

CLINICAL OUTCOMES OF REMDESIVIR IN HOSPITALIZED COVID-19 PATIENTS: A RETROSPECTIVE STUDY IN ULAANBAATAR CITY, MONGOLIA

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Abstract: On 10 March 2020, The Ministry of Health of Mongolia publicly announced the first laboratory-confirmed case of COVID-19. Mongolia was the 31st affected country in Asia. As of the 7th of May 2022; there have been 469,885 cases and 2,167 deaths reported. The Ministry of Health developed COVID-19 diagnostic and treatment guidelines which have been updated four times. The latest guideline was released on the 18th of January 2022, and included remdesivir (RDV), molnupiravir, and favipiravir as antiviral drugs. There is no sufficient study of remdesivir (RDV) efficacy in Mongolia. The retrospective study has been evaluated from hospitalized patients with COVID-19 symptoms and had received 5-day RDV treatment. A total of 148 patients had had 5-days RDV as a treatment. At least 39.2% of the patients were within the 45-60 years age group. Females were about 64.9% and (54.7%) patients had moderate COVID-19 disease; while (62.16%) patients had comorbid conditions. Findings of our study that show that a 5-day course of treatment is associated with vital clinical benefits that can provide greater benefits in Mongolian inpatients.

Keywords: Remdesivir, COVID-19, anti-viral drug.

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Introduction

Coronavirus disease (COVID-19) is an infectious disease caused by a virus called the severe acute respiratory syndrome coronavirus-2 (SARS-COV-2), which was first discovered in Wuhan, China in December 2019. The disease rapidly spread worldwide leading to the COVID-19 pandemic, which concluded around 20th April 2022. The global incidence of COVID-19 had reached almost 500 million confirmed cases with 6 million death cases. COVID-19 symptoms are variable, but often include fever, cough, headache, shortness of breath, and loss of smell and taste. Most people develop mild to moderate symptoms (8%), while 14% develop severe symptoms (dyspnea, hypoxia) and only 5% can have critical symptoms (respiratory failure, multi-organ dysfunction).

Until recently, there was no sufficient treatment or cure for COVID-19, but in April 2022, various medications have been approved in different countries, because SARS-COV-2 replication leads to many clinical manifestations. Antiviral drugs prevent viral replication through various mechanisms having the greatest impact before the illness progresses that can lead to severity of inflammation. Remdesivir (RDV) is an adenosine analog with

broad-spectrum antiviral activity against several single-stranded RNA viruses that are approved by the Food and Drug Administration (FDA) for the treatment of COVID-19 on 1 May 2020. Coronavirus Disease 2019 treatment Guidelines by the National Health Institute (NIH) recommended using intravenous remdesivir for the treatment of adult and pediatric patients. It is approved for the treatment of mild to moderate COVID-19 in high-risk, non-hospitalized patients and for the treatment of hospitalized patients.

Mongolia is a lower-middle-income country in East Asia, bordered by Russia to the North and China to the South. It has an extreme continental climate and usually has a long and severe winter climate with temperatures measuring at lower to less than -30°C. The population of Mongolia reached almost 3.5 million people (2018), with nearly half of the population living in the capital city of Ulaanbaatar. About 49.2% of the resident population are Males and the remaining 50.8% are Females. Aggregation by age group shows 31.2% are children fewer than 15 years, 64.7% of the population are aged within the 15-64 years age group, and 4.1% are over the age of 65 years respectively. The Mongolian health system has three levels of service which has family health centers, village health centers, maternity and general hospitals,

next is; ambulances service centers, and regional diagnostic and lastly treatment centers (RDTCs). The leading causes of mortality in the country in 2018 has been diseases of the circulatory system at 34.4%, cancer at 24.6%, injuries, poisonings, and certain other consequences of external causes was at 16.8%, diseases of the digestive system at 6.8%, and diseases of the respiratory system at 4.3%. Deaths from these diseases accounted for a combined 87.1% of all deaths. On 10 March 2020, The Ministry of Health of Mongolia publicly announced the first laboratory-confirmed case of COVID-19. Mongolia was the 31st affected country in Asia. As of the 7th of May 2022; there have been 469,885 cases and 2,167 deaths reported. The Ministry of Health developed COVID-19 diagnostic and treatment guidelines which have been updated four times. The latest guideline was released on the 18th of January 2022, and included remdesivir (RDV), molnupiravir, and favipiravir as antiviral drugs. There is no sufficient study of remdesivir (RDV) efficacy in Mongolia. Our study presents the clinical outcomes of remdesivir (RDV) in hospitalized patients in Ulaanbaatar, the capital city of Mongolia.

Method

Surveillance design and participants

The retrospective study has been evaluated from hospitalized patients with COVID-19 symptoms and had received 5-day RDV treatment. We analyzed the data from the patient's file, of those who were admitted to the hospital with SARS-COV-2. Infections were confirmed by polymerase chain reaction testing and also with X-ray diagnosed pneumonia from 01 July to 30 October in 2021 in the Songino-Khairkhan district Health Center of Ulaanbaatar, Mongolia. Patients younger than 18 years, pregnant, or who used other antiviral drugs were excluded from the study. The study was reviewed and approved by the Bio-Medical

Ethics Review Committee of the Mongolian National University of Medical Sciences (2021/3-11).

Procedure and outcomes

Data entailing patient age, gender, COVID-19 severity, comorbid conditions, concomitant medicines, vital signs, CRP, duration of hospitalization, and other adverse events were collected. The primary outcome was defined as either; (1) patient was discharged from the hospital with clinical improvement, (2) no improvement, or (3) death which is reported in the patient's file. A secondary outcome is a difference between the admission and the fifth day of hospitalization of symptoms, vital signs, and CRP.

Statistical analysis

All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) version 25.0. Continuous and quantitative data variables were summarized using descriptive analysis. Categorical data are presented as frequency count (N) and percentages (%). Clinical outcomes were projected using compare means with dependent t-test. A *p*-value of <0.05 was considered statistically significant.

Results

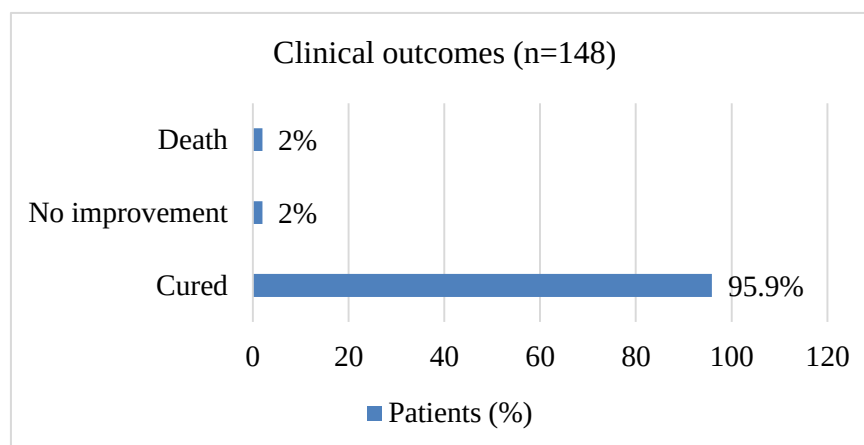
Patient characteristics

A total of 148 patients had had 5-days RMV as a treatment. At least 39.2% of the patients were within the 45-60years age group. Females were about 64.9% and (54.7%) patients had moderate COVID-19 disease; while (62.16%) patients had comorbid conditions. Hypertension (29.1%) was the most common comorbid condition followed by diabetes (16.9%), and obesity (5.4%). Among 148 patients on concomitant medications, antibiotics were used for all patients followed by dexamethasone (95.9%).

Table 1. Patient characteristics

Characteristics		N	%
Age group (years)	18-24	4	2.7
	25-44	31	20.9
	45-60	58	39.2
	61-75	34	23
	76-90	19	12.8
	90<	2	1.4
Gender	Male	52	35.1
	Female	96	64.9
COVID-19 severity	Moderate	81	54.7
	Severe	53	35.8
	Critically severe	14	9.5
Comorbidities	Hypertension	43	29.1
	Diabetes	25	16.9
	Obesity	8	5.4
	COPD	5	3.4
	Hypothyroidism	5	3.4
	Other	6	4.1

Concomitant medicine	Antibiotic	148	100
	Heparin	124	83.8
	Dexamethasone	144	97.3
	Vit C	142	95.9
	Vit D	140	94.6

Figure 1. Patient discharge from hospital

Cough symptoms was most prevalent on the first day of hospitalization 132 (89.2%) then on the fifth day 77 (52.1%) for most patients, ($p=0.000$). At least 76 (51.4%) patients had shortness of breath on the first day as compared to 21 (14.1%) patients on the fifth day, ($p<0.004$). Other symptoms had improvement on the fifth day of hospitalization ($p<0.023$). Vital signs (SpO₂, respiratory rate, heart rate) had improved on the fifth day than admission day, respectively ($p=0.000$). Among 148 patients, 77 (52%) patients had inflammation marker test (CRP). About 29 (37.3%) patients had CRP (+++) on the first day, 4(5.2%) patients on the fifth day ($p<0.013$) (Table 2).

Table 2. Clinical outcomes of patients

Symptoms	First day	Fifth day	<i>p</i> -value
	N (%)	N (%)	
Cough	132 (89.2)	77 (52.1)	0.000
Shortness of breath	76 (51.4)	21(14.1)	0.004
Chest pain	70 (47.3)	15(10.1)	0.013
Headache	46(31.1)	2 (1.3)	0.000
Fever	28 (18.9)	0 (0)	0.000
Other	53(35.8)	16 (10.8)	0.023
Vital signs	Mean±SD	Mean±SD	
SpO₂ ()	90.59±6.3	93.47±4.1	0.000
Respiratory rate	21.17±4.5	19.01±2.1	0.000
Heart rate	82.35±12.7	75.41±8.4	0.000
Blood pressure ()	125/81±13.7	122/70±11.6	0.018
Temperature (C)	38.7±0.44	36.3±0.26	0.005
CRP	N (%)	N (%)	
(-)	23(29.9)	49 (63.6)	0.013
(+)	12 (15.6)	13(16.9)	
(++)	13(16.9)	11(14.3)	
(+++)	29 (37.7)	4 (5.2)	

Duration of hospitalization was 10±3.9 days. Respective admissions for patients lasted many days in the following category; moderate COVID-19 for 9±3.1 days, severe cases were for 11±38 days and critical severe was 15± 4.4 days. Among 148 patients 95.9% of them had cured and discharged from hospital with improvement.

Discussion and Conclusion

The Food and Drug Administration (FDA) of U.S approved remdesivir (RDV) based on the agency's analysis of data from three randomized, controlled trials that included participants hospitalized with mild to severe COVID-19. In 2020, the United States government approved RDV for use in moderate and severe cases of COVID-19, and coincidentally several clinical studies endorsed remdesivir (RDV) as the most suitable treatment. Remdesivir (RDV) has been the topic of debate ever since the ACTT-1 research, funded by the National Institutes of Health, indicated a shorter time towards a positive clinical outcome. According to the World Health Organization (WHO), Mongolia has developed and amended several COVID-19 strategy and treatment guidelines with reference to reliable and verified sources of information. A limitation of this study is that Mongolia cannot perform a clinical trial with placebo for the reason that we do not have ethical clearance to do so within the short timeframe we conducted the study.

World Health Organization (WHO) in 2020 had advised in an ad hoc consultation on the next steps for Covid-19 vaccine evaluation. It discussed that critical additional data be sought to inform regulatory and policy recommendations for the first successful vaccines and subsequent optimization.

In January 2022, the Canadian component of the World Health Organization (WHO) reported that hospitalized people treated with remdesivir had lower death rates and reduced oxygen treatment and mechanical ventilation compared to standard care treatment.

However, the bigger Solidarity study, funded by WHO, found no effect in terms of mortality. Even though the findings of the Solidarity trial showed that remdesivir does not show any significant impact on the mortality rate among serious COVID-19 patients, it rather played an important role in decreasing the severity of illness and duration of illness. This is important for lower- and middle-income countries that are overwhelmed with COVID-19 patients. It can reduce the burden on hospitals

Our study included only those patients who received at least five days of remdesivir that supported the recommendations for an initial five-day course for most patients. The study showed similar outcome to those studies highlighted by WHO where patients who were treated with remdesivir had significant improvement of clinical symptoms and vital signs. Findings of our study that show that a 5-day course of treatment is associated with vital clinical benefits that can provide greater benefits in Mongolian inpatients.

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