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Remdesivir Therapy versus Standard Care in Hospitalized Pregnant Women with Moderate and Severe COVID-19 in a Tertiary Care Center of Dubai: A Quasi-experimental Study

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Pregnant women with COVID-19 are more likely to be hospitalized and require respiratory support than non-pregnant women. There is little published data on Remdesivir use in pregnant women with COVID-19. We aimed to investigate the clinical course and obstetric outcomes for pregnant women with COVID-19 administered Remdesivir versus standard therapy.
Methods: We conducted a non-randomized quasi experimental study among 100 pregnant women with moderate or severe COVID-19 who were admitted to a tertiary care hospital in Dubai between 18 January and 31 March 2021. We compared women receiving Remdesivir (treatment arm) and women receiving standard therapy (control arm).
Results: More women in the Remdesivir group had normal vaginal delivery (n=17, 39.5%) than controls (n=9, 20.5%). Newborn Apgar scores at 1 and 5 minutes were similar in both groups. The

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mean standard deviation time to recovery and discharge was lower for patients receiving Remdesivir than controls (8.4±3.3 versus 13.6±9.2 days). Fewer treated patients required intensive care; at 60- day follow-up, all women on Remdesivir were doing well whereas six (12.0%) women on standard therapy had died.

Conclusions: Pregnant women with moderate or severe COVID-19 treated early with Remdesivir showed an overall better clinical course and outcomes than those on standard therapy.

Keywords: SARS-CoV-2; COVID-19; pregnancy; remdesivir; Dubai; survival.

1. INTRODUCTION

The emergence and rapid spread of the novel coronavirus SARS-CoV-2, which causes the disease COVID-19, led to declaration of a global pandemic by the World Health Organization (WHO) in March 2020 [1]. Patients with COVID-19 infection show a wide range of clinical features [2]. The knowledge gained from previous human coronavirus outbreaks suggests that in specific situations such as pregnancy, women infected with SARS-CoV-2 are prone to having a higher risk for infection-related respiratory complications in comparison with non-pregnant women [3]. This increased risk of overall worse maternal outcomes has also been reported in pregnant women with symptomatic COVID-19 requiring hospitalization [4,5]. Increased risks in pregnant population include the_requirement for oxygen supplementation, mechanical ventilation, intensive care unit (ICU) admission, and death owing to COVID-19 [6].

Remdesivir is an inhibitor of SARS-CoV-2 RNA-dependent RNA polymerase, which is essential for viral replication. The available international data suggest that patients with severe COVID-19 treated with Remdesivir exhibit clinical improvement in terms of a significant reduction in morbidity and reduced length of hospital stay, recovery time, and mortality [7]. Remdesivir is the first antiviral drug approved by the United States Food and Drug Administration for the treatment of COVID 19 in adults and approved for compassionate use in pregnant women [8]. United States data suggest that treatment with Remdesivir is safe and well-tolerated in pregnant women with COVID-19 [9]. It is recommended that Remdesivir not be withheld because of theoretical risk in pregnancy, if medically indicated [10].

It has been reported that breastfeeding can result in SARS-CoV-2 transmission from mother to infant; however, newborns are unlikely to absorb a substantial amount of remdesivir [11]. In the revised United Arab Emirates (UAE) National Guidelines for Clinical Management and Treatment of COVID-19, compassionate use of Remdesivir in pregnant women hospitalized with COVID-19 was approved in February 2021[12]. Recently published data from Dubai showed that pregnant women with COVID-19 are more likely to be admitted to the hospital and receive respiratory support than non pregnant women [4].

There are limited studies on COVID-19 infection among pregnant women and little published data on the use of remdesivir in these women and their maternal outcomes [13]. The aim of this study was to investigate the clinical course and obstetric outcomes for pregnant women with COVID-19 in the UAE who were administered Remdesivir and those who received standard care.

2. METHODS

We conducted a non-randomized quasi-experimental study to compare maternal morbidities and obstetric outcomes between pregnant women with COVID-19 who were treated with remdesivir (treatment arm) and those who received standard therapy (control arm). We followed The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines in reporting our observations [14].

This study was conducted in a tertiary care hospital in Dubai, UAE, between 18 January and 31 March 2021. Latifa Women and Children Hospital (LWCH) is a 440-bed public tertiary care center that specializes in maternal, neonatal and pediatric services. During the second COVID-19 wave in UAE, on 18 February 2021, LWCH initiated the use of Remdesivir in pregnant women with COVID-19. All hospitalized pregnant women in both groups were monitored daily by teams in both internal medicine and obstetrics. Patients were followed up to day 60 from the day of admission. Data were collected using the electronic medical records from 1 June 2021 to 31 August 2021.

2.1 Patient Eligibility

COVID-19 was confirmed in all patients using an Allplex reverse transcription polymerase chain reaction kit (Seegene Technologies, Walnut Creek, CA, USA with nasopharyngeal swabs to detect respiratory tract infection with SARS-CoV-2. We adopted the clinical spectrum criteria of moderate and severe COVID-19 pneumonia per the National Institutes of Health COVID-19 treatment guidelines [15].

Regardless of oxygen saturation, pregnant women in their second and third trimester who were hospitalized in LWCH with moderate or severe COVID-19 were considered eligible to participate in this study as defined by the NIH guidelines.(15) We excluded pregnant women with COVID-19 who had any of the following medical conditions: creatinine clearance (Cockcroft–Gault formula) <30 mL/minute, serum levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) >5 times the upper limit of normal, or evidence of multiorgan failure.

2.2 Treatment arm (Remdesivir therapy)

This study was performed during the second wave of COVID-19 when LWCH initiated the compassionate use of Remdesivir in pregnant women with COVID-19, according to the revised UAE National Guidelines for Clinical Management and Treatment of COVID-19, approved on 17 February 2021 [12].

Study participants were selected from among 250 pregnant women hospitalized in the isolation ward with moderate and severe COVID-19 between 17 February and 31 March 2021. Patients who were administered intravenous remdesivir received a 200-mg loading dose on day 1, followed by 100 mg daily for 4 days (total duration of treatment, 5 days).

2.3 Control Arm (Conventional Therapy)

Pregnant women admitted between 18 January 2021 and 16 February 2021 who received standard therapy per the local protocol were included in the control arm. These patients were administered one or a combination of the following medications: azithromycin, antimalarials (hydroxychloroquine), and antiretrovirals (lopinavir/ritonavir). Patients in both the treatment and control arms received one or a combination of the following drugs: low-molecular-weight heparin, systemic steroids, antibiotics, and immunosuppressant (tocilizumab) or interferon, per the clinical indication (Appendix 1).

Patients who were treated with Remdesivir were matched with an equal number of patients who received standard therapy, according to severity per the WHO Clinical Progression Scale. (Appendix 2).

2.4 Data Collection

The study data of hospitalized pregnant women with moderate and severe COVID-19 pneumonia admitted to LWCH spanned from 18 January to 31 March 2021. Data were collected for both study arms from the DHA unified electronic medical records system (Salama system). Prior to data analysis, all collected data were approved by the hospital administration and anonymized to ensure patient privacy and confidentiality. Data integrity was maintained per regulations and guidelines of the DHA.

The standardized collected data included demographics, obesity (defined as body mass index [BMI] ≥30 kg/m2), coexisting medical conditions (hypertension, asthma, chronic lung diseases, type 2 diabetes with chronic kidney disease, hypothyroidism), maternal age at delivery, pre- and post treatment liver enzymes, radiological findings, concurrent therapy, length of hospitalization, ICU admission, readmission, and maternal death.

Maternal and neonatal outcomes included gestational age at delivery, mode of delivery (natural vaginal or lower uterine segment cesarean delivery), condition of the fetus at birth, and presence of gross anomalies. Women in both the treatment and control arms were monitored for maternal COVID-19 clinical outcomes, as documented and defined according to the 10-point WHO Clinical Progression Scale (Appendix 2) at admission and at predefined time intervals on days 5, 10, 28, and 60. Data on vital signs, oxygen saturation on room air, and oxygen requirement were collected, and laboratory testing for COVID-19 severity markers was performed every 48–72 hours, along with fetal non-stress tests, whenever indicated. After hospital discharge, all patients had telemedicine follow-up on days 14 and 28. Extended follow-up was conducted for patients with severe COVID-19 pneumonia up to day 60.

2.5 Chest X-ray Scoring

A chest radiograph scoring system (on a scale of 1–6) was used where each lung was divided into six zones, with three on each side (upper, middle, and lower). Opacities were classified into reticular, ground glass, patchy, and dense consolidation patterns [16].

2.6 Data Analysis

Data were analyzed using IBM SPSS for Windows version 28.0 (IBM Corp., Armonk, NY, USA). Categorical variables are described using number and proportion. Continuous variables are described using measures of central tendency and dispersion. Continuous data were tested for normality using the Shapiro–Wilk test. The Mann–Whitney test and *t*-test were used to compare means between continuous variables, as appropriate. Categorical variables were cross-tabulated to examine the independence between variables; for these variables, the chi-square or Fisher's exact test were used, as appropriate. Survival curves were generated using the Kaplan–Meier method. A p-value <0.05 was considered significant for all analyses.

3. RESULTS

Between 18 January and 31 March 2021, a sample of 100 hospitalized pregnant women with moderate or severe COVID-19 pneumonia who were admitted to a tertiary care hospital in Dubai were included in this quasi-experimental study. Fifty patients were administered Remdesivir and 50 were given standard therapy at baseline.

The mean±standard deviation (SD) maternal age (years) in the Remdesivir arm was comparable to that of the standard therapy arm: 33.9±4.6 years for those receiving remdesivir and 33.1±5.6 years in those receiving standard therapy. The distribution of UAE nationals and non nationals was comparable in both groups, with 15 (30%) UAE nationals in the treatment (remdesivir) arm and 17 (34%) in the control arm, and 33 (66%) non-nationals in the treatment arm and 33 (66%) in the control arm (Table 1).

Risk factors at admission for complications of COVID-19 were comparable in both arms (Table 1). BMI in both groups was similar for overweight as well as obesity; 29 (58%) women were overweight in the Remdesivir arm compared with 29 (58%) in the control arm, and 17 (34%) were obese in the Remdesivir arm compared with 19 (38%) controls. Only one patient had asthma in the treatment group. One patient in each group had type 2 diabetes mellitus with chronic kidney disease. Eight (16%) patients had gestational diabetes mellitus (GDM) in the remdesivir arm and 11 (22%) in the control arm. Three (6%) patients in the Remdesivir group had chronic hypertension versus one (2%) patient in the control arm (Table 1).

Fig. 1 shows the time to starting Remdesivir from symptom onset and from the date of admission. Remdesivir was initiated in all 50 patients in the remdesivir arm during the first week after admission. Most patients (n=24, 48%) started treatment on the date of admission (day 0), 13 (26%) started on day 1; 4 (8%) on day 2; 3 (6%) on day 3; 4 (8%) on day 4; and 1 (2%) patient each started treatment on day 6 and 8. However, only 6 (12%) patients started remdesivir from days 2–4 after symptom onset, 23 (56%) from days 5–7 after symptom onset, 9 (18%) from days 8–10, and 7 (14%) patients started remdesivir from days 11–16 after symptom onset.

Table 2 shows that according to chest radiograph scoring, prior to treatment, 17 (34%) patients in the remdesivir arm had involvement of fewer than 3 zones and 33 (66%) had involvement of 3 or more zones. In the control arm, 15 (30%) patients had involvement of fewer than 3 zones and 35 (70%) had involvement of 3 or more zones, making both groups comparable in terms of zonal involvement. Post-treatment, 26 (52%) patients in the remdesivir arm and 11 (22%) patients in the control arm had involvement of 3 zones or fewer. Twenty-four (48%) patients in the treatment arm and 36 (72%) in the control arm had involvement of 3 or more zones. In terms of pre treatment X-ray patterns, 22 (44%) patients in the treatment arm had patchy opacities versus 28 (56%) in the control arm, and 6 (12%) patients had consolidation in the remdesivir arm versus 4 (8%) in the control arm. Post-treatment, both groups showed improvement, with 20 (40%) patients in each having patchy opacities. However, 4 (8%) patients had a consolidation pattern post-treatment in the remdesivir arm versus 7 (14%) in the control arm.

Both groups had similar pre- and post-treatment AST levels (Table 2). Pre-treatment mean±SD AST levels in the Remdesivir arm (16.0±34.8 U/L) were comparable to those in the control arm (23.0±48.9 U/L). Post-treatment AST levels were abnormal in both arms, with 23.0±51.0 U/L in the

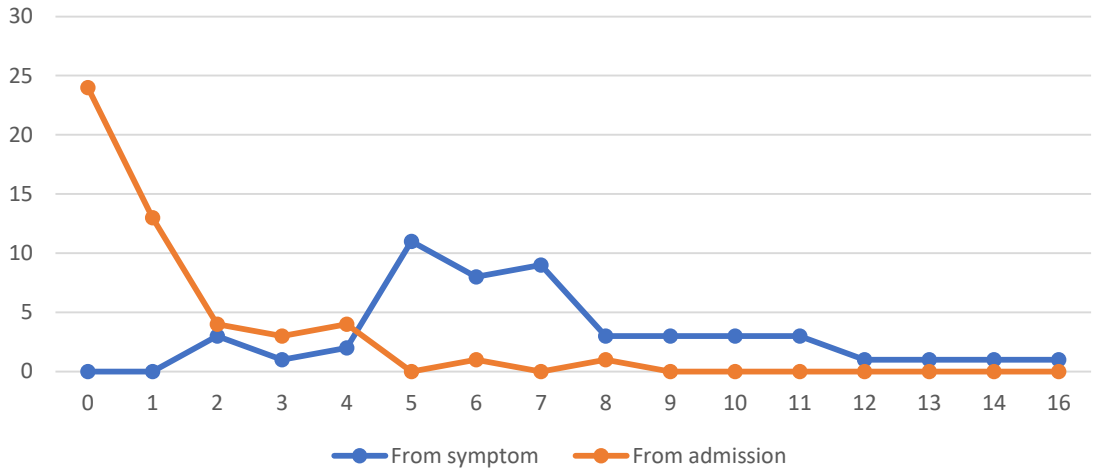

Fig. 1. Delay of starting remdesivir

Legend: This figure shows the delay (in days) in starting Remdesivir in hospitalized pregnant women with COVID-19 illness. The blue line represents the delay in treatment from symptoms onset and the orange line represents the delay in treatment from the admission date The x-axis represents the number of patients, and the y-axis is the number of days

remdesivir arm and 16.0±50.0 U/L in the control arm. However, abnormal ALT levels prior to starting treatment were more pronounced in the remdesivir group (20.0±46.5 U/L) than in the standard care group (13.0±25.5 U/L). Abnormal ALT levels post-treatment were comparable in both groups, with 24.0±51.1 U/L in the remdesivir arm and 18.0±62.1 U/L in the control arm. There was a 1.85 times rise in ALT levels post- versus pre-treatment in the remdesivir arm (Table 2).

In the remdesivir arm, more patients (n=31, 62%) were administered Bioferon as compared with the control arm (n=23, 46%) (Table 3). However, intravenous dexamethasone was administered in significantly fewer patients in the remdesivir arm (n=41, 82%) compared with the control arm (n=49, 98%; p=0.008). Tocilizumab was administered equally in both groups (Table 3).

In the remdesivir arm, all patients (n=50, 100%) recovered and were discharged home versus 42 (84%) women in the control arm (p=0.013). The mean±SD time to recovery and discharge was significantly shorter for patients receiving remdesivir, 8.4±3.3 days as compared with 13.6±9.2 days in the standard care arm (p<0.001). Also, significantly fewer patients were transferred to the ICU in the remdesivir arm: 10 (20%) versus 23 (46%) in the control arm (p=0.002). The readmission rate was comparable in both treatment groups, with 2 (4%) patients in the Remdesivir arm readmitted versus 6 (12%) in the control arm (Table 3).

On admission, 20 (40%) patients in the Remdesivir group were hospitalized with no requirement for oxygen therapy (WHO Clinical Progression Scale score 4), 21 (42%) were hospitalized with oxygen via mask or nasal cannula (WHO scale score 5), and 9 (18%) were on non invasive ventilation (NIV) with high-flow oxygen (WHO scale score 6). Among controls, 20 (40%) patients were hospitalized with no oxygen, 27 (54%) were on oxygen via mask or nasal cannula, 2 (4%) were on NIV with high-flow oxygen, and 1 (2%) patient received mechanical ventilation (WHO scale score 7), as shown in Table 4.

At day 5 after admission, 26 (52%) patients in the Remdesivir arm were asymptomatic and discharged (WHO scale score 1), 5 (10%) were hospitalized but received no oxygen, 9 (18%) were on oxygen via mask or nasal cannula, and 10 (20%) were on high-flow oxygen. Among controls, 4 (8%) patients were discharged (WHO scale scores 0, 1, and 2), 10 (20%) were hospitalized with no need for oxygen therapy, 14 (28%) were on oxygen via mask or nasal cannula, 11 (22%) were on NIV, 6 (12%) were receiving mechanical ventilation, and 5 (10%) patients were intubated and on vasopressors (WHO scale score 8), as shown in Table 4.

In the remdesivir arm at day 10, 46 (92%) patients were discharged (WHO scale score 1), 3 (6%) were hospitalized with low-flow oxygen via nasal cannula, and 1 (2%) patient was on high

flow oxygen; in the control arm, 25 (50%) patients were asymptomatic and discharged (WHO scale scores 1, 2, and 3), 7 (14%) were hospitalized and received no oxygen, 4 (8%) were on oxygen via mask or nasal cannula, 5 (10%) were on NIV, 6 (1%) were on mechanical ventilation, and 3 (6%) patients were ventilated and on inotropic support. At day 28, all 50 (100%) patients in the remdesivir arm were discharged as compared with 42 (84%) in the control arm; 6 (12%) patients in the control arm were still intubated and ventilated, 2 had died, and 4 more died after day 28. At day 60, all patients in the remdesivir arm were alive compared with 44 (88%) in the standard care arm (Table 4).

Of the 100 pregnant women with COVID-19 pneumonia included in this study, data for perinatal outcomes was available for 87 (43 remdesivir and 44 standard care) (Table 5). The mean±SD gestational age in weeks at presentation was significantly lower in the remdesivir group (25.6±7.8) than in the control group (31.1±4.2) weeks (p<0.001). In the remdesivir group, significantly more women had normal vaginal delivery (n=17, 39.5%) than those who received standard care (n=9, 20.5%; p=0.043). Significantly fewer patients on remdesivir had caesarean delivery (n=26, 60.5%) compared with controls (n=35, 79.5%; p=0.043). It is important to note that 10 (23.3%) deliveries in the remdesivir group occurred owing to iatrogenic intervention from worsening COVID-19 (Table 5). However, nearly half of deliveries among women in the control arm (n=21, 47.7%) were owing to worsening COVID-19 in the mother (p=0.015). Pre-term delivery (<37 weeks) was less frequent in the remdesivir group (n=11, 26.5%) whereas more than three-quarters of women in the control arm delivered prematurely (n=31, 70.5%; p<0.001), as shown in Table 5. Similarly, mean±SD birth weight in the remdesivir group (2.92±0.6 kg) was significantly higher than in the control arm (2.56±0.8 kg; p=0.016) (Table 5). Newborns' condition at birth was similar in both groups (Table 5), with similar Apgar scores at 1 and 5 minutes, although this was not significant. There were no major anomalies reported with either the group receiving remdesivir or controls. All newborns of mothers who were COVID-19-positive at delivery were tested using RT PCR within 48 hours of birth, and none tested positive.

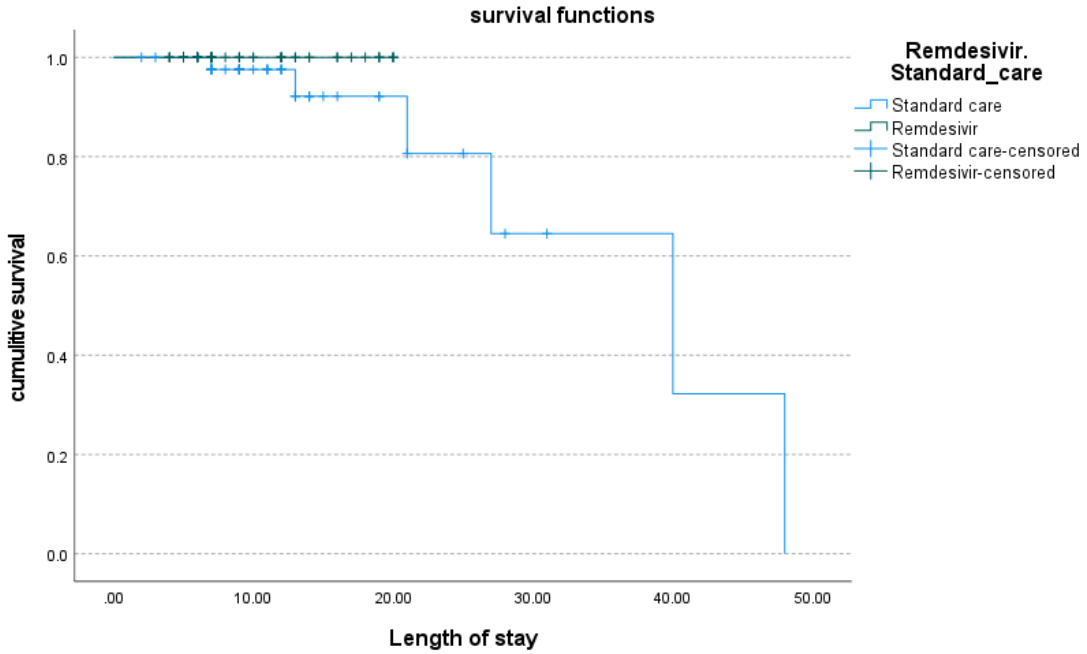

Fig. 2. Kaplan-Meier survival curve for patients treated by Remdesivir or by Standard care

Legend: Kaplan-Meier survival curve (Fig. 2) show that at day 60 all patients receiving Remdesivir were alive whereas 6 deaths occurred in the standard of care group. The median time to death in the control arm was 24 [7 – 48] days

Table 1. Baseline demographics and clinical characteristics of hospitalized pregnant patients with COVID-19

Characteristics	Remdesivir (N = 50)	Standard care (N = 50)	Total (N =100)	p-value
Mean age (SD) – years	33.9 (4.6)	33.1 (5.6)	33.48 (5.12)	0.437
Nationality – no. (%)				
UAE nationals	15 (30)	17 (34)	32 (32)	0.415
Non-UAE nationals	35 (70)	33 (66)	68 (68)	
Risk factors – no (%)	18 (36)	18 (36)	36 (36)	1
Overweight[1]	29 (58)	29 (58)	58 (58)	0.48
Obesity[2]	17 (34)	19 (38)	36 (36)	
Asthma	1 (2)	0	1 (1)	0.2150
Gestational diabetes	8 (16)	11 (22)	19 (19)	0.4472
Type 2 diabetes with CKD	1 (2)	1 (2)	2 (1)	1
Chronic Hypertension	3 (6)	1 (2)	4 (6.7)	<0.001
Admission Oxygen-support no (%)				
< 5 L	18 (36)	11 (22)	29 (29)	
5 – 20 L	7 (14)	24 (48)	31 (31)	<0.001
≥ 20 L	8 (16)	15 (30)	40 (40)	

UAE: United Arab Emirates; SD: standard deviation; CKD: chronic kidney disease; L: liter.
1: BMI 25 to 29.9 kg/m2
2: BMI ≥30 kg/m2

Table 2. Chest X-ray findings and liver enzyme values pre- and post-treatment among hospitalized pregnant patients with COVID-19

	Pre-treatment			Post-treatment		
	Remdesivir (N=50)	**Standard care (N=50)**	**p value**	**Remdesivir (N=50)**	**Standard care (N=50)**	**p-value**
X ray pattern :						
Reticular pattern	17 (34)	7 (14)	0.057	13 (21.3)	17 (34)	0.163
Ground glass opacities	5 (10)	11 (22)		13 (27.7)	6 (12)	
Patchy opacities	22 (44)	28 (56)		20 (42.6)	20 (40)	
Consolidation	6 (12)	4 (8)		4 (8.5)	7 (14)	
X ray zones (n %)						
Mild (<3)	17 (34)	15 (30)		26 (52)	11 (23.4)	
Severe (≥3)	33 (66)	35 (70)	0.415	24 (48)	36 (76.6)	0.003
Mean increase in serum liver levels (SD)						
AST	16 (34.8)	23 (48.9)	0.120	23 (51.1)	16 (50)	0.554
ALT	20 (46.5)	13 (25.5)	0.028	24 (51.1)	18 (62.1)	0.243

AST normal values, 10–-31 U/L; ALT normal values, 10–-32 U/L.
AST, aspartate aminotransferase; ALT, alanine aminotransferase; SD, standard deviation.

Table 3. Concurrent -medications and outcomes among hospitalized patients with COVID-19

Characteristics	Remdesivir (N=50)	Standard care (N=50)	Total (N=100)	p-value
Concurrent -medications –(n %)				
Bioferon	31 (62)	23 (46)	54 (54)	0.08
Tocilizumab	2 (4)	2 (4)	4 (4)	0.691
Dexamethasone (IV)	41 (82)	49 (98)	90 (90)	0.008
Outcomes:				
Mean length of hospital stay (SD)-days	8.43 (3.3)	13.6 (9.2)		<0.001
ICU admission – (n %)	10 (20)	23 (46)	33 (33)	0.002

Characteristics	Remdesivir (N=50)	Standard care (N=50)	Total (N=100)	p-value
Discharged home	50 (100)	42 (84)	92 (92)	0.9336
Discharge outcome at 28 days – (n %)				
Death	0	6 (12)	6 (6)	0.015
Re-admission – (n %)	2 (4)	6 (12)	8 (8)	0.134
Maternal outcome at 60 days – (n %)				
Survival	50 (100)	44 (88)	98 (94)	0.013
Death	0	6 (12)	6 (6)	0.013

UAE, United Arab Emirates; IV, intravenous; ICU, intensive care unit.

Table 4. WHO clinical progression scale for cases and controls from admission to 28 days

WHO-CPS	On admission		5 days		10 days		28 days	
	control	Case	control	case	control	case	control	case
0			1	0				
1			2	26	17	46	42	50
2			1	0	7	0		
3	0	0			1	0		
4	20	20	10	5	7	0		
5	27	21	14	9	4	3		
6	2	9	11	10	5	1		
7	1	0	6	0	6	0	6	0
8			5	0	3	0		
9								
10							2	0

WHO-CPS : WHO clinical progression scale

Table 5. Pregnancy and fetal outcomes of hospitalized patients with COVID-19

Characteristics	Remdesivir (N = 43)	standard care (N = 44)	p-value
Mode of delivery – (n %)			
NVD	17 (39.5)	9 (20.5)	0.043
LSCD	26 (60.5)	35 (79.5)	
Indication of delivery – (n %)			
COVID-19 related	10 (23.3)	21 (47.7)	0.015
Obstetric factor	33 (76.7)	23 (52.3)	
Gestational age at delivery – weeks			
Mean gestational age (SD)	25.6 (7.8)	31.1 (4.2)	< 0.001
Preterm (< 37 weeks) – (n %)	11 (26.5)	31 (70.5)	<0.001
Term- no (%)	30 (73.2)	13 (29.5)	
Mean fetal weight (SD)-kg	2.92 (0.6)	2.56 (0.8)	0.016
Apgar score (1 minute)– no			
≤ 7	8	6	0.15
>7	11	20	
Apgar score (5 minute)– no			
≤ 7	1	1	0.661
>7	26	18	

UAE, United Arab Emirates; SD, standard deviation; kg, kilogram; NVD: Normal vaginal delivery; LSCS, lower (uterine) segment caesarean section; no: number

4. DISCUSSION

Published data have demonstrated that medications used in standard treatment for COVID-19, including hydroxychloroquine and lopinavir-ritonavir, do not lead to a significant reduction in the rate of hospitalization nor in improving patients' clinical outcomes, even when used early in the disease course [17,18]. Data on Remdesivir in pregnant women are limited and

include only a few case reports or case series involving severe or critical COVID-19. The present study was among the first to compare treatment with Remdesivir, irrespective of oxygen saturation, versus standard care among pregnant women with moderate to severe COVID-19 pneumonia. Because pregnant women with moderate illness tend to deteriorate quickly, we opted to begin remdesivir in pregnant patients who showed evidence of lower respiratory infection during clinical assessment or on chest imaging. Treatment was initiated as early as possible after the time of admission, and preferably early after symptom onset with moderate illness, irrespective of the patient's respiration rate or oxygen status.

All 50 patients in the second and third trimester of pregnancy with moderate and severe COVID - 19 were treated with a 5 day course of remdesevir .Remdesevir was started in 20 patients with a WHO Clinical Progression Scale score of 4 and in 21 with a WHO scale score of 5. All 41 patients showed a significant clinical response within 5 days from initiation of remdesivir. The nine treated patients with a WHO scale score of 6 on admission and severe COVID-19 with late presentation also survived. These results are comparable with those of other studies on favorable maternal outcomes with remdesivir therapy in pregnant women [8].

In this study, pregnant women with moderate to severe COVID-19 pneumonia who received Remdesivir as early as within 5 days from the onset of symptoms, or within the first 72 hours after hospital admission irrespective of oxygen saturation, had a more favorable clinical course and shorter hospital stay than pregnant women who received standard care but did not receive remdesivir. The six patients who were delayed remdesivir 72 hours after admission had a delayed clinical recovery and prolonged hospital stay (9–15 days). The delay in starting Remdesivir was mainly attributed to unavailability of remdesivir for several days and maternal hesitancy in taking the medication owing to concerns regarding the safety of the fetus.

In the remdesivir group, 10 patients were transferred to the ICU, 9 of whom presented with severe COVID-19 pneumonia on the day of admission, with a WHO scale score 6; 1 patient presented on admission with a WHO scale score of 5. All patients in the ICU presented late to the hospital, with an average delay from the onset of symptoms of 6.6 days; 1 patient deferred Remdesivir therapy for more than 72 hours after admission.

No deaths occurred in the remdesivir group. Although both groups had similar distributions of age and BMI, the gestational age at presentation was higher in the control arm. Of the six patients who died in the control arm, four were in the third trimester and two were in the late second trimester; two patients had GDM, another two had GDM had morbid obesity (BMI 40 and 41 kg/m^2), and the remaining two had no comorbidities. Among these patients, WHO scale scores on admission were 4 (n=4) and 5 (n=2). All six patients were transferred to the ICU within 48–72 hours owing to worsening respiratory status and were intubated and mechanically ventilated. All six deaths were attributed to severe acute respiratory distress syndrome (ARDS); three patients had septic shock, two had disseminated intravascular coagulation, and one patient had pulmonary embolism.

Both groups received steroids mainly for two indications: fetal lung maturity where intravenous dexamethasone was used from weeks 24–36 of gestation, and an extended course for 5– 7 days for progressive COVID-19 pneumonia with desaturation. The course was extended to 10 days or more for severe patients and those in the ICU [15].

No significant adverse effects were reported in the group receiving remdesivir. At baseline, patients in both groups had abnormal liver enzymes. However, post-treatment, there was no significant increase in liver enzymes in the remdesivir group.

We noted several important observations in our study, including the high number of preterm births, increased rates of caesarean delivery, and less favorable perinatal outcomes in the control arm compared with the remdesivir arm owing to a worsening maternal condition due to COVID-19 infection. Preterm caesarean births were decided with worsening of the mother; these results are comparable to those of other reports during the early months of the COVID-19 pandemic [19,20]. A systematic review including 36 articles showed that COVID-19 status alone was a common indication for caesarean delivery early in the pandemic, despite a lack of evidence regarding vertical transmission. This increase in the rate of caesarean delivery may reflect obstetricians' attempts to save the life of their patients under constantly evolving guidelines [2].

In our sample of 100 patients, there was no evidence of vertical transmission of SARS-CoV-2 from mother to fetus. This is a crucial observation; however, more data are needed to validate this finding. From the limited number of available studies, no assessment can yet be made regarding the rate of vertical transmission in early pregnancy and potential risks for fetal morbidity and mortality [21].

We initiated antiviral therapy in pregnant women with early moderate COVID-19, with or without desaturation, and in those with severe COVID-19 infection, and observed favorable maternal and fetal outcomes. Pregnant women taking remdesivir appear to do better than those receiving standard therapy in terms of ICU admission, the need for intubation and mechanical ventilation, length of hospital stay, and mortality. This study among pregnant women with COVID-19 will be followed by ongoing research including longer follow-up times to investigate the effects of disease severity, concurrent medications, and the long-term effects on mother and fetus in the treatment of COVID 19.

The Findings In a recent systematic review which included 13 observation studies with 113 pregnant women, patients who received remdesivir earlier in the course of the disease with moderate and sever COVID 19 infection had shown better clinical outcome, supports our observations [22].

5. STRENGTHS AND LIMITATIONS

To assure that the Remdesivir and standard care arms were comparable at baseline, in this quasi experimental study, we matched patients for age and BMI, according to WHO Clinical Progression Scale score. However, limitations of this study include the relatively small sample size and lack of available data on long-term effects.

6. CONCLUSIONS

Our findings provide support for initiating antiviral therapy in pregnant women hospitalized with COVID-19 earlier in the course of illness to prevent disease complications and mortality. There is a risk of elevated transaminases in patients treated with remdesivir; however, our findings did not show a significant elevation of liver enzymes. Counseling of pregnant women who are hospitalized with COVID-19 must include the potential benefits of rapid recovery with Remdesivir and favorable perinatal outcomes for both mother and fetus when treatment is initiated early. Pregnant women with moderate and severe COVID-19 would benefit from early treatment with a 5-day course of Remdesivir, ideally started within 48 hours of symptom onset. There is a need for health systems to raise community awareness regarding the seriousness of COVID-19 during pregnancy and the importance of early presentation to the hospital to prevent clinical deterioration and maternal and fetal morbidity and mortality.

Because the benefits clearly outweigh the risks, pregnancy should not be a contraindication for Remdesivir therapy. However, until more studies can confirm the safety and efficacy of Remdesivir in pregnant women with COVID-19 pneumonia, the decision to administer Remdesivir should be made on an individual basis and agreed by a multidisciplinary team with confirmed patient consent.

PATIENT CONSENT AND ETHICAL APPROVAL

Ethical approval for this study was granted on 20 May 2021 by the Institutional Review Board of the Dubai Health Authority (DHA) (approval no. D SREC-05/2021).

All pregnant women with moderate or severe COVID-19 pneumonia who were given remdesivir were counseled. Written informed consent was obtained for treatment with intravenous remdesivir. Patients on remdesivir were allowed to discontinue the trial medication at any time during the study. Because this was a quasi-experimental study design, no informed consent was required from patients receiving standard care, who were given the best available treatment per the hospital protocol prior to Remdesivir approval.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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APPENDIX 1

Drugs and treatment regimens used for women with COVID-19

Generic name	Dose	Duration
Hydroxychloroquine	Two loading doses of 400 mg on day 1 followed by 200 mg twice daily	7-14 days
Chloroquine base	300 mg (base) twice daily	5-7 days
Lopinavir-Ritonavir (200mg/50mg)	400mg/100mg twice daily	5-7 days (maximum 14 days)
Remdesivir	200mg IV on day 1 , followed by 100mg IV	Total duration 5 days
Tocilizumab	4-8 mg/kg (max 400 mg) followed by a second dose after 8-12 hours.	2 doses within 24 hours
PEGylated interferon	180 mcg, maximum of 2 doses 1 week apart	2 doses within one week
Nebulized Interferon	5 million units BD	5-10 days
Low Molecular Weight Heparin (LMWH) [Prophylactic]	According to Body weight: 50-90kg: 40mg once daily. 91-130kg: 60mg once daily. 131-170kg: 80mg once daily.	Till clinical improvement
Low Molecular Weight Heparin (LMWH)-Therapeutic in critical COVID-19pneumonia patients	50-90kg: 40mg twice daily 91-130kg: 60mg twice daily 131-170kg: 80mg twice daily	Till clinical improvement
Methylprednisolone	0.5-1 mg/kg in 2 divided doses	3 days in Non-ICU & 5-7 days in ICU patients.
N-acetyl cysteine	PO 400mg thrice daily Nebulization 200-400mg thrice daily	5-7 days

APPENDIX 2

WHO Clinical Progression scale (reference Marshall JC, Murthy S, Diaz J, Adhikari NK, Angus DC, Arabi YM, Baillie K, Bauer M, Berry S, Blackwood B, Bonten M. A minimal common outcome measure set for COVID-19 clinical research. The Lancet Infectious Diseases. 2020 Aug 1;20(8):e192-7.).

Patient State	Descript	Score
Uninfected	Uninfected; no viral RNA detected	0
Ambulatory mild disease	Asymptomatic; viral RNA detected	1
	Symptomatic; independent	2
	Symptomatic; assistance needed	3
Hospitalised: moderate disease	Hospitalised; no oxygen therapy*	4
	Hospitalised; oxygen by mask or nasal prongs	5
Hospitalised: severe disease	Hospitalised; oxygen by NIV or high flow	6
	Intubation and mechanical	7

Patient State	Descript	Score
	ventilation pO_2/FiO_2≥150 or SpO_2/FiO^2≥200	
	Mechanical ventilation pO_2/FiO_2≥150 (SpO_2/FiO^2≥200) or vasopressors	8
	Mechanical ventilation pO_2/FiO_2≥150 and vasopressors, dialysis, or ECMO	9
Dead	Dead	10

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