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OBSTETRICS

New-onset myocardial injury in pregnant patients with coronavirus disease 2019: a case series of 15 patients



Brisandy Ruiz Mercedes, MD; Ayna Serwat, MBBS; Lena Naffaa, MD; Nairovi Ramirez, MD; Fatima Khalid, MBBS; Sofia B. Steward, MD; Omar Gabriel Caro Feliz, MD; Mohamad Bassam Kassab, MD; Lina Karout, MD

BACKGROUND: Severe acute respiratory syndrome coronavirus 2 is the new coronavirus responsible for the coronavirus disease 2019 pandemic, characterized by acute respiratory distress syndrome and atypical pneumonia. In nonpregnant women, studies have shown that severe acute respiratory syndrome coronavirus 2 causes cardiac injury, which can result in myocardial inflammation and damage. Despite many studies investigating the extent of cardiac compromise in patients with severe coronavirus disease 2019, little is known regarding its impact on pregnant women.

OBJECTIVE: This study aimed to illustrate the clinical, laboratory, radiologic findings and outcomes of pregnant patients with coronavirus disease 2019 who developed myocardial injury with ventricular dysfunction.

STUDY DESIGN: We retrospectively reviewed the paper records of 15 pregnant women with coronavirus disease 2019, who developed myocardial injury on a single tertiary care hospital in the Dominican Republic. Patients' baseline characteristics, clinical picture, and laboratory and radiologic findings were presented, and maternal and fetal outcomes were analyzed.

RESULTS: Of 154 pregnant patients diagnosed as having coronavirus disease 2019 at our hospital during the study period, 15 (9.7%), developed myocardial injury. These patients' mean age and gestational age were 29.87 ± 5.83 and 32.31 ± 3.68 , respectively. Furthermore, 66.7% of patients presented with shortness of breath and 16.3% with palpitations. All patients were admitted to the intensive care unit, and 86.6% needed intubation. Patients developed myocardial injury, confirmed with highly elevated troponin ($34.6 [14.4-55.5 \text{ ng/mL}]$), and pro-B-type natriuretic peptide concentrations ($209 [184-246 \text{ pg/mL}]$). In addition, all patients developed left ventricular dysfunction demonstrated by an echocardiogram with a mean left ventricular ejection fraction of 37.67 ± 6.4 . Unfortunately, 2 patients who presented with palpitations died a few days after admission.

CONCLUSION: Our study showed coronavirus disease 2019 induced myocardial injury and left ventricular dysfunction in pregnant women with a 13.3% mortality rate, which was attributed to malignant arrhythmias.

Key words: cardiovascular disease, coronavirus, coronavirus disease 2019, myocardial injury, pregnancy, severe acute respiratory syndrome coronavirus 2, ventricular dysfunction

Introduction

Severe acute respiratory syndrome coronavirus (SARS-CoV-2) is the new coronavirus responsible for the coronavirus disease 2019 (COVID-19), which was declared a global public health emergency by the World Health Organization on March 11, 2020.¹⁻³ As of August 9, 2020, more than 19 million confirmed cases of COVID-19 had been reported globally, with 727,317 deaths.⁴ Emerging studies demonstrated the harmful effects of SARS-CoV-2 on the cardiovascular (CV) system, such as myocardial injury, which is associated with myocardial inflammation and damage.⁵ Almost 33% of nonpregnant

patients with COVID-19 admitted to the intensive care unit (ICU) developed cardiac injury.⁶ Despite many studies investigating the effect of COVID-19 on adult patients' heart, little is known regarding its impact on pregnant women.

Pregnancy leads to physiological, immunologic, and mechanical changes that increase susceptibility to infectious respiratory organisms, predisposing to more severe illnesses.⁷ Angiotensin-converting enzyme 2 (ACE-2) receptors are believed to be the door for SARS-CoV-2 entry into the host cells. Interestingly, ACE-2 receptors expression is increased during pregnancy. SARS-CoV-2 down-regulates ACE-2 receptors, eliminating its cardioprotective effect and leading to increasing concentrations of tumor necrosis factor- α and inflammation, which could be the possible cause of myocardial dysfunction in pregnant and nonpregnant patients with COVID-19.⁵ In recent COVID-19 surveillance by the Centers for Disease

Control and Prevention (CDC), pregnant women were more likely to require hospitalization than nonpregnant women (31.5% vs 5.8%, respectively).

Moreover, pregnant women were significantly more likely to be admitted to the ICU and receive mechanical ventilation (adjusted relative risk [RR], 1.5; 95% confidence interval [CI], 1.2-1.8) than nonpregnant patients who are COVID-19 positive.⁷ Interestingly, there is a lack of studies investigating the effect of COVID-19 on pregnant women's CV system. To our knowledge, only 1 study by Juusela et al⁸ showed the occurrence of cardiomyopathy in pregnant women with COVID-19; according to their results, of 7 pregnant women with COVID-19, 2 developed cardiac dysfunction (RR, 28.6; 95% CI, 8.2-64.1) with moderately reduced left ventricular ejection fraction (LVEF) of 40% to 45% and hypokinesis. Therefore, it is crucial to understand the impact of COVID-19 on the heart of pregnant women. This case series aimed

Cite this article as: Mercedes BR, Serwat A, Naffaa L, et al. New-onset myocardial injury in pregnant patients with coronavirus disease 2019: a case series of 15 patients. *Am J Obstet Gynecol* 2021;224:387.e1-9.

0002-9378/\$36.00

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<https://doi.org/10.1016/j.ajog.2020.10.031>

AJOG at a Glance

Why was this study conducted?

This study aimed to assess the characteristics and outcomes of coronavirus disease 2019 (COVID-19) and myocardial dysfunction in 15 pregnant patients.

Key findings

In this study, 15 patients diagnosed with COVID-19 developed myocardial injury. In addition, 66.7% of patients presented with shortness of breath and 16.3% with palpitations. All patients needed to be transferred to the intensive care unit. Furthermore, 86.6% of patients were intubated. All patients had myocardial dysfunction with highly elevated troponin and B-type natriuretic peptide concentrations. All patients developed left ventricular dysfunction. Unfortunately, 2 patients died because of torsades de pointes and sustained supraventricular tachycardia.

What does this add to what is known?

This study illustrates the clinical and baseline characteristics of pregnant women who developed COVID-19–induced myocardial injury. Although our patients were previously healthy with no cardiovascular risk factors and diseases, they developed severe COVID-19–induced myocardial injury and ventricular dysfunction.

to describe the baseline and clinical characteristics, laboratory and radiologic findings, and outcomes of 15 pregnant women admitted to a single tertiary care hospital with COVID-19 and who developed myocardial injury. Investigating these cases would help provide a better understanding of possible risk factors of COVID-19 in the pregnant population and provide data to possibly help in counseling pregnant women with such complications.

Materials and Methods**Study population and design**

To determine the clinical characteristics and evolution of myocardial injury in pregnant patients with critical COVID-19, we conducted a single-center, retrospective observational study between March 20, 2020, and June 30, 2020, in an obstetrical tertiary level hospital in Santo Domingo, Dominican Republic. The study population consisted of 15 pregnant patients admitted to the hospital with confirmed COVID-19 by real-time reverse transcription-polymerase chain reaction (RT-PCR) assay of nasopharyngeal swab specimens and who developed myocardial injury. The study was approved by the institutional review

board and the bioethics committee of the Public Health Ministry of the Dominican Republic (CONABIOS) before accessing the data, and informed consent was obtained.

Data collection

Data from the paper records in the hospital archives section were retrieved after patient discharge or death. Data consisted of prenatal demographics and clinical characteristics, laboratory electrocardiogram (ECG) and radiologic findings, and patient outcomes.

Patients' baseline and clinical characteristics consisted of patients' age, body mass index, presence of chronic diseases, gestational age (GA), Gravida-parabortion-cesarean delivery (GPAC), and prenatal course, in addition to patients' chief complaint (CC), CC duration, ICU admission, and need for intubation.

Laboratory findings consisted of cardiac enzymes: cardiac troponin I and N-terminal pro-B-type natriuretic peptide (NT-proBNP) with normal concentration being <0.4 ng/mL and <100 pg/mL, respectively. As per the Academic College of Cardiology recommendations, patients were considered to have myocardial injury if troponin

concentration were above the 99th percentile upper reference limit, >0.4 ng/mL.⁹

ECG measurement consisted of rhythm, presence of bundle branch block (BBB), ST elevation, and T-wave inversion. Radiologic findings of chest radiographs (X-rays) consisted of the presence of consolidation, ground glass, and cardiothoracic index (CTI), whereas transthoracic echocardiography (TTE) measurements consisted of LVEF, left ventricular (LV) dilation, left atrial dilation (LAD), and LV hypokinesis. LV dysfunction was considered in patients with a LVEF of $\leq 49\%$.¹⁰

We also recorded information related to the mode of delivery and GA. Maternal and infant outcomes, neonate weight (kg), length (cm), and activity, pulse, grimace, appearance, and respiration (Apgar) scores at 0 and 5 minutes and whether they were admitted to the neonatal intensive care unit (NICU). An Apgar score was considered reassuring if 7 to 10, moderately abnormal if 4 to 6, and low if 0 to 3.¹¹

Statistical analysis

Analyses were conducted using Statistical Package for the Social Sciences (SPSS) for Windows (version 24; SPSS Inc, IBM, Chicago, IL). Categorical variables are presented as frequencies with percentages, and continuous variables are presented as means \pm standard deviations for normally distributed values and median and interquartile ranges (IQRs) for nonnormally distributed values.

Results

Among 154 symptomatic pregnant patients that attended our hospital with COVID-19 between March 20, 2020, and June 30, 2020, 77 (50%) had moderate disease and were admitted to the hospital floor, 34 (22%) had severe disease and needed ICU admission, and 15 (9.7%) developed myocardial injury with LV dysfunction.

Baseline and clinical characteristics

The patients were 29.87 ± 5.83 years old and at 32.31 ± 3.68 weeks of gestation. All

patients were previously healthy, and only 13.3% had prenatal bleeding (Table 1). From 15 patients, 66.6% presented to the hospital with shortness of breath (SOB), 13.3% with palpitations, 13.3% with decreased fetal movement (DFM), and 6.6% with fatigue. Patients were admitted to the hospital approximately 9.93 ± 3.13 days after the start of symptoms. All patients had severe disease and were admitted to the ICU, and 86.6% of the patients were intubated.

Laboratory, electrocardiogram, and radiographic findings

All patients tested positive for SARS-CoV-2 by PCR and had reactive COVID enzyme-linked immunosorbent assay immunoglobulin G. All patients had elevated cardiac enzymes were the median and IQR for troponin and proBNP were 34.6 (14.4–55.5 ng/mL) and 209 (184–246 pg/mL), respectively (Table 2). Almost 55% of patients had abnormal ECG findings, where 13.3% had irregular rhythms, 33.3% BBB, 40% ST depression, and 40% T-wave inversion. In terms of patients' chest X-rays, all patients had lung consolidation, and 6 (40%) had ground-glass opacities. The CTI of patients were 0.5 ± 0.06 . In terms of patients' TTE, all patients had abnormal findings, where all presented with LV dysfunction with a mean LVEF of 37.67 ± 6.4 and LV diffuse hypokinesis. In addition, 20% had LAD and 13% LV dilation.

Maternal and infant outcome

All patients were delivered by cesarean delivery, where 60% were delivered prematurely. The mean GA at delivery was 34.2 ± 4 weeks of gestation. From 15 patients, 13.3% died after delivery because of malignant arrhythmias (ventricular tachycardia and torsade de pointes). One clinically unstable mother was delivered at 23.3 weeks of gestation by an emergent cesarean delivery because of a significant decrease in fetal heart rate; the child was delivered and was unresponsive with an Apgar score of 0 at 0 and 5 minutes. No autopsy or additional test was performed to determine the cause of death (Table 3). A great proportion of patients had to deliver

their babies prematurely (60%) because of their unstable clinical (unstable vitals, severe hypoxemia arrhythmia) condition and fetal bradycardia. This was decided when the physician believed that the continuation of pregnancy results in danger of the mother and fetus's life.

From 14 infants, 5 (35.7%) had low birthweight (weight of < 2.5 kg), and 1 (7.1%) had very low birthweight (< 1.5 kg). Furthermore, 8 infants (57%) had a reassuring Apgar score at 0 and 5 minutes, 3 (21.5%) had a moderately depressed Apgar score at 0 minutes and a reassuring score at 5 minutes, and 3 (21.5%) had a moderately depressed score at 0 and 5 minutes. In addition, 5 (35.7%) infants were admitted to the NICU (premature infants with low birthweight) and discharged later.

Discussion

Principal findings of the study

Our study showed the different baseline and clinical characteristics, laboratory and radiologic findings, and outcomes of 15 pregnant women with confirmed COVID-19 who developed myocardial injury with LV systolic dysfunction. The patients were young, previously healthy women in the third trimester of pregnancy. The most common hospital presentation was SOB, followed by palpitations. All of them had a positive RT-PCR test and chest X-ray confirming COVID-19. Cardiac injury biomarkers were elevated in the 15 cases, with some showing ECG changes and all having decreased LVEF. All patients were critical ill and were admitted to the ICU, and 13 (86.6%) were intubated. Unfortunately, 2 patients (13.2%) died a few days after admission owing to arrhythmia.

Results of the study in the context of what is known

There is a surge in studies demonstrating the harmful effects of COVID-19 on the CV system.¹² In nonpregnant women, COVID-19 has been associated with cardiovascular diseases (CVD), such as myocarditis, acute myocardial infarction, cardiomyopathy, arrhythmias, and venous thromboembolic events.¹² Myocardial injury is the most common reported CV event in patients with

COVID-19 and is independently associated with high mortality.^{12,13} Myocardial injury with elevated cardiac markers occurred in 7% to 17% of patients hospitalized with COVID-19 and 22% to 31% in more severe cases admitted to the ICU.¹² In a cohort study of 191 symptomatic hospitalized patients with COVID-19, 33 (17%) developed myocardial injury in which 32 (97%) died.¹³ This high mortality rate can be attributed to the fact that 63% of 191 patients with COVID-19 had severe or critical disease status. In another study, 20% of patients with COVID-19 developed myocardial injury, and they were 5 times more likely to need mechanical ventilation and 11 times more likely to die compared with patients without cardiac complications.¹³ There are several mechanisms of myocardial injury, with myocarditis or systemic inflammation being the most common. It is worth noting that all of these findings were in nonpregnant women with COVID-19 with limited studies investigating the CV effect of COVID-19 in pregnant women. To our knowledge, there is only 1 study that shows the cardiac effect of COVID-19 in pregnancy.⁸ In this case series, 2 pregnant women with COVID-19 developed cardiac dysfunction with moderately reduced LVEF (40%–45%) and hypokinesis. These 2 patients were previously healthy with some CV risk factors, such as race and ethnicity or obesity, and 1 patient had advanced maternal age. Both patients delivered their babies by cesarean delivery and were isolated in negative-pressure rooms. The outcome was still unknown as, at the time of article writing, they were still admitted to ICU and were recovering. Similarly, in our study, of 154 pregnant women with COVID-19 referred to the hospital, 15 (9.7%) developed myocardial injury with reduced LVEF, which ranged from 22% to 45% with a 37.67 ± 6.4 mean. All 15 cases had very high elevated troponin and BNP concentrations with or without ECG changes and were admitted to the ICU. It is unknown whether the incidence of cardiac injury in these patients is due to the direct effect of SARS-CoV-2 virus or secondary to multiorgan failure

TABLE 1
The baseline and clinical characteristics of 15 pregnant women with COVID-19–induced myocardial injury

| Patient | Baseline characteristic | | | Gestation | | | Hospitalization | | | |
|---------|-------------------------|--------------------------|-------------------------------|------------|---------|----------------------------|---|-----------------|---------------------------|---------------------|
| | Age (y) | BMI (kg/m ²) | Chronic diseases | GA (wk) | GPAC | Prenatal period | CC | CC duration (d) | ICU admission | Intubated |
| 1 | 31 | 32 | None | 35.0 | 4-3-0-0 | Normal | SOB | 12 | Yes | Yes |
| 2 | 33 | 28 | None | 33.0 | 3-1-1-0 | Bleeding | DFM | 13 | Yes | Yes |
| 3 | 26 | 26 | None | 36.0 | 2-0-0-1 | Normal | SOB | 9 | Yes | Yes |
| 4 | 29 | 30 | None | 29.0 | 2-0-0-1 | Normal | Palpitations | 9 | Yes | Yes |
| 5 | 22 | 24 | None | 29.5 | 1-0-0-0 | Normal | Fatigue | 8 | Yes | No |
| 6 | 26 | 29 | None | 32.2 | 5-3-1-0 | Normal | SOB | 6 | Yes | Yes |
| 7 | 36 | 23 | None | 36.5 | 3-0-0-3 | Normal | SOB | 12 | Yes | Yes |
| 8 | 38 | 31 | None | 33.1 | 2-0-1-0 | Normal | SOB | 12 | Yes | Yes |
| 9 | 32 | 27 | None | 30.4 | 4-0-3-0 | Bleeding | SOB | 13 | Yes | Yes |
| 10 | 35 | 26 | None | 34.0 | 2-0-0-1 | Normal | SOB | 13 | Yes | Yes |
| 11 | 19 | 28 | None | 28.0 | 1-0-0-0 | Normal | SOB | 13 | Yes | No |
| 12 | 21 | 27 | None | 23.3 | 1-0-0-0 | Normal | DFM | 11 | Yes | Yes |
| 13 | 33 | 30 | None | 36.2 | 1-0-0-0 | Normal | SOB | 3 | Yes | Yes |
| 14 | 35 | 29 | None | 33.0 | 1-0-0-0 | Normal | Palpitations | 9 | Yes | Yes |
| 15 | 32 | 32 | None | 35.4 | 1-0-0-0 | Normal | SOB | 6 | Yes | Yes |
| Total | 29.87±5.83 | 28.00±2.60 | 15 (100.0) previously healthy | 32.31±3.68 | — | 2 (13.3) prenatal bleeding | 10 (66.6) SOB 2 (13.3) palpitations 2 (13.3) DFM 1 (6.6) fatigue | 9.90±3.13 | 15 (100.0) ICU admissions | 13 (86.6) intubated |

Data are presented as mean±standard deviation or number (percentage).

BMI, body mass index; CC, chief complaint; COVID-19, coronavirus disease 2019; DFM, decreased fetal movement; GA, gestational age; GPAC, gravida, para, abortus, cesarean delivery; ICU, intensive care unit; SOB, shortness of breath.

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TABLE 2
Demonstrate blood tests, ECG, and radiologic findings of 15 pregnant women with myocardial injury

| Patient | Blood test | | | | ECG | | | | Chest X-ray | | | TTE | | | |
|--|--------------------------------------|---------------------------------|--|---|--|------------------|----------------------------|----------------------------------|---------------------------------------|-----------------------------------|------|---|------------------|------------------|--|
| | COVID PCR | COVID ELISA IgM | Troponin (ng/mL) | ProBNP (pg/mL) | Rhythm | BBB | ST depression | T-wave inversion | Consolidation | Ground glass | CTI | LVEF | LAD | LVD | LV diffuse hypokinesia |
| 1 | Positive | Reactive | 14 | 150 | Regular | Yes | Yes | Yes | Yes | Yes | 0.50 | 37 | No | No | Yes |
| 2 | Positive | Reactive | 9.8 | 184 | Regular | No | Yes | Yes | Yes | Yes | 0.49 | 40 | No | No | Yes |
| 3 | Positive | Reactive | 15 | 209 | Regular | No | No | No | Yes | No | 0.50 | 40 | No | No | Yes |
| 4 | Positive | Reactive | 641 | 566 | Irregular | Yes | Yes | Yes | Yes | Yes | 0.66 | 22 | Yes | Yes | Yes |
| 5 | Positive | Reactive | 13 | 135 | Regular | No | No | Yes | Yes | No | 0.48 | 38 | No | No | Yes |
| 6 | Positive | Reactive | 189 | 308 | Regular | No | No | No | Yes | Yes | 0.50 | 35 | No | No | Yes |
| 7 | Positive | Reactive | 45 | 225 | Regular | No | No | No | Yes | No | 0.50 | 39 | No | No | Yes |
| 8 | Positive | Reactive | 13 | 246 | Regular | No | No | Yes | Yes | No | 0.48 | 42 | No | No | Yes |
| 9 | Positive | Reactive | 12 | 233 | Regular | No | No | No | Yes | No | 0.49 | 44 | No | No | Yes |
| 10 | Positive | Reactive | 55 | 144 | Regular | No | No | No | Yes | No | 0.45 | 37 | No | No | Yes |
| 11 | Positive | Reactive | 35 | 204 | Regular | Yes | Yes | No | Yes | No | 0.44 | 45 | No | No | Yes |
| 12 | Positive | Reactive | 20 | 243 | Regular | Yes | Yes | No | Yes | No | 0.48 | 38 | No | No | Yes |
| 13 | Positive | Reactive | 35 | 166 | Regular | No | No | No | Yes | Yes | 0.49 | 43 | No | No | Yes |
| 14 | Positive | Reactive | 750 | 423 | Irregular | Yes | Yes | Yes | Yes | Yes | 0.68 | 25 | Yes | Yes | Yes |
| 15 | Positive | Reactive | 44 | 198 | Regular | No | No | No | Yes | No | 0.46 | 40 | Yes | No | Yes |
| Total | 5 (100.0) PCR-positive results | 15 (100.0) reactive cases | 15 (100.0) elevated troponin levels | 15 (100.0) elevated ProBNP levels | 2 (13.3) irregular rhythms | 5 (33.0) BBBs | 6 (40.0) ST depressions | 6 (40.0) T-wave inversions | 15 (100.0) consolidations | 6 (40.0) ground-glass cases | 0.50 | 37±6 | 3 (20.0) LADs | 2 (13.3) LVDs | 15 (100.0) LV diffuse hypokinesia cases |
| All patients have COVID-19 with elevated cardiac enzymes | | | | | 8 (53.3) had abnormal ECG, 7 (46.6) had a normal ECG | | | | All patients had abnormal chest X-ray | | | All patients had abnormal TTE with LV dysfunction | | | |

Data are presented as mean±standard deviation or number (percentage).

BBB, bundle branch block; chest X-ray, chest radiograph; COVID-19, coronavirus disease 2019; CTI, cardiothoracic index; ECG, electrocardiogram; ELISA, enzyme-linked immunosorbent assay; IgM, immunoglobulin G; LAD, left atrial dilation; LV, left ventricle; LVD, left ventricular dilation; LVEF, left ventricular ejection fraction; PCR, polymerase chain reaction; proBNP, pro-B-type natriuretic peptide; TTE, transthoracic echocardiography.

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TABLE 3
Demonstrates delivery information of maternal and infant outcomes

| Patient | Delivery | | | Outcome | | Infant | | | | |
|---------|----------|--------------------------------|---|--------------------------|----------------------|-------------|-------------|--|------------------------------|--------------------------|
| | GA (wk) | Mode of delivery | Reason for delivery | Maternal | Infant | Length (cm) | Weight (kg) | Apgar at 0 and 5 min | Apgar interpretation | NICU admission |
| 1 | 37 | Cesarean delivery | Clinical instability | Recovered | Healthy | 47 | 2.9 | 7/8 | Normal | No |
| 2 | 35.3 | Cesarean delivery | Clinical instability | Recovered | Healthy | 45 | 2.3 | 6/8 | Moderate depressed or normal | No |
| 3 | 38 | Cesarean delivery | Previous cesarean delivery | Recovered | Healthy | 47 | 2.6 | 8/9 | Normal | No |
| 4 | 29 | Cesarean delivery | Fetal bradycardia | Death | Healthy | 37 | 1.2 | 5/6 | Moderate depressed or normal | Yes |
| 5 | 33 | Cesarean delivery | Clinical instability | Recovered | Healthy | 42 | 2.1 | 5/6 | Moderate depressed | Yes |
| 6 | 35.2 | Cesarean delivery | Clinical instability | Recovered | Healthy | 48 | 2.9 | 7/8 | Normal | No |
| 7 | 39 | Cesarean delivery | Previous cesarean delivery | Recovered | Healthy | 48 | 3 | 7/8 | Normal | No |
| 8 | 35.2 | Cesarean delivery | Clinical instability | Recovered | Healthy | 48 | 2.7 | 7/8 | Normal | No |
| 9 | 32 | Cesarean delivery | Clinical instability | Recovered | Healthy | 43 | 1.7 | 5/6 | Moderate depressed | Yes |
| 10 | 37 | Cesarean delivery | Previous cesarean delivery | Recovered | Healthy | 47 | 2.5 | 7/8 | Normal | No |
| 11 | 31 | Cesarean delivery | Clinical instability | Recovered | Healthy | 42 | 1.5 | 5/6 | Moderate depressed | Yes |
| 12 | 23.3 | Cesarean delivery | Clinical instability or fetal bradycardia | Recovered | Death | 26 | 0.3 | 0 | — | |
| 13 | 38 | Cesarean delivery | Clinical instability | Recovered | Healthy | 49 | 3.1 | 7/8 | Normal | No |
| 14 | 33.3 | Cesarean delivery | Fetal bradycardia | Death | Healthy | 43 | 1.9 | 6/8 | Moderate depressed or normal | Yes |
| 15 | 37 | Cesarean delivery | Clinical instability | Recovered | Healthy | 49 | 3 | 7/8 | Normal | No |
| Total | 34.2±4.0 | 15 (100.0) cesarean deliveries | 9 (60.0) Clinical Instability 3 (20.0) fetal bradycardias 3 (20) previous cesarean deliveries | 2 (13.3) maternal deaths | 1 (6.6) fetal demise | 44.0±5.0 | 2.2±0.7 | 8 (57.0) had a normal Apgar at 0 and 5 min 3 (21.5) had a moderate depressed Apgar at 0 min and a normal Apgar at 5 min 3 (21.5) had a moderate depressed Apgar at 0 and 5 min | | 5 (35.7) NICU admissions |

Data are presented as mean±standard deviation or number (percentage). Normal Apgar, 7 to 10; moderate depressed Apgar, 4 to 6; severe depressed Apgar, 0 to 3.

Apgar, activity, pulse, grimace, appearance, respiration; GA, gestational age; NICU, neonatal intensive care unit.

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due to the overwhelming critical illness. Older patients with COVID-19 and comorbidities are more likely to develop cardiac injury. Interestingly, our patients were young, previously healthy females with minimal CV risk factors; this makes a statement regarding the impact of COVID-19 in the CV system. It can cause cardiac compromise, even in the absence of previous CVD. It is worth mentioning that 2 studies showed that the prevalence of acute myocardial injury in patients with COVID-19 increased patients' mortality significantly more than age, previous CVD, CV risk factors, and chronic pulmonary disease.^{6,14} Therefore, it is essential to identify cardiac injury in pregnant patients to avoid complications early in their disease course.

Arrhythmia and sudden cardiac arrest are also common CV complications of patients with COVID-19.^{13,15} A Chinese study of 138 hospitalized patients with COVID-19 showed that 23 patients (16.7%) developed arrhythmias and 16 patients (69.5%) required ICU admission.¹⁵ Over 7% of patients with COVID-19 present with palpitations.¹³ Studies have shown a range of arrhythmias in patients with COVID-19 with sinus tachycardia being the most common type.¹³ This fact is consistent with our findings because 26.6% of patients had sinus tachycardia and 13.3% had atrial fibrillation. Unfortunately, the 2 patients who presented with atrial fibrillation had an emergency cesarean delivery and died 3 and 6 days after hospitalization because of torsade de pointes and sustained ventricular tachycardia. In our study, the new-onset atrial fibrillation in patients with respiratory distress syndrome is associated with an increase in the 90-day mortality.¹⁶ In contrast, in the study by Juusela et al,⁸ 1 patient developed supraventricular tachycardia and received high-dose metoprolol but fortunately recovered. We believe that the prevalence of arrhythmia in these patients could be secondary to electrolyte imbalance, COVID-19 by itself, myocardial injury, and hypoxia.

Literature shows the controversial prevalence of COVID-19–induced LV

systolic dysfunction. One systematic prospective echocardiography study of 100 patients with COVID-19 (>18 years), who had an ECG within 24 hours of admission showed that the prevalence of systolic LV dysfunction was uncommon (<10%).¹⁷ This percentage consisted of patients with mild, moderate, and severe COVID-19 with or without troponin elevations. In addition, from 100 patients, only 20% had elevated troponin concentrations in which 15% had associated reduced LVEF. On contrary, a study of 125 patients with COVID-19 admitted to a hospital were assessed for the prevalence of LV dysfunction.¹⁸ This population consisted mostly of patients with severe COVID-19 (69%) who were admitted to the ICU with 88% requiring mechanical ventilation. From 125 patients, 22% had an impaired LVEF (<50%). Furthermore, from 125 patients, only 93 had cardiac biomarkers measure. Almost 50% of patients with elevated cardiac enzymes (troponin concentration of ≥ 50 ng/L) had LV dysfunction. Similarly, in a retrospective study of 72 patients with COVID-19 who had ECG because of a major concern of acute CV event or because of hemodynamic instability, 34.7% had a reduced LVEF in which 45.7% had an elevated troponin concentration and reduced LVEF.¹⁹ It is worth noting from these patients that it was unknown who had preexisting LV dysfunction. Both studies showed that the prevalence of ventricular dysfunction in patients with COVID-19 is consistent with our study.^{18,19} However, when compared with our study, from 15 patients with elevated cardiac troponin concentrations, all patients had reduced LVEF. This raises the question of an increased prevalence of COVID-19–induced systolic dysfunction in pregnant women when compared with nonpregnant patients.

Troponin elevation in COVID-19 is directly proportional to adverse outcomes and mortality.¹² The presence of positive troponin concentrations is associated with severe illness and poor outcomes in patients with COVID-19. These patients are 5 times more likely to need ventilation, develop

arrhythmias, and die. In contrast, patients with mild disease rarely have elevated troponin concentrations (1%–2%).²⁰ The National Health Commission of China reported that 12% of patients with COVID-19 present with an elevated troponin level. In addition, they stated that 46% of nonsurvivors who had COVID-19 had elevated troponin concentrations vs 1% of survivors. These findings support the association of elevated troponin concentrations with increased mortality.²¹ The magnitude and rate of troponin elevation are directly associated with poor outcome.²² Troponin concentrations in patients with COVID-19 were repeatedly measured at 4, 10, 13, and 22 days of infection and were 2.5, 4.1, 4.4, and 3.8 ng/mL, respectively, in survivors and 8.8, 22, 55, and 290.6 ng/mL in nonsurvivors.²³ In a meta-analysis of 4 studies, patients with severe COVID-19 had significantly higher troponin concentrations than patients with mild COVID-19.²⁴ In our study, all patients had elevated troponin concentrations, which had an IQR of 14.4 to 55.5 ng/mL. In addition, all had a moderate to a severe course of disease needing ICU admission. Unfortunately, we had 2 fatalities due to arrhythmias in our study, which were associated with the highest troponin concentrations (641 and 750 ng/mL, respectively). A study in Wuhan supports this, demonstrating an increased risk of malignant arrhythmias, such as ventricular tachycardia and fibrillation in patients with elevated troponin concentrations compared with patients with normal concentrations.¹³ This potentially can be one of the major factors leading to increased mortality in these patients. Although troponin demonstrated to be an excellent prognostic marker, BNP has shown a similar role.²⁵ Increased BNP concentrations in patients with COVID-19 are a marker of cardiac injury and are associated with in-hospital death.²⁶ A study by Guo et al⁶ showed that elevated troponin and BNP are significantly associated with each other. Moreover, Shi et al¹⁴ demonstrated elevated BNP concentrations in patients with COVID-19 with cardiac involvement compared with patients

with no cardiac involvement. In addition, these patients had a significantly higher mortality rate, which reached 51.2% of cases. Therefore, routinely measuring these biomarkers at admission would play an essential role in decreasing mortality in high-risk patients.

Multiple studies illustrated the clinical picture of COVID-19 in pregnant women.^{4,27} In a cohort study of 64 pregnant women with severe or critical COVID-19 admitted to the hospital in the United States, no incidence of CV complication was noted except for 1 episode of cardiac arrest.⁴ In addition, no maternal mortality occurred. In our study of 154 pregnant women diagnosed with COVID-19, 9.7% developed myocardial injury, and 13.3% died. In terms of delivery, 60% of our patients delivered prematurely, which is consistent with the cohort study where 59.4% of patients who delivered during hospitalization had a preterm delivery at <37 weeks of gestation and 31.2% at <34 weeks of gestation. Furthermore, the mean birthweights of neonates were somewhat similar (2.2 ± 0.7 kg in our study vs 2.4 ± 0.8 kg in the cohort study), which is likely because of the early GA of mothers. However, contrary to our study, no fetal demise has occurred. In the cohort study, 63.3% (vs 35% in our study) of neonates were admitted to the NICU. In the cohort study, patients were characterized according to the severity of COVID-19: severe vs critical. The average rate of NICU admission of neonates was 63.6% for all patients and 40% for patients who are severely ill and 83.3% for patients who are critically ill. In our study, 35% of neonates were admitted to the NICU. Another cohort illustrated the clinical characteristics and outcomes of COVID-19 in 158 pregnant women with COVID-19.²⁷ The study classified patients into asymptomatic or mild disease (78%) and moderate or severe disease (22%). Interestingly, in the study, no CV complication was reported. From 15 hospitalized patients with moderate to severe disease, only 1 (6.6%) was intubated (vs 86.6% intubated in our study), and 9 (60%) were admitted to the ICU (vs 100% in our

study). In addition, only 2 women (13.3%) had a preterm delivery (vs 60% in our study). All of these data show the great variance in the prevalence and severity of COVID-19 among the different population.

Clinical and research implications

This case series has important implications for obstetrical practice and research. It demonstrates that there is a major lack of knowledge and literature, showing the need for further studies to investigate the potential effect of COVID-19 on the heart of pregnant women. A case-control study investigating whether there is a difference in the effect of COVID-19 on the CV system between pregnant and nonpregnant women with COVID-19 is essential. In addition, a larger-scale study of COVID-19 outcomes in pregnant women taking into consideration different gestational trimesters, the presence of CV risk factors, and comorbidities would be necessary to draw conclusions. This would be very important especially in the third trimester of pregnancy where maternal risk of decompensation and complications increases.

Strengths and limitations

This study has limitations, like many others. First, our study is composed of a small sample size; a more extensive cohort study is needed to confirm our findings. Second, only symptomatic pregnant women were tested for SARS-CoV-2, which could result in overestimation in COVID-19 and cardiomyopathy association in pregnancy. Third, we could not provide a clear understanding of the rate of cardiac injury in our population and whether it is attributed to COVID-19, pregnancy by itself, or systemic illness. Fourth, remdesivir was not administered as it was not available in the Dominican Republic at the time of these patients' admission.

Conclusions

Most of the studies on COVID-19 have described its CV effect in nonpregnant women. Our study illustrates the abnormal findings of pregnant women

with COVID-19—induced myocardial injury with LV dysfunction. Patients had a mortality rate of 13.3%, which was attributed to malignant arrhythmias. ■

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Author and article information

From the Division of Infectious Diseases, Department of Medicine, Hospital Aristides Fiallo, La Romana, Dominican Republic (Dr Mercedes); Department of Medicine, Liaquat National Medical College, Karachi, Pakistan (Dr Serwat); Nemours Children's Hospital, Radiology Department, University of Central Florida, Orlando, FL (Dr Naffaa); Department of Obstetrics and Gynecology, Hospital Materno Infantil San Lorenzo De Los Minas, Santo Domingo, Dominican Republic (Dr Ramirez); Department of Medicine, King Edward Medical University, Lahore, Pakistan (Dr Khalid); Department of Medicine, University of Carabobo, Valencia, Venezuela (Dr Steward); Department of Medicine, Menonita Medical Center, Guayama, Puerto Rico (Dr Feliz); Division of Cardiology, Department of Medicine, Massachusetts General Hospital, Boston, MA (Dr Kassab); and Department of Radiology, American University of Beirut Medical Center, Beirut, Lebanon (Dr Karout).

Received Aug. 11, 2020; revised Oct. 8, 2020; accepted Oct. 20, 2020.

B.R.M., A.S., M.K., and L.K. contributed equally to this study.

M.K. and L.K. are senior authors.

The authors report no conflict of interest.

Corresponding author: Lina Karout, MD. lk81@aub.edu.lb; linakarout25@gmail.com