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# Maternal death due to severe and critical COVID-19 in Qom, Iran: A case series

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# **ABSTRACT**

**Objective:** To report the maternal death due to COVID-19.

Methods: A total of 14 maternal deaths due to severe and critical COVID-19 who were referred to the obstetric department of Nekouie-Forghani-Hedayati Hospital, Qom, Iran from December 2019 to May 2022 were collected. The clinical manifestations and maternal and perinatal outcomes were analyzed.

**Results:** Dexamethasone was used in 7 cases, while remdesivir was used in 5 cases. Acute respiratory distress syndrome, multiple organ failure, and sepsis were the main cause of mother death. The pregnancy in 8 cases were terminated by caesarean and only one neonatal death was reported from a mother at 13th week of gestational age, while all other fetus delivered were healthy and alive.

**Conclusions:** COVID-19 in pregnancy is an emergency. Critical appraisal is needed to detect the other comorbidities and positive PCR test by throat swap should be performed as soon as possible.

**KEYWORDS:** Maternal death; COVID-19; Newborn; Mother; Mortality; Case series

# 1. Introduction

Patients with coronavirus disease 2019 (COVID-19) have severe acute respiratory syndromes[1]. COVID-19 pandemic causes serious health problems and uncertainty in the management of severe or critically ill pregnant women continually confuses obstetricians[2].

Therefore, it is not surprising that maternal deaths have increased in communities especially in lower-income countries[1,2].

Postpartum maternal death or during pregnancy has a catastrophic impact on families. It is considered one of the human development indexes and is an important indicator of the quality of a health system[3]. Maternal deaths are increased during the COVID-19 pandemic in all countries[1,2,4], such as Iran. COVID-19 is currently the leading cause of 46% of maternal deaths in Mexico during 2021 and this ratio is increased twice compared with the pre-pandemic stage[1].

#### **Significance**

The maternal death occurs during COVID-19 pandemic in Iran due to limited recourses for management in pregnant women. We reported 14 maternal deaths due to severe and critical COVID-19. Acute respiratory distress syndrome, multi organ failure, and sepsis are the most common cause of maternal mortality. On-time appraisal for early diagnosis and treatment is essential for pregnant women with COVID-19.

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Treatment of COVID-19 focuses on infection prevention, control measures, supportive care by oxygen therapy and mechanical ventilator support, and antiviral therapy based on the Centers for Disease Control recommendation[5]. Due to limited information on COVID-19, management of infection and medication in pregnant women is a critical challenge for obstetricians, especially in mothers with other comorbidities[4]. We assessed the clinical manifestations and perinatal outcomes of 14 maternal deaths due to COVID-19 to explore prevention of future deaths.

#### 2. Patients and methods

#### 2.1. Study design

This study is a retrospective single center case series and reported fourteen consecutive maternal deaths due to severe and critical COVID- 19 in pregnant women who were referred to the obstetric department of Nekouie-Forghani-Hedayati Hospital, Qom, Iran from December 2019 to May 2022.

# 2.2. Inclusion and exclusion

These 14 cases were infected with severe and critical COVID-19 and hospitalized in intensive care unit (ICU) or were intubated. Inclusion criteria were death due to COVID-19, having positive PCR, and death occurrence during pregnancy or 6 weeks after pregnancy. Maternal death due to other factors were excluded form study.

# 2.3. Intervention

The national guidelines for COVID-19 by Iran's National Ministry of Health and Medical Education were used and all patients were treated according to WHO and Ministry of Health and Medical Education recommendations[6-8]. Corticosteroid, antiviral, anticoagulant, and other drugs were administered based on national and WHO guidelines[6,7].

#### 2.4. Ethical statement

The present study was performed after approval from the ethical committee of Qom University of Medical Sciences (IR.MUQ. REC.1398.154). Moreover, informed consent was taken from all patients or their families.

# 2.3. Statistical analysis

Measurement data were described as mean and standard deviation or median (Q1, Q3), while categorical data as frequency. SPSS version 20 (SPSS Inc., Chicago, IL, USA) was used.

#### 3. Results

# 3.1. Demographic, clinical, and laboratory characteristics

All of these mothers had dropped SpO<sub>2</sub>, were intubated in the ICU, and finally died. From all, 5 cases (35.7%) were post-partum and admitted to the hospital after delivery.

The demographic, clinical, and laboratory characteristics are presented in Table 1. The mean age of mothers was (32.7±5.5) years and varied between 24 to 40 years. The mean length of hospitalization duration was (13.7±6.9) days (4-28 days). Of all 14 cases, 8 cases were Iranian and 5 of them were Afghan. Five cases were gravida 3 and 4 cases were gravida 1.

The majority of cases (n=9, 64.3%) were of gestational age (GA)  $\ge$ 35 weeks and 5 cases (35.7%) were of longer than 35 weeks. A history of comorbidities and other medical conditions including gestational diabetes mellitus, hypertension, hypothyroidism, urinary tract infection, and other diseases was reported in 7 (50%) cases.

Table 1. Demographic, clinical, and laboratory characteristics.

Items	
Age, year, mean±SD	32.7±5.5
Nationalit, n, %	
Iranian	8 (57.1)
Non Iranian	6 (42.9)
Mother weight, kg, mean±SD	80.3±13.1
BMI, kg/m <sup>2</sup> , mean±SD	$33.04\pm5.73$
Length of stay, d, median, Q1, Q3	15 (7, 17)
SpO <sub>2</sub> , %, mean±SD	$83.7 \pm 16.5$
Neonatal Apgar at 5th min, mean±SD	$7.9\pm2.9$
Gravida, n, %	
G1	4 (28.6)
G2	2 (14.3)
G3	5 (35.7)
G4 and higher	3 (21.4)
Gestational age, $n$ , %	
≤30 weeks	5 (35.7)
30-34 weeks	5 (35.7)
≥35 weeks	4 (28.6)
Comorbidities and other medical conditions, $n$ , %	
None	7 (50.0)
GDM, HTN, hypothyroidism, UTI and others	7 (50.0)
Laboratory results on admission	
WBC, $\times 10^3 / \mu L$ , mean $\pm SD$	11.1±4.1
ALT, U/L, median, Q1, Q3	28.0 (15.5, 44.8)
AST, U/L, median, Q1, Q3	47.5 (28.3, 77.0)
Creatinine, mg/dL, mean±SD	$1.18\pm0.81$
INR, mean±SD	$1.14\pm0.11$
d-Dimer, μg/L, mean±SD	2025±1666

BMI: body mass index; GDM: gestational diabetes mellitus; HTN: hypertension; UTI: urinary tract infection; WBC: white blood cell; ALT: alanine transaminase; AST: aspartate aminotransferase; INR: international normalized ratio.

Maternal death due to COVID-19

Table 2. Treatment and outcomes

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Variables	n	%
Medication		
Corticosteroid		
Dexamethasone	7	50.0
Interferon beta-1b	4	28.6
Methylprednisolone	5	
Hydrocortisone	3	21.4
Antiviral drugs		
Atazanavir	2	14.3
Remdesivir	5	35.7
Ritonavir, caletra, oseltamivir, IVIG, atazanavir, recigen,	1	7.1
plasmapheresis, actemra		
Anticoagulant		
Enoxaparin sodium	8	57.1
Heparin	4	28.6
Azithromycin	5	35.7
Vancomycin	7	50.0
Ceftriaxone	5	35.7
Tazocin	6	42.9
Meropenem	3	21.4
Other (Linezolid, clotrimazole, etc)	1	7.1
Causes of mother death		
ARDS	4	28.6
Multiple organ failure	5	35.7
Sepsis	5	35.7
Modes of delivery		
CS	8	57.1
NVD	6	42.9
Neonatal outcomes		
Abort NVD	1	7.1
Alive	13	92.9

ARDS: acute respiratory distress syndrome; CS: caesarean; NVD: normal vaginal delivery.

#### 3.2. Treatment and outcomes

The treatment and outcomes are presented in Table 2. The most commonly used corticosteroid was dexamethasone that used in 7 cases (50%). Remdesivir and enoxaparin sodium were the more commonly used antiviral and anticoagulant drugs that were used in 5 (35.7%) and 8 (57.1%) cases, respectively. Acute respiratory distress syndrome (ARDS), multiple organ failure, and sepsis were main cause of maternal death. Although, in 5 cases a combination of ARDS, multiple organ failure, and sepsis were the cause of death.

#### 3.3. Outcomes of babies

The mean Apgar score at the 5th minute after delivery was  $7.9\pm2.3$  and the median was 9.3 (7.3, 9.5). The pregnancy in 8 (57.1%) ases was terminated by cesarean and only one neonatal death was reported that was delivered from a mother at the 13th week of GA, while all other fetuses delivered were healthy and alive (Table 2).

#### 4. Discussion

COVID-19 is an important cause of preterm birth during pregnancy based on previous study results[9]. Moreover, maternal deaths due to COVID-19 was associated with non-Iranian ethnicity, preterm birth, perinatal death, and cesarean. Mother comorbidities such as preeclampsia, diabetes, hypertension, and hypothyroidism were probable risk factors for maternal death[9].

However, despite some studies on COVID-19 in pregnancy, there was no sufficient data to draw unbiased conclusions regarding vertical transmission as well as perinatal and neonatal complications of pregnant women<sup>[10]</sup>. Moreover, insufficiently equipped hospital and healthcare facilities and resources for the management of COVID-19 in pregnant women including testing capacity, negative pressure isolation rooms, and ICU, operating rooms in middle-income countries such as Iran are limitations of management of the disease<sup>[4]</sup>.

Based on our experience in the obstetric department, we recommended that the following concerns should be considered when treating pregnant women with positive PCR COVID-19. Firstly, thromboprophylaxis should be considered and administered. Second, in patients with severe and critical COVID-19, treatment with remdesivir and steroids should start without any delay. Third, the medication and management of COVID-19 in pregnant women should be individualized based on the presence of comorbidities or accompanying diseases. And finally, the probability of vertical transmission and social supporting effect of the family on prognoses of disease should also be taken into account[4]. Although the incidence of vertical transmission of COVID-19 is low, pregnancies with COVID-19 should be carefully monitored to prevent neonatal infection[9,11,12].

COVID-19 in pregnancy is usually an emergency. Critical appraisal of comorbidities is needed and a positive PCR test by throat swap should be performed as soon as possible. Moreover, educational programs for families should be implemented to treat pregnant women with respiratory distress on time and minimize the stress of vertical transmission.

#### **Conflict of interest statement**

The authors declare no conflict of interest.

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# **Authors' contributions**

AA and AM worked in concept and design of study and preparing the article draft. MY, MM, RA, ZY, MS and FB worked in acquisition and interpretation of data as well as management of cases. All authors read and approved the final manuscript.

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