. Liver diseases can lead to increased levels of free hormones due to impaired corticosteroid metabolism.Cortisol has a plasma half-life of approximately 66 minutes

under standard conditions but can increase to 120 minutes with high steroid loads. The volume of distribution (VD) also changes accordingly. Corticosterone has a faster turnover rate than cortisol, and clearance rates are not affected by acute stress or adrenal insufficiency. Aldosterone has a relatively short plasma half-life of less than 20 minutes.When administered intravenously, the recommended corticosteroid doses are 40mg/kg and 60mg/kg. Side effects of corticosteroids can include gastrointestinal disturbances, vomiting, nausea, insomnia, headaches, dizziness, generalized weakness, impact on mental health, skin conditions such as acne and increased hair growth, and irregularities in menstrual cycles.

APPLICATIONS IN COVID-19:

The use of glucocorticoids (GCs) in the treatment of Covid-19 has been a topic of controversy. The World Health Organization (WHO) interim guidance for Covid-19 management advises against routinely administering systemic GCs. However, GCs effectively inhibit the inflammatory response by reducing cytokine levels and suppressing pro-inflammatory gene expression. By reducing serous exudate, tissue edema, and injury, GCs can alleviate inflammation-related symptoms. Autopsy findings of Covid-19 patients have shown severe lung serous exudate, likely associated with decreased serum albumin levels observed in critical cases. Based on these pathological changes observed in Covid-19 patients, glucocorticoids have shown utility in treating critical disease cases. However, using GCs in Covid-19 management remains a subject of ongoing discussion and further research.

B) Remdesivir:

Remdesivir is a nucleoside analogue used to inhibit the action of RNA polymerase in the treatment of Covid-19. It has a moderate duration of action and is administered via intravenous infusion. The common adverse reactions of Remdesivir include diarrhoea, renal impairment, rash, hypotension, acute kidney injury, multiple organ dysfunction syndromes, hypernatremia, and deep vein thrombosis. Pharmacodynamically, Remdesivir acts as a prodrug that gets metabolised to its active triphosphate form (RDV-TP). It inhibits viral RNA synthesis by interfering with the replication and translocation of the RNA polymerase, ultimately terminating viral replication. This mechanism is similar among different coronaviruses, suggesting broad antiviral activity. Remdesivir is rapidly absorbed, with peak plasma concentrations reached within a short time. The recommended dose of Remdesivir is 100mg/kg to 200mg/kg intravenously. Common side effects include shivering, nausea, sweating, vomiting, dizziness, rashes, shortness of breath, changes in heart rate, facial swelling, yellowing of the skin or eyes, dark yellow urine, and pain.The SARS-CoV-2 virus in treating Covid-19 causes the primary application of Remdesivir. It works by preventing the virus from spreading in the body and causing severe disease.

METHODOLOGY:

STUDY SITE: This study was conducted in the Medical Records Department (MRD) in a tertiary care hospital (Aster Prime Hospital), Ameerpet, Hyderabad, TS, India.

STUDY DESIGN: A retrospective observational study was held to differentiate the use and effectiveness of Corticosteroid (Methylprednisolone) given in combination with Remdesivir and Remdesivir alone as treatment in COVID-19 hospitalized patients.

STUDY DURATION: The study was conducted for six months, i.e., from August 2021 to January 2022.

SAMPLE SIZE: The study was done on 150 hospitalized patients affected by COVID-19.

STUDY PROCEDURE:

- The following data of the study was collected:
- Patient demographic information, i.e., name, age, gender, etc.
- Diagnosis of the patient.
- No. of days the patient was admitted to the Hospital.
- Hemodynamic parameters on the admission date (DOA) and discharge date (DOD).
- Complete blood picture tests, i.e., RBC, PCV/Hct, MCV, MCHC, RDW, WBC, and other values,i.e. Random Blood Glucose and ALT on the date of admission (DOA) and date of discharge (DOD).
- Inflammatory markers like IL-6, CRP, ESR, LDH, and D-dimers on the date of admission (DOA) and discharge (DOD).
- Cough and shortness of breath during DOA and DOD.
- Duration of symptoms during the admission.
- Situation of the patient on discharge.
- O2 support and PCR positivity of the COVID-19 hospitalized patients.
- Doses and no. of days of Solumedrol (Methylprednisolone) administered along with Remdesivir to COVID-19 patients.

- Doses and no. of days of Remdesivir administered to COVID-19 patients.

COVID-19 patients with known Co-morbid conditions and Drugs for Co-morbid conditions.

SOURCES OF DATA:

- Patient data collection form.
- Consultant's note on the Admission Form.
- Preliminary tests form for hospitalised patients.
- Doctor's progress inscription.
- Drug prescription chart.

SELECTION CRITERIA:

Inclusion criteria: Both male and female patients affected by COVID-19.

- Patients between the age bracket of 21-80 years.
- Patients with co-morbid conditions of Diabetes Mellitus, Hypertension, CAD, and Hypothyroidism.

Exclusion criteria:

- Patients below or adequate to 20 years.
- Pregnant or lactating females.
- Patients with poor prognoses are expected to demise.
- Patients who are intolerant or allergic to the therapeutic drugs used in this research.
- Patients with hepatic or renal failure.
- Patients diagnosed with dementia or decompensated psychiatric diseases.

Study group:

GROUP 1: Corticosteroid (Methylprednisolone) with Remdesivir group: About 100 patients have received the treatment of Corticosteroid (Methylprednisolone) 40/60/125 mg intravenously + Remdesivir 100/200 mg intravenously.

GROUP 2: Remdesivir as a monotherapy group: About 50 patients have received the monotherapy of Remdesivir 100/200 mg intravenously.

METHOD OF STUDY:

This retrospective observational study was carried out for six months in the Department of Medical Records. A total of 150 patients diagnosed with Covid 19 Pneumonia were selected. The patients were divided into two groups, with 100 patients in Group-1 [Corticosteroid (Methylprednisolone) with Remdesivir] and 50 in Group-2 (Remdesivir).

The patient's demographic information, hemodynamic parameters, laboratory values, symptoms, and conditions were collected. The patients were administered with desired doses of drugs, and the following data was collected in the patient data collection form.

RESULTS AND DISCUSSION:

1) The total number of patients:

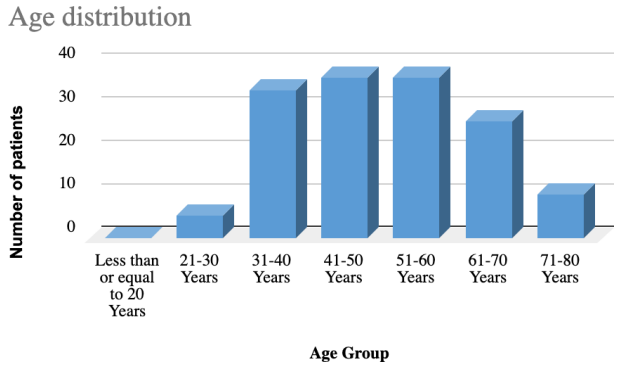
a) Number of days and number of patients given Corticosteroid (MP) with Remdesivir

Number of Days in Hospital	Number of patients given Corticosteroid (Methylprednisolone) with Remdesivir
Less than 5	25
6-10	56
11-15	13
16-20	3
21-25	1
26-30	2

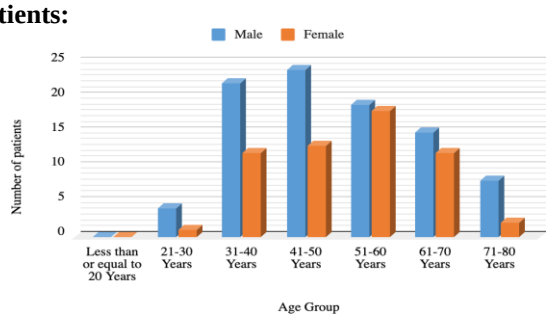
b) Number of days and number of patients given Remdesivir

Number of Days inHospital	Number of patients given Remdesivir
Less than 5	18
6-10	22
11-15	9
16-20	1
21-25	0
26-30	0

2) Age distribution of patients



3) Gender Distribution of patients:



4) Hemodynamic Parameters

1. Respiratory Rate (CPM)

a. Respiratory Rate (CPM) in patients given Corticosteroid (Methylprednisolone) with Remdesivir on DOA and DOD

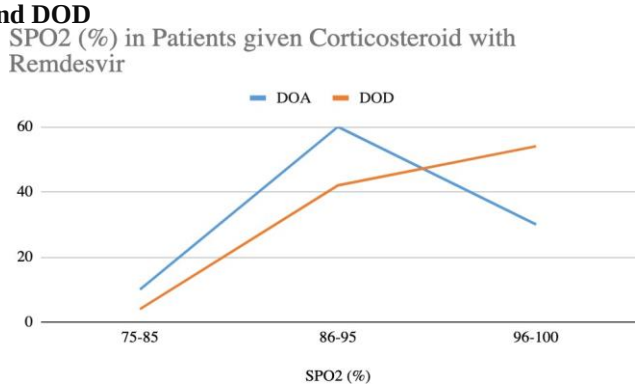
Respiratory Rate	Respiratory Rate (CPM) of patients given Corticosteroid with Remdesivir	Respiratory Rate (CPM) of patients given Corticosteroid with Remdesvir
	Do A	Do D
15-20	9	52
21-30	88	46
31-40	2	1
41-50	1	1

b. Respiratory Rate (CPM) in patients given Remdesivir on DOA and DOD

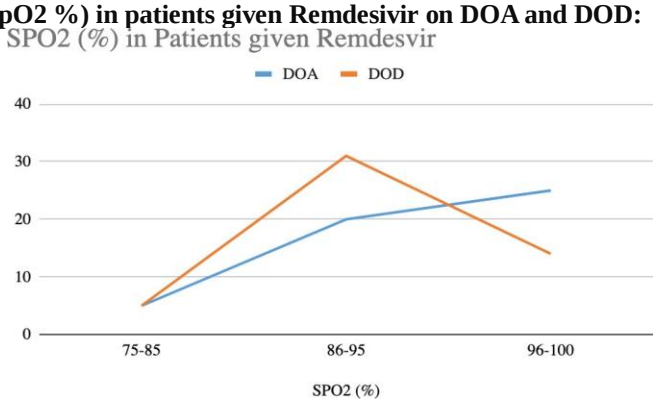
Respiratory Rate	Respiratory Rate (CPM) of patients given Remdesvir	Respiratory Rate (CPM) of patients given Remdesvir
	DOA	DOD
15-20	2	9
21-30	47	40
31-40	0	1
41-50	1	0

5) Oxygen Saturation (SpO2 %):

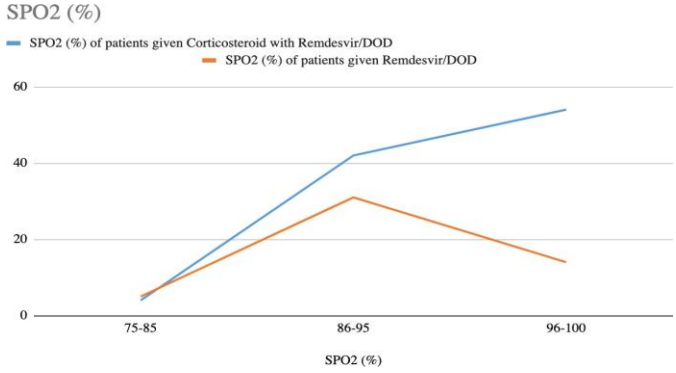
a. Oxygen saturation (SpO2 %) in patients given Corticosteroid (Methylprednisolone)with Remdesivir on DOA and DOD



b. Oxygen saturation (SpO2 %) in patients given Remdesivir on DOA and DOD:



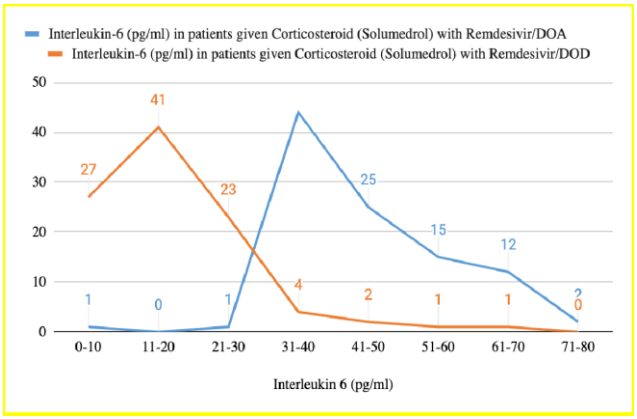
c. Oxygen saturation (SpO2%) in patients given Corticosteroid (Methylprednisolone)with Remdesivir V/S Remdesivir on DOD



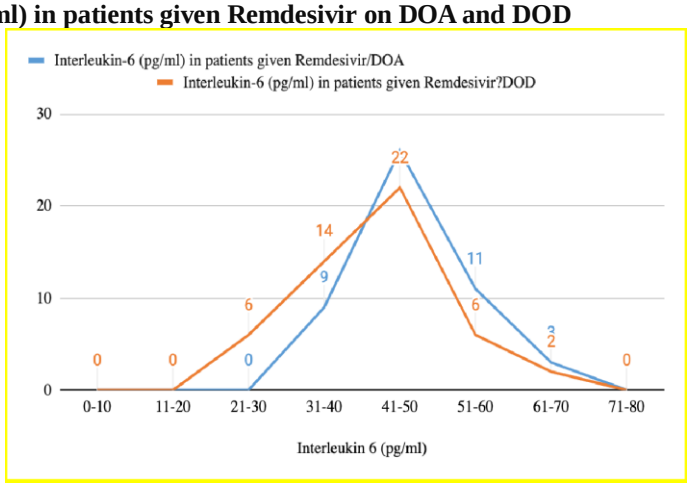
6) Biomarkers

Interleukin-6 (pg/ml)

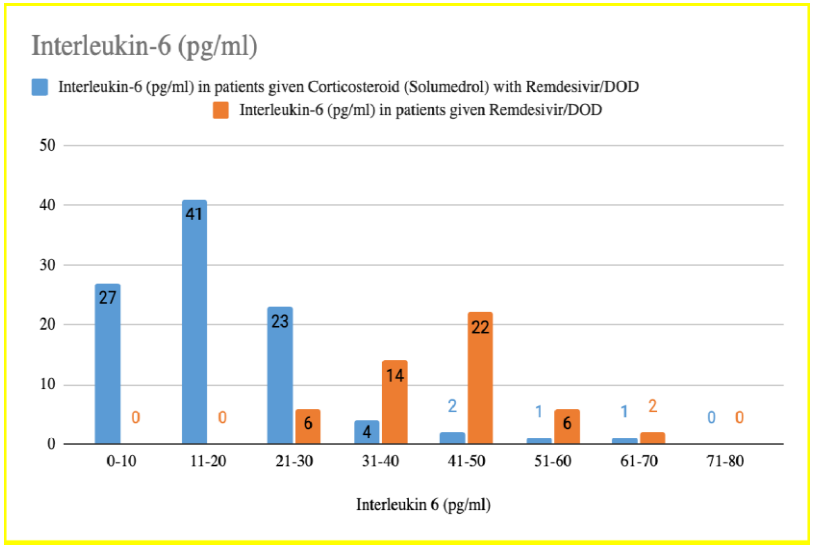
Interleukin-6 (pg/ml) in patients given Corticosteroid (Methylprednisolone) with Remdesivir on DOA and DOD



Interleukin-6 (pg/ml) in patients given Remdesivir on DOA and DOD



Interleukin-6 in patients given Corticosteroid (Methylprednisolone) withRemdesivir V/S Remdesivir on DOD



CRP(mg/dL):

a. **CRP(mg/dL) in patients given Corticosteroid (Methylprednisolone) with Remdesiviron DOA and DOD**

CRP(mg/dL)	CRP(mg/dL) in patients givenCorticosteroid (Methylprednisolone) with Remdesivir	Percentage	CRP(mg/dL) in patients given Corticosteroid (Methylprednisolone) with Remdesivir	Percentage
	Frequency on DOA		Frequency on DOD	
less than <5	41	41%	77	77.00%
6-10	36	36%	13	13.00%
11-15	15	15%	9	9.00%
16-20	4	4%	1	1.00%
21-25	1	1%	0	0.00%
26-30	0	0%	0	0.00%
30-35	3	3%	0	0.00%

b. **CRP(mg/dL) in patients given Remdesivir on DOA and DOD**

CRP(mg/dL)	CRP(mg/dL) in patients given Remdesivir	Percentage	CRP(mg/dL) in patients given Remdesivir	Percentage
	Frequency on DOA		Frequency on DOD	
less than <5	18	36%	16	32%
6-10	25	50%	24	48%
11-15	7	14%	7	14%
16-20	0	0%	3	6%
21-25	0	0%	0	0%
26-30	0	0%	0	0%
30-35	0	0%	0	0%

c. **CRP in patients given Corticosteroid (Methylprednisolone) with Remdesivir V/SRemdesivir on DOD**

CRP (mg/dL)	CRP (mg/dL) in patients given Corticosteroid (Methylprednisolone) with Remdesivir	Percentage	CRP (mg/dL) in patients given Remdesivir	Percentage
	Frequency on DOD		Frequency on DOD	
less than <5	77	77.00 %	16	32%
6-10	13	13.00 %	24	48%
11-15	9	9.00%	7	14%
16-20	1	1.00%	3	6%
21-25	0	0.00%	0	0%
26-30	0	0.00%	0	0%
30-35	0	0.00%	0	0%

WBC:

a. WBC count in patients given Corticosteroid (Methylprednisolone) with Remdesivir onDOA and DOD

WBC(cell/cumm)	WBC(cell/cumm) in patients given Corticosteroid (Methylprednisolone) with Remdesivir	Percentage (%)	WBC(cell/cumm) in patients given Corticosteroid (Methylprednisolone) with Remdesivir	Percentage (%)
	Frequency on DOA		Frequency on DOD	
Less than <10,000	23	23%	83	83%
10,000-20,000	72	72%	14	14%
20,000-30,000	2	2%	2	2%
30,000-40,000	2	2%	0	0%
40,000-50,000	0	0%	0	0%
50,000-60,000	1	1%	0	0%
>60,000	0	0%	1	1%

b. WBC count in patients given Remdesivir on DOA and DOD

WBC(cell/cumm)	CRP(mg/dL) in patients given Remdesivir	Percentage(%)	CRP(mg/dL) in patients given Remdesivir	Percentage(%)
	Frequency on DOA		Frequency on DOD	
Less than <10,000	6	12%	9	18%
10,000-20,000	44	88%	39	78%
20,000-30,000	0	0%	2	4%
30,000-40,000	0	0%	0	0%
40,000-50,000	0	0%	0	0%
50,000-60,000	0	0%	0	0%
>60,000	0	0%	0	0%

c. WBC count in patients given Corticosteroid (Methylprednisolone) with Remdesivir V/SRemdesivir on DOD

WBC(cell/cumm)	WBC(cell/cumm) in patients given Corticosteroid (Methylprednisolone) with Remdesivir	Percentage(%)	CRP(mg/dL) in patients given Remdesivir	Percentage(%)
	Frequency on DOD		Frequency on DOD	
Less than <10,000	83	83%	9	18%
10,000-20,000	14	14%	39	78%
20,000-30,000	2	2%	2	4%
30,000-40,000	0	0%	0	0%
40,000-50,000	0	0%	0	0%
50,000-60,000	0	0%	0	0%
>60,000	1	1%	0	0%

LDH

a. LDH count in patients given Corticosteroid (Methylprednisolone) with Remdesiviron DOA and DOD

LDH (U/L)	LDH count in patients givenCorticosteroid (Methylprednisolone) with Remdesivir	Percentage (%)	LDH count in patients given Corticosteroid (Methylprednisolone)with Remdesivir	Percentage (%)
	Frequency on DOA		Frequency on DOD	
Less than <200	4	4%	26	26%
200 – 400	73	73%	64	64%
400 – 600	14	14%	3	3%
600 – 800	1	1%	3	3%
800 – 1000	3	3%	2	2%
1000 – 1200	4	4%	2	2%
>1200	1	1%	0	0%

b. LDH count in patients given Remdesivir on DOA and DOD

LDH (U/L)	LDH count in patients given Remdesivir	Percentage(%)	LDH count in patients given Remdesivir	Percentage(%)
	Frequency on DOA		Frequency on DOD	
Less than <200	1	2%	9	18%
200 – 400	33	66%	30	60%
400 – 600	9	18%	4	8%
600 – 800	2	4%	3	6%
800 - 1000	3	6%	3	6%
1000 - 1200	2	4%	1	2%
>1200	0	0%	0	0%

c. LDH count in patients given Corticosteroid (Methylprednisolone) with RemdesivirV/S Remdesivir on DOD

LDH (U/L)	LDH count in patients given Corticosteroid (Methylprednisolone) with Remdesivir	Percentage(%)	LDH count in patients given Remdesivir	Percentage(%)
	Frequency on DOD		Frequency on DOD	
Less than <200	26	26%	9	18%
200 - 400	64	64%	30	60%
400 - 600	3	3%	4	8%
600 - 800	3	3%	3	6%
800 - 1000	2	2%	3	6%
1000 - 1200	2	2%	1	2%
>1200	0	0%	0	0%

D-dimers (ug/ml)

a. D-dimers (ug/ml) levels in patients given Corticosteroid (Methylprednisolone) with Remdesivir on DOA and DOD

D-dimers(µg/ml)	D-dimers(µg/ml) in patients given Corticosteroid (Methylprednisolone) with Remdesivir Frequency on DOA	Percentage (%)	D-dimers(µg/ml) in patients given Corticosteroid (Methylprednisolone) with Remdesivir Frequency on DOD	Percentage (%)
<50	22	22%	54	54%
51-100	0	0%	0	0%
101 - 150	1	1%	1	1%
151 - 200	62	62%	43	43%
201 - 250	1	1%	0	0%
251 - 300	2	2%	1	1%
301 - 350	1	1%	1	1%
351 - 400	6	6%	0	0%
401 - 450	1	1%	0	0%
451 - 500	2	2%	0	0%
501 - 600	1	1%	0	0%
601 - 650	1	1%	0	0%

a. D-dimers (ug/ml) levels in patients given Remdesivir on DOA and DOD

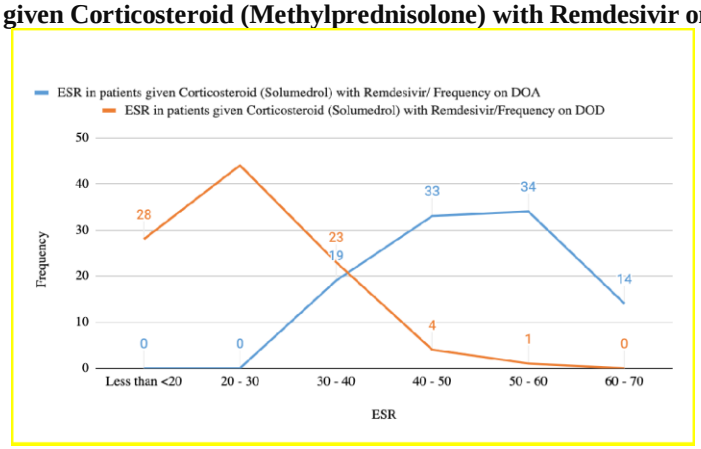
D-dimers (µg/ml)	D-dimers(µg/ml) in patients given Remdesivir Frequency on DOA	Percentage(%)	D-dimers(µg/ml) in patientsgiven Remdesivir Frequency on DOD	Percentage(%)
<50	0	0%	0	0%
51-100	0	0%	0	0%
101 – 150	0	0%	0	0%
151 – 200	0	0%	0	0%
201 – 250	0	0%	1	2%
251 – 300	32	64%	40	80%
301 – 350	9	18%	1	2%
351 – 400	3	6%	5	10%
401 – 450	3	6%	0	0%
451 – 500	1	2%	3	6%
501 – 600	2	4%	0	0%
601 – 650	0	0%	0	0%

c)D-dimer in patients given Corticosteroid (Methylprednisolone) with Remdesivir V/SRemdesivir on DOD

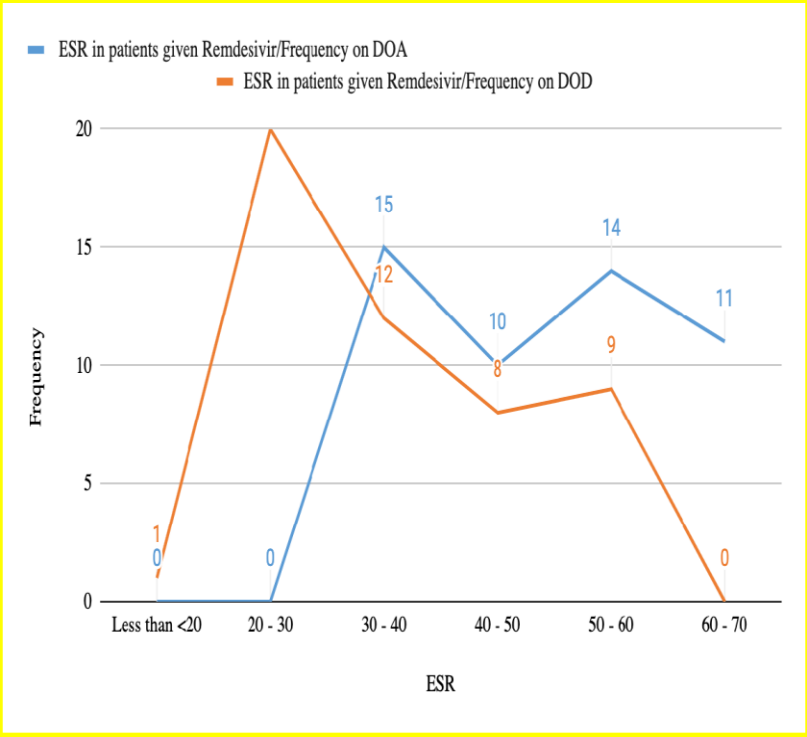
D-dimers(µg/ml)	D-dimers(µg/ml) in patients given Corticosteroid (Methylprednisolone) with Remdesivir	Percentage (%)	D-dimers(µg/ml) inpatients given Remdesivir	Percentage (%)
	Frequency on DOD		Frequency on DOD	
<50	54	54%	0	0%
51-100	0	0%	0	0%
101 – 150	1	1%	0	0%
151 – 200	43	43%	0	0%
201 – 250	0	0%	1	2%
251 – 300	1	1%	40	80%
301 – 350	1	1%	1	2%
351 – 400	0	0%	5	10%
401 – 450	0	0%	0	0%
451 – 500	0	0%	3	6%
501 – 600	0	0%	0	0%
601 – 650	0	0%	0	0%

ESR

ESR in patients given Corticosteroid (Methylprednisolone) with Remdesivir onDOA and DOD



ESR in patients given Remdesivir on DOA and DOD



ESR in patients given Corticosteroid (Methylprednisolone) with Remdesivir V/S Remdesivir on DOD

ESR	ESR in patients given Corticosteroid (Methylprednisolone) with Remdesivir Frequency on DOD	Percentage (%)	ESR in patients givenRemdesivir Frequency on DOD	Percentage (%)
Less than <20	28	28%	1	2%
20 – 30	44	44%	20	40%
30 – 40	23	23%	12	24%
40 - 50	4	4%	8	16%
50 - 60	1	1%	9	18%
60 - 70	0	0%	0	0%

CONCLUSION:

The study has shown a significant and effective therapeutic outcome from the usage of Corticosteroid (Methylprednisolone) when given in combination with Remdesivir as opposed to the monotherapy of Remdesivir.

The two drugs were compared for their efficacy in COVID-19 hospitalized patients. The hemodynamic parameters, inflammatory markers and other lab values were stabilized after treating them with the Combination therapy of Corticosteroid (Methylprednisolone) with Remdesivir.

Patients treated using a combination of Corticosteroid (Methylprednisolone) with Remdesivir showed a high frequency of efficacy and greater therapeutic outcome when compared to Remdesivir as monotherapy. The results have the potential to assess the severity of COVID-19 from the hemodynamic parameters and biomarkers; from this, we are able to conclude that when the patient is given the combination therapy of the Corticosteroid (Methylprednisolone) with Remdesivir, there is a significant improvement inthe health of the patient and they are more hemodynamically stable, their cough and SOB is also treated as opposed to the Group-2 patients who have been administered Remdesivir asa monotherapy.

The bio-markers of the patients in Group-1 who were given Corticosteroid (Methylprednisolone) in combination with Remdesivir were also stabilised in contrast to thepatients of Group-2 who were given only Remdesivir. When given Corticosteroid (Methylprednisolone) in combination with Remdesivir, the need for using ventilators was significantly decreased.

Thus in the hospitalised COVID-19 patients, the ones given Corticosteroid (Methylprednisolone) in combination with Remdesivir showed better therapeutic outcomes when compared to only giving Remdesivir.

LIST OF ABBREVIATIONS:

S.NO	ACRONYM	DESCRIPTION
1.	CV	Coronavirus
2.	SARS CoV	Severe Acute Respiratory Syndrome- Coronavirus
3.	MERS-CoV	Middle East Respiratory Syndrome
4.	RNA	Ribonucleic acid
5.	PM	Plasma membrane
6.	CEACM1	Carcinoembryonic antigen-related cell adhesion molecule 1
7.	ACE-2	Angiotensin-converting enzyme
8.	TMPRSS-2	Transmembrane protease serineprotease-2
9.	HC	Host cell
10.	dSRNA	Double stranded Ribonucleic acid
11.	ssRNA	Single stranded Ribonucleic acid
12.	Nsp1	Non-structural protein 1
13.	Mrna	Messenger Ribonucleic acid
14.	O2	Oxygen
15.	DVT	Deep vein thrombosis
16.	WHO	World Health Organisation
17.	COPD	Chronic Obstructive Pulmonary Disease
18.	RT-PCR	Reverse Transcription Polymerase Chain Reaction
19.	CDC	Centre for Disease Control and Prevention
20	OS	Observational Studies
21	RCT	Randomised Controlled Trials
22	GC	Glucocorticoids
23	MP	Methylprednisolone
24	ADR	Adverse Drug Reaction
25	GCR	Glucocorticoid Receptors

26	DNA	Deoxyribonucleic acid
27	VD	Volume of Distribution
28	CBG	Corticosteroid-Binding Globulin
29	IV	Intravenous
30	ATP	Adenosine triphosphate
31	RDV-PP	Remdesivir triphosphate
32	Exo N	Exonuclease
33	SOB	Shortness of breath
34	IL-6	Interleukin-6
35	ESR	Erythrocyte Sedimentation Rate
36	CRP	C-reactive protein
37	ADE	Adverse Drug Event
38	RBS	Random Blood Sugar
39	SPO2	Oxygen Saturation
40	WBC	White Blood Cells
41	LDH	Lactate Dehydrogenase
42	MRD	Medical Records Department
43	DOA	Date of Admission
44	DOD	Date of Discharge

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