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COVID-19 Disease During Pregnancy and Peripartum Period: A Cardiovascular Review

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Abstract: Pregnancy with various physiological effects on cardiovascular system, makes mothers with borderline cardiovascular reserve at significant risk for adverse events during labor and early postpartum period. Cardiac imaging modalities, have shown that Coronavirus Disease 2019 disease is associated with subclinical myocardial injury in significant numbers of infected people, even in mild or asymptomatic disease and previous healthy ones. Herein, we have discussed the cardiovascular aspects of prepartum pregnant women with Coronavirus Disease 2019, especially patients with moderate to severe illness. Also, we have proposed how to handle the hemodynamic load during labor and the first 48 hours postpartum in the hypoxemic overloaded parturients with possible subclinical myocardial injury. (Curr Probl Cardiol 2021;00:100888.)

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Introduction

Pregnancy, as a physiologic condition with multiple effects on cardiovascular system, is considered a unique hemodynamic challenge for both obstetrician and cardiologists. Significant hemodynamic changes during pregnancy and postpartum to adopt the metabolic demands of maternal and fetus, make mothers with borderline cardiovascular reserve at significant risk, especially near delivery with additive hemodynamic load of labor.^{1,2}

The new Corona virus known as “Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-COV₂)”, responsible for Coronavirus Disease 2019 disease originated in Wuhan, China at December 2019 and rapidly became a pandemic with high mortality rate that reached to more than 2 million death worldwide at the end of 2020. COVID-19 disease has been proposed to be associated with different types of cardiovascular manifestations namely acute coronary syndrome, cardiac arrhythmia, myocarditis, stress cardiomyopathy and thromboembolism as well as evidence of myocardial injury in significant numbers of infected people, even in mild or asymptomatic infection and previous healthy ones.³⁻⁵

Pregnant and postpartum women express different cardiovascular or respiratory-related symptoms such as shortness of breath, palpitation and syncope, so clinicians should keep their high suspicion to screen cardiac involvement in patients with COVID-19 disease. Moreover, some patients such as those with preeclampsia are more prone to cardiovascular complications.

Herein, we have discussed the cardiovascular manifestations of pregnant women with COVID-19 disease, especially those with moderate to severe illness. Also, we have proposed how to handle the hemodynamic load during labor and the first 48 hours postpartum in the hypoxemic overloaded parturients with possible subclinical myocardial injury.

Physiologic Cardiovascular Changes in pregnancy

During normal pregnancy, a dynamic process in cardiovascular response is observed. Significant increase in stroke volume and cardiac output (30%-50%), started at 5 weeks of gestation that peaks at the second trimester and plateaus thereafter, physiological anemia, initial decrease in systemic vascular resistance (SVR) and blood pressure (BP), followed by a rise in SVR and BP in the third trimester accompanied by a rise in heart rate (HR: 10-20/min) in second half of pregnancy is observed as a physiologic response.^{1,6} These alterations are well accommodated by cardiac remodeling process that includes an increase in left ventricular

(LV) wall thickness, four chamber cardiac enlargement, increase in biventricular mass while preserving filling pressures, contractility and ventricular ejection fraction in normal ranges.^{1,7}

A further 60%-80% rise in cardiac output compared with pre labor maseurs are observed during labor and early postpartum. This is attributed to the blood autotransfusion, surges in circulatory catecholamines and tachycardia due to painful uterine contractions.⁷ Based on these hemodynamic changes, the ventricles are encountered with a huge cardiac load during labor compared with pre pregnancy measures (more than 100% increase in cardiac output). Theses alterations are counteracted by blood loss and anesthesia hypotension that may be used during labor. The hemodynamic changes of labor, usually last for 48-72 hours after delivery.⁴ It is estimated that the structural remodeling changes return to baseline at 3-6 months of postpartum.²

Cardiovascular Manifestations of COVID-19 Disease

There are numerous evidences that SARS-COV₂ infection is presented with all spectrum of cardiovascular disease including acute coronary syndrome, arrhythmia, myocarditis, stress cardiomyopathy and thromboembolism.⁴ Cardiac injury associated with COVID-19 disease has been attributed to cytokine storm, viral myocarditis as well as ischemia.^{3,4,8} Ischemic myocardial injury, has been proposed to be due to systemic inflammation, supply-demand mismatch (related to the high cardiometabolic demand of systemic infection, catecholamine surge and intravascular volume imbalances) and hypoxemia (due to direct lung injury as well as epicardial and microvascular coronary dysfunction and thrombus formation in coronary circulation).^{4,9} The same mechanism in addition to electrolyte disturbance and drug sides effects are responsible for cardiac arrhythmia.¹⁰ Increased risk of thromboembolism during COVID-19, especially in acutely ill patients with ARDS is confirmed.¹¹ Hypercoagulation state during COVID-19 is attributed to systemic inflammation, immobility and hypoxemia.⁴

Cardiac magnetic resonance (CMR) studies revealed evidence of myocardial inflammation and fibrosis, even in minimally symptomatic patients with COVID-19 disease, a finding that is correlated with poor long-term prognosis in previous myocarditis series.¹² Abnormal CMR findings, including myocardial inflammation, mild degrees of LV enlargement and dysfunction has been reported from 15%-78% of recently recovered COVID-19 patients, with biventricular involvement in some series.¹³⁻¹⁵ In a strain echocardiography study, reduced longitudinal

strain, especially in basal segments was reported in 71% of patients, even in those with mild symptoms.¹⁶ Right ventricular involvement was more prominent in part of studies due to microthrombus formation in pulmonary circulation along with endothelial lung injury.^{17,18}

Elevated cardiac biomarkers such as cardiac troponin (CTn) and pro-brain natriuretic peptide (pro-BNP), indicative for evolving myocardial inflammation and injury, is reported in a significant number of infected patients (27.8% of 187 patients, 19.7% of 416 cases in two Chinese series, 71% of 100 patients in a German cohort) associated with more severe disease, increased mortality and poor in hospital outcomes.^{13,19-21}

COVID-19 Disease and Pregnancy Outcomes

Considering pregnancy as an immunocompromised state, implementing specific well-defined strategies and a multidisciplinary approach for management of COVID-19 in obstetrics is highly recommended.²² Lower risk of mortality was observed during pregnancy and COVID-19 compared to previous types of Corona virus infection.²³ Center of disease control and prevention reported the increased risk of severe illness and death in pregnant patients infected with SARS-COV₂ compared with non-pregnant counterparts.²⁴ It is estimated that near 70% of admissions for COVID-19 in women who completed pregnancy, were in the third trimester based on the last Center of disease control and prevention update.²⁵ Although there are high risk reports such as our critical case series with high mortality rate at beginning of the pandemic, there are still debates about actual risk of SARS-COV₂ infection during pregnancy and whether they are at higher risk compared with age matched non pregnant women.^{23,26-28} In a Swedish study, higher prevalence of preeclampsia was reported in pregnant women who were admitted in labor with positive SARS-CoV-2 test (5.8% positive test of 2682 women).²⁹ In another report from Texas, 7.4% of 3374 pregnancies were positive for SARS-COV₂ without adverse outcomes including cesarian section.³⁰

In two United States (US) series of pregnant women with COVID-19, the prevalence of severe disease was 15% (6 of 46 women) and 69% (44 of 64 women) with one still birth in the first and one maternal cardiac arrest without mortality in the second report.^{31,32} All of the six women with severe disease in the first US report were overweight or obese.³¹

In a Spanish cohort of 82 pregnant patients with COVID-19, 11% (9 patients) experienced adverse maternal outcome, 4 with severe disease and 5 with mild symptoms. In this study, cesarean delivery was independent predictor of poor clinical outcome.³³ Ten percent (41 women) of

427 pregnant patients with positive SARS-COV₂ test, experienced severe disease in a national United Kingdom (UK) cohort. Three cases of maternal mortality were reported due to complications of COVID-19 in this study.³⁴

The high rate of cesarian delivery, especially when performed in pre-term status, is concerning during the COVID-19 pandemic. In a Chinese observation, an unusual rate (93%) of cesarean section was reported among 68 deliveries. Although the prevalence of severe disease was 8.7% (seven patients) but concern about COVID-19 was the main indication for cesarean section in 61% of deliveries.³⁵ A systematic review of 36 articles, revealed the 68.9% rate of cesarean section, among 203 cases of SARS-COV₂ positive deliveries, in whom the concern about COVID-19 status, was the only indication in 22.6% of cases.³⁶ In another review of pregnant women with COVID-19, 46 out of 48 women, gave birth by cesarean delivery with one stillbirth and one neonatal death without maternal mortality.³⁷

COVID-19 Disease and Cardiac Involvement in Pregnancy

All spectrum of COVID cardiovascular manifestations, are reported in pregnant women during the pandemic. Mercedes et al represented a series of 154 pregnant women with COVID 19 infection, of whom 15 women became critically ill and were admitted to ICU. Decreased LVEF and elevated cardiac enzymes (pro-BNP and CTn I) were reported for all of these critically ill patients, with mortality rate of 13% (two patients) due to arrhythmia.³⁸ In a series of 31 pregnant women with positive SARS-COV₂ infection and severe disease, 22% of women with troponin measurement, had elevated values, as well as 30% of BNP measures. Bradycardia (HR<60) was reported in one-third of the women. Two maternal mortality was observed, both in women with elevated troponin.³⁹ In a case report, 2 out of 7 pregnant women developed cardiomyopathy (LV ejection fraction of 40%-45%) during severe COVID-19 disease. Both of them were obese with elevated cardiac biomarkers, presented at 33 and 39 weeks of pregnancy.⁴⁰

Labor Management: Cardiovascular Considerations

It is recommended that the management of pregnant women with COVID-19 disease during labor should be carried out in a multidisciplinary approach with involvement of obstetrician, obstetric anesthetists,

pulmonologist, midwives, microbiologists, neonatologists, infectious disease specialists and cardiologist.^{41,42} Given the physiological hemodynamic changes in pregnancy, particularly during the labor and the first 48-72 hours after delivery, hypoxemic women with moderate to severe COVID-19 disease, are at critical risk for hemodynamic derangement. Thus, the initial forty-eight hours are essential for patient care, and it might be helpful to employ special considerations in patients who are at risk or have any evidence of cardiac involvement.

1. When the decision was made for termination of pregnancy, cesarian delivery should not be carried out solely for COVID-19 disease. Given to the increased risks of neonatal complications, blood loss and thromboembolic events, it should be performed for obstetric reasons or patients with deteriorating clinical status.
2. Beside history taking, careful cardiovascular exam and monitoring of vital signs, surface twelve leads electrocardiogram is essential to assess any rhythm disturbance, QT interval, any ST segment or T wave changes indicative for ischemia, that make the patient vulnerable to arrhythmia. Drug interactions as well as electrolyte imbalance, especially hypokalemia, should be corrected promptly in patients with long QT interval, considering the susceptibility of malignant dysrhythmias in patients with certain types of congenital long QT syndromes during pregnancy and postpartum period.
3. We recommend cardiac biomarkers (CTn, BNP and pro-BNP) to be measured in all pregnant patients with moderate to severe COVID-19 disease admitted to the labor. Trans thoracic echocardiography, based on local availability and considering safety protocols, preferentially with handheld machines if feasible, have additive value in women with positive biomarkers.
4. In critical parturients with subclinical myocardial injury (elevated biomarkers) or echocardiographic evidence of ventricular dysfunction, we propose a delicate trial of low dose intravenous diuretic therapy (such as 20 mg of intravenous furosemide) during labor, at the time of peak cardiac output, to help the injured exhausted myocardium to accommodate the huge changes in HR and hemodynamic load. Careful monitoring, namely evaluation of fine rales in the lung field, volume status, fluid intake and urine output in the first 72 hours after delivery is recommended to use additive doses of diuretic when is needed.
5. Special attention should be given to patients with high body mass index (BMI) that were at increased risk of severe disease, cardiomyopathy and venous thromboembolic events in multiple studies.^{2,31,40}

Better insight into the management of pregnant patients with critical COVID-19 disease during labor will be achieved by developing large multicenter studies with adequate valid data. Individualized approach to these patients based on general baseline health condition, the body weight, obstetric history, temporal phase of COVID-19 disease progression, degree of lung involvement, hypoxemia, cardiac injury and fetal maternal status in a well-defined team approach is warranted.

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