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# A study of effect of remdesivir on mortatlity and hospital stay of moderate to severe cases of COVID-19/ severe acute respiratory illness in North Karnataka region

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**Abstract:** *Background:* As the epidemic that started at Wuhan spread globally many agents with antiviral activity were evaluated for the treatment of coronavirus disease. Many agents were claimed to be "Game changer" in the management of covid. Likewise Remdesivir received much attention leading to high demand of a scarcely produced antiviral agent, which many a times was out of stock in our region. *Methods:* In this retrospective observational study data of patients admitted in Al Ameen Medical College Hospital with moderate to severe form of SARS CoV 2 / SEVERE ACUTE RESPIRATORY ILLNESS was evaluated retrospectively. Patients were divided into two groups i.e. those who received remdesivir and those who could not avail. Statistical analysis was done to determine mortality benefit of Remdesivir and influence on hospital stay. *Results:* 293 patients were studied and out of them 56 received remdesivir. Mortality was 32.1% among those who received and in the other group 17.7%. Mean hospital stay was 11.7 days with SD of 11.6 among those who received remdesivir and in the other group it was 7.3 days mean hospital stay with SD of 4.7days. *Conclusion:* Our study showed no benefit in the outcome and hospital stay among patients receiving remdesivir. However we concede that the number patients receiving remdesivir was less and this is a limitation. Although this was a small scale study with limited number of patients, it represents a point of reference for the use of remdesivir at other hospitals.

**Keywords:** COVID-19, Remdesivir, SARS CoV 2.

## Introduction

Severe acute respiratory illness syndrome coronavirus 2 (SARS CoV 2) was identified in the month of December in Wuhan province of People's Republic of China [1] and was understood that if this local epidemic was not contained locally then the world would have to brace itself for a new pandemic based upon the way it was spreading locally. Eventually it turned into a pandemic and thereby starting search of a novel antiviral agent that would be efficacious and helpful in decreasing the mortality and morbidity of patients. Many antiviral agents were thought to be usefull and were tried. Many were claimed to be "Game changer" and were later found to be otherwise. Several therapeutic measures were evaluated but none was found to have efficacious anti-viral activity in vivo [2].

In this scenario remdesivir entered the picture with a hope among doctors that it might be beneficial in managing cases of Severe Acute Respiratory Illness (SARI) caused by the Covid-19 virus as it showed inhibitory activity on virus in vitro. It was believed by the general populace that finally the much awaited cure has arrived. The drug however was scarcely available in India initially. Use of remdesivir in management of SARI patients started with enthusiasm.

Initially as the drug was not easily available and also before its use started, patients were treated by the guidelines decided by competent authorities. We followed the protocol as provide by circular of Government of Karnataka [3]. The factors because of

 

which it could not be given in many patients were,

1. The initial shortage in availability of drug
2. High cost of the drug
3. Approval to use the drug after a considerable time since the commencement of pandemic

Remdesivir was used according to the guidelines provided by Government of Karnataka circular [3]. Baseline investigations & parameters were evaluated and the drug was used if no contraindications were present. Remdesivir was administered i.v as a 200mg loading dose and subsequently 100mg daily for 5 to 10 days according to the clinical improvement in the general condition. Remdesivir was also given on compassionate grounds in those patients who had high CORADS score but were swab RT PCR negative for covid-19.

## Material and Methods

This was a retrospective observational study carried out in Al Ameen Medical College and Hospital Vijaypura, Karnataka which caters to health needs of patients especially of North Karnataka region and district of Vijaypura in particular. Patients with moderate to severe form covid 19 / SEVERE ACUTE RESPIRATOY ILLNESS were retrospectively divided in to 2 groups i,e. those who received remdesivir and those who could not. All the patients were treated in accordance to the standard protocol released by circular Government of Karnataka [3].

Hydroxycholroquine was avoided in patients receiving remdesivir. The reasons for patients not receiving remdesivir were either local unavailability, financial constraints or patients getting admitted before remdesivir got authorised for use in covid 19. The data available in the form their case paper with daily notes was analysed and statistical analysis was done to see any statistical significant difference in the mortality of patients in both the groups as well as duration of hospital stay.

*Statistical method used:* All the characteristics were summarised descriptively. For continuous variables, the summary statistics of mean +/- standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Chi-square test was used for association between two categorical variables.

The difference of the means of analysis variables between two independent groups was tested by unpaired t test. If the p-value was $< 0.05$, then the results were considered to be statically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.23 (IBM statistics, Chicago, USA) and Microsoft office 2007.

## Results

Total number of patients studied were 293. 198 patients were male and 95 patients were female (table 1). Mean age of patients admitted with moderate to severe form of covid-19 infection was 53.8 years with standard deviation of 13.5 years (table 2). 56 patients received remdesivir and 38 among them recovered, 18 died (table 3). Number of patients who could not receive remdesivir was 237 out of whom 195 recovered and 42 died (table 3).

**Table-1: Distribution of Cases according to Sex**

| Sex | N | Percent |
|---|---|---|
| Male | 198 | 67.6 |
| Female | 95 | 32.4 |
| Total | 293 | 100 |

**Table-2: Distribution of Cases according to Age**

| Age(yrs) | N | Percent |
|---|---|---|
| ≤30 | 20 | 6.8 |
| 31-40 | 34 | 11.6 |
| 41-50 | 63 | 21.5 |
| 51-60 | 75 | 25.6 |
| >60 | 101 | 34.5 |
| Total | 293 | 100 |

| Descriptive Statistics | Min | Max | Mean | SD |
|---|---|---|---|---|
| Age(yrs) | 20 | 82 | 53.8 | 13.5 |

| Table-3: Distribution of Outcome according to Remdesivir | | | | | |
|---|---|---|---|---|---|
| Outcome | Remdesivir given | | Remdesivir not given | | p value |
| | Mean | SD | Mean | SD | |
| Death | 18 | 32.1% | 42 | 17.7% | 0.016* |
| Recovered | 38 | 67.9% | 195 | 82.3% | |
| Total | 56 | 100.0% | 237 | 100.0% | |

Mean duration of hospital stay among patients receiving remdesivir was 11.7 with standard deviation of 11.6 days. In the other group it was 7.3 days mean with standard deviation of 4.7 (table 4). There was no benefit with respect to mortality and length of hospital stay among patients receiving remdesivir. It is however conceded that the small sample size of group receiving remdesivir is a limitation.

| Table-4: Distribution of Length of Hospital Stay in both groups | | | | | | | |
|---|---|---|---|---|---|---|---|
| Parameters | Remdesivir given | | Remdesivir not given | | t | df | p value |
| | Mean | SD | Mean | SD | | | |
| LOS(days) | 11.7 | 11.6 | 7.3 | 4.7 | 4.519 | 291 | <0.001* |

## Discussion

Three common group of symptoms are identified with Covid-19 infection and they were;

1. Respiratory symptom cluster with cough, sputum, shortness of breath, and fever;
2. Musculoskeletal symptom group with muscle and joint pain, headache, and fatigue;
3. Group of digestive symptoms with abdominal pain, vomiting, and diarrhoea [4]

The covid-19 virus can affect the upper respiratory tract [5] and it is the lungs that are affected most. It is suggested by some studies that the organ most involved is the organ with high density of angiotensin converting enzyme 2 (ACE2) receptors. Since lungs have high number of type ll alveolar cells, the virus utilizes special surface glycoprotein to connect to ACE2 receptor and enter the host cell [6].

However data is at present conflicting whether use of angiotensin receptor blocker translates into clinically demonstrable benefit. One view is that increasing ACE2 recpetors using angiotensin receptor blockers medications could be protective [7]. Remdesivir was introduced for the treatment of moderate to severe forms of covid-19 [8] and it received its share of attention. The drug was originally produced as a broad spectrum antiviral by biopharmaceutical company Gilead sciences [9] and was originally developed to treat Hepatitis C and was later on used in the treatment of haemorrhagic fever caused by Ebola and Marburg virus [10]. It had shown inhibitory activity in vitro for SARS COV1 and Middle Eastern Respiratory Syndrome virus (MERS COV) [11-12].

Remdesivir is a pro-tide i,e. prodrug of a nucleotide [13]. Its active metabolite impairs the activity of RNA-DEPENDENT RNA-POLYMERASE causing it to escape proof reading by exoribonuclease which subsequently leads to termination of chain synthesis after an additional 5 bases have been added leading to decrease in the production of viral RNA. It can be given for 5 to 10 days in severe covid 19 infection without major side effects [14].

Remdesivir was administered intravenously 200mg on day one subsequently 100mg once a day i.v. for a period of 5 to 10 days depending upon clinical improvement. Hydroxychloroquin was not given to those receiving remdesivir, however other treatment

aspects remained same for all the patients as per government guidelines [3]. Day to day progress of patients was monitored and recorded in respective case papers.

In our study total number of patients studied was 293 and among them 195 were male and 98 were females (table 1). Our study showed that there was no mortality benefit offered by remdesivir in treating moderate to severe case of SAR CoV 2/ severe acute respiratory illness (table 3). This in concordance to recent studies [15]. Remdesivir was found to be superior to placebo in decreasing the recovery time [16]. However in our study remdesivir was not found to decrease the duration of hospital stay (table 4). This however may be attributable to small sample size of patients who received remdesivir. Number of patients who were able to receive remdesivir was 56 (table 5).

**Table-5: Distribution of Remdesivir**

| Remdesivir | N | Percent |
|---|---|---|
| Yes | 56 | 19.1 |
| No | 237 | 80.9 |
| Total | 293 | 100.0 |

Sample size of group which could receive remdesivir was less and this is a limitation. Reasons for patients not receiving remdesivir were as mentioned earlier.

## Conclusion

Authors observed in this study that there was no mortality benefit offered by remdesivir in patients of severe acute respiratory illness/ moderate to severe SARS CoV-2 covid-19 infection. Hospital stay of patients receiving remdesivir was more than the other group. This is discordant with other studies [8] and may be attributable of small sample size to group which received. Authors also concede that less number of patients in this study is a limitation. Although it was a small scale study with limited patients, it represents a point of reference for the use of remdesivir at other hospitals.

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