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Case Series

Rising trends of peripartum cardiomyopathy: insights from the COVID-19 pandemic

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ABSTRACT

Peripartum cardiomyopathy (PPCM) is a rare, life-threatening condition of unknown etiology occurring in late pregnancy or early postpartum. The COVID-19 pandemic has introduced new diagnostic challenges, particularly in distinguishing PPCM from COVID-19-related cardiomyopathy, both of which may share overlapping clinical features. This study was done to investigate the temporal relationship between SARS-CoV-2 infection and the onset of PPCM, highlighting possible implications for maternal health in the post-COVID-19 era. A prospective observational case series was conducted at a tertiary care center in South India. Four postpartum women with recent or past COVID-19 infection were diagnosed with PPCM over a six-month period. Three of the four patients succumbed despite intensive care and multidisciplinary interventions. The clustering of these cases in a short time frame and their shared history of COVID-19 infection raises questions regarding a potential pathogenic link. Future studies are needed to elucidate the pathophysiological mechanisms linking COVID-19 and PPCM.

Keywords: Peripartum cardiomyopathy, COVID-19, LV dysfunction, High risk pregnancy

INTRODUCTION

The pandemic caused by the novel Coronavirus SARS-CoV-2 has led to devastating fatalities, profoundly impacting millions of individuals worldwide. Despite the implementation of various measures aimed at reducing mortality rates in the early stages, the effectiveness of these strategies remains uncertain, particularly in light of the evolving nature of distinct waves and variants of the virus.[1,2] While COVID-19 primarily presents with respiratory symptoms, a spectrum of cardiac complications has also emerged, including arterial and venous thromboembolism, myocardial infarction (MI), cardiomyopathy, heart failure, and arrhythmias—an area that necessitates further research and investigation.[3]

Peripartum cardiomyopathy (PPCM) is a rare and idiopathic condition characterized by the development of cardiac failure during the last month of pregnancy or within five months postpartum. This diagnosis is typically confirmed by exclusion, underscoring its complexity.[4] Research into COVID-19-related cardiomyopathy in pregnant women remains sparse. Given the overlapping clinical presentations, it can be particularly challenging to differentiate between PPCM and COVID-19-related cardiomyopathy.[5] The immunosuppressive state and physiological changes that accompany pregnancy complicate the establishment of a clear scientific understanding of this issue. For those who survive COVID-19, the journey does not conclude with the acute illness; rather, the potential for long-term sequelae surfaces, calling for thorough investigation.

Recently, conditions emerging after COVID-19 have been identified as post-COVID-19 syndrome, defined by the manifestation of new or persistent symptoms occurring at least three months post-infection, regardless of the initial severity of the disease.[6] An alarming increase in the

incidence of PPCM has been reported, likely due to enhanced diagnostic capabilities alongside the rising age and co-morbidities of expectant mothers. Advanced imaging techniques such as cardiac magnetic resonance imaging (CMRI) and strain echocardiography have revealed significant subclinical left ventricular dysfunction in approximately 80% of patients affected by COVID-19.[7,8] However, there remains a lack of comprehensive data regarding the myocardial impacts of COVID-19 infection specifically in pregnant patients.

In this report, we present a focused case series from a single healthcare center, examining four patients observed over a brief span of six months, all of whom developed peripartum cardiomyopathy following what appeared to be successful recovery from COVID-19 infection.

CASE SERIES

Case 1

A 27-year-old primipara, was referred to our emergency department on day 4 post cesarean section as she had developed sudden onset breathlessness and anuria. As per her discharge summary, the cesarean performed was under spinal anesthesia for fetal distress and was uneventful. The following day after surgery, she had nil urine output and she denied history of postpartum hemorrhage or preeclampsia. She had received 2 cycles of hemodialysis with blood transfusion before being referred to our centre. She had an uneventful antenatal history but history of mild COVID-19 infection one year ago.

Upon arrival, the patient was maintaining saturation with 5 liters of oxygen by mask and urobag was empty. Clinical examination revealed tachycardia of 118 beats per minute, bilateral grade 4 pedal oedema along with hypotension (BP 100/60 mmHg). She was promptly admitted to the surgical intensive care unit (SICU), where a multidisciplinary team including obstetricians, internists, cardiologists, nephrologists, and pulmonologists managed her care.

Laboratory results showed hemoglobin at 8.5 g/dl, leukocytosis with a total count of 20,030 cells/µl, and elevated creatinine at 3.2 mg/dl. Chest X-ray demonstrated bilateral mild pleural effusions, evidenced by blunting of the costophrenic angles. A transthoracic echocardiogram (TTE) indicated global left ventricular hypokinesia with moderate left ventricular systolic dysfunction, reflected by an ejection fraction (EF) of 32%. Abdominal sonography revealed kidneys of normal size with mildly echogenic parenchyma and preserved corticomedullary differentiation.

A diagnosis of peripartum cardiomyopathy, acute kidney injury (AKI), and associated sepsis was established. Management included blood transfusions and hemodialysis on alternate days, which gradually restored her urine output over the course of one week. Empirical antibiotic therapy commenced with intravenous imipenem/cilastatin, and vancomycin was subsequently added based on blood culture results that identified *Acinetobacter baumannii*. Upon clinical improvement, the patient was discharged on a regimen of oral torsemide, bisoprolol, isosorbide dinitrate, and hydralazine. A follow-up transthoracic echocardiogram was recommended post-discharge; however, the patient did not return for follow-up care.

Case 2

A 24-year-old primipara at 35 weeks of gestation underwent an emergency cesarean section due to abruptio placenta, resulting in the delivery of a stillborn infant weighing 1.8 kg. Postoperatively, she experienced severe postpartum hemorrhage (PPH) necessitating a massive blood transfusion and was subsequently transferred to our facility on the second postoperative day. Notably, she had a history of testing positive for COVID-19 via RT-PCR during the second month of a prior pregnancy, which ended in miscarriage. Her antenatal course prior to this intervention was reported as uneventful by her accompanying relatives.

Upon arrival at the emergency department, the patient was in hypovolemic shock, exhibiting vital signs of tachycardia at 128 bpm, a blood pressure of 60 mmHg (systolic), non-recordable diastolic pressure, and SpO_2 levels at 88% despite being on 15 litres of supplemental oxygen. Immediate resuscitation commenced with the administration of double ionotropic support, after which she stabilized to an SpO_2 of 94% on non-invasive ventilation (SIMV mode). Echocardiographic evaluation revealed biventricular systolic dysfunction with an ejection fraction of 30%, without any evidence of thrombus formation. Unfortunately, her clinical condition deteriorated into septic shock accompanied by acute kidney injury (AKI). She required multiple sessions of sustained low efficiency dialysis (SLED).

Initially, she was treated with Meropenem, Clindamycin, and Vancomycin; however, as her condition worsened, antibiotics were escalated to include Tigecycline and Colistin. Due to prolonged intubation, a tracheostomy was performed. Although a gradual improvement was noted initially, the patient experienced a sudden collapse on postoperative day 17, leading to her demise.

Case 3

A 29-year-old primigravida was admitted at 38 weeks of gestation with meconium-stained amniotic fluid during early labor. Her vital signs were stable: pulse rate 80 bpm, blood pressure 110/70 mmHg, oxygen saturation 98% on room air, and she was afebrile. At four months of gestation, she had tested positive for COVID-19 via rtPCR, experiencing only mild symptoms of fatigue and myalgia. The patient had no significant medical or surgical history prior to her pregnancy, and her blood investigations showed normal results.

She underwent an emergency lower segment caesarean section (LSCS) due to grade 3 meconium staining in early labor. Intraoperatively, she experienced myoclonic jerks and required intubation and ventilatory support. An emergency CT scan of the brain was performed and yielded normal results, after which she was started on prophylactic anticonvulsants. The patient was subsequently managed in the ICU, where she began experiencing recurrent episodes of hypotension and bradycardia. A 2D echocardiogram revealed severe global hypokinesia of the left ventricular with an ejection fraction of 25%, with no thrombus detected.

Following a cardiology consultation, she was treated with diuretics, Digoxin 0.25 mg/day, two doses of intravenous Amiodarone 250 mg infusion, and Ivabradine 5 mg/day.

Despite these interventions, her clinical status rapidly deteriorated, rendering her hemodynamically dependent on triple vasopressor agents.

Unfortunately, the patient succumbed on postoperative day two. The family declined a postmortem examination.

Case 4

A 34-year-old woman, G3P2L2, at 31 weeks' gestation, presented to our outpatient department with a one-week history of low-grade fever, accompanied by a dry cough and breathlessness. She had been diagnosed with gestational diabetes mellitus, which was managed using insulin according to a six-point sugar profile.

Upon taking her medical history, she revealed that during the eighth month of her previous pregnancy two years earlier, she had tested positive for COVID-19 via RTPCR, experiencing only mild symptoms that required symptomatic treatment.

On admission, the patient exhibited tachycardia at 110 beats per minute, a blood pressure of 100/60 mmHg, and an oxygen saturation of 96% on room air. Her blood workup revealed a hemoglobin level of 10.9 g/dl, a total white blood cell count of 5,200, and a CRP level of 55, while renal and liver function tests were unremarkable. Urinalysis suggested a urinary tract infection, prompting the initiation of intravenous antibiotics. Both COVID rapid antigen and RT-PCR tests returned negative results, and fetal well-being evaluations indicated normal findings.

However, on the second day of admission, the patient's condition deteriorated, with a sudden drop in oxygen saturation to 88%, necessitating immediate transfer to the ICU. Arterial blood gas analysis indicated type 1 respiratory failure, and a chest X-ray revealed bilateral patchy opacities with fibrotic changes. The patient was placed on 15 liters of oxygen via mask, and intravenous antibiotics were intensified with Piptaz 4.5 g TID, along with the initiation of bronchodilators. Despite these interventions, her dyspnea worsened, and she developed hypotension.

A trans-thoracic echocardiogram was conducted, revealing dilated cardiomyopathy, global hypokinesia, and severe left ventricular systolic dysfunction with an ejection fraction of 22%; no thrombus was detected. The patient was subsequently started on anti-failure medications, including Bromocriptine 2.5 mg/day and Digoxin 0.25 mg/day. Tragically, despite all efforts, the patient did not survive.

Table 1 shows comparison of all four cases.

Table 1: Comparison of all four cases.

Case no.	Age (years)	Gestational age	History of COVID-19 infection	Clinical presentation	Echocardiographic findings	Management	Outcome
1	27	Postpartum (day 4)	Mild COVID-19, 1 year ago	Breathlessness, anuria, bilateral pedal edema, hypotension	LV hypokinesia, EF 32%	Blood transfusion, hemodialysis, antibiotics (Acinetobacter baumannii)	Discharged but lost to follow-up
2	24	35 weeks	COVID-19 during prior pregnancy	Tachycardia, hypovolemic shock, septic shock, AKI	Biventricular dysfunction, EF 30%	Multiple blood transfusions, dialysis, antibiotics (Tigecycline, Colistin)	Died after postoperative collapse
3	29	38 weeks	Mild COVID-19, 4 months ago	Meconium-stained amniotic fluid, myoclonic jerks, hypotension	LV hypokinesia, EF 25%	Diuretics, Digoxin, Amiodarone, Ivabradine	Died after rapid deterioration

Continued.

Case no.	Age (years)	Gestational age	History of COVID-19 infection	Clinical presentation	Echocardiographic findings	Management	Outcome
4	34	31 weeks	Mild COVID-19, 2 years ago	Fever, dry cough, breathlessness, tachycardia, hypoxia	LV dysfunction, EF 22%	Anti-failure medications, antibiotics	Died after worsening respiratory failure

DISCUSSION

The four cases discussed above were clustered over a short period of 4 months (September 2022 to December 2022), and all of them had a recent history of COVID-19 infection. Although PPCM is a rare entity in obstetrics, the incidence varies globally between 1:15,000 and 1:100, the highest being reported from Nigeria.[9]

In research conducted at a tertiary care facility in South India, the incidence was reported to be one case per 1,374 live births.[10] The observation made in our study, which showed a sudden rise in cases of this uncommon disease, three of whom had maternal death, makes it an object of ongoing speculation.

The etiology of PPCM is unclear and appears to be multifactorial and polygenic: genetic predisposition, inflammation, autoimmune reaction, oxidative stress, low selenium levels, and viral infections like Adenovirus, Coxsackie, Epstein-Barr, Parvovirus, and Cytomegalovirus as well as the effects of antiangiogenic factors are all potential contributory factors.[11]

Endothelial damage due to Vasoinhibin, a derivative of Prolactin has been found as a potential culprit for the pathogenesis of PPCM. A similar path of destruction by endothelial cell injury was noted in COVID 19 complicated cardiomyopathy (CCM).

In non-obstetric patients, COVID-19 CCM has been studied extensively, whereas the same for pregnancy related is sparse. This case series highlights the temporal relationship between COVID-19 and frequent catastrophic outcomes, of PPCM leading to the query if cardiomyopathy was related to COVID-19 versus peripartum. Angiotensin-converting enzyme-2 (ACE2), which is found majorly in heart and lungs becomes the binding site for SARS-CoV-2, which then leads to severe systemic inflammation and subsequent mitochondrial dysfunction.[12,13]

Recently, myocardial injury has been noted in a patient who had recovered from COVID-19 illness, as researched in a case report by Cook et al, where a parturient presented with left ventricular global hypokinesis and ejection fraction of 38% two months after initial COVID-19 infection.[14]

Another study which showed similar findings was from a large tertiary centre in Israel where 3 patients with recent affliction of COVID 19 presented with PPCM before or after delivery.[15] A case reported in AIIMS, Bhopal by Karna et al, of a 32-years gravida 2 para 2 who developed COVID-19 infection following cesarean section which then got complicated to heart failure lays forward the question - is the cardiomyopathy COVID-19 associated? This area needs further exploration as studies on pregnant women is scarce.[16]

The management of PPCM in the context of COVID-19 requires a multidisciplinary approach involving cardiologists, obstetricians, pulmonologists, and infectious disease specialists. Treatment regimens may include standard heart failure therapies such as beta-blockers, ACE inhibitors, and diuretics, with careful consideration of the patient's pregnancy or postpartum status.[17] The prognosis of PPCM varies, with some patients experiencing full recovery while others may suffer from persistent cardiac dysfunction or progressive heart failure.

CONCLUSION

The COVID-19 pandemic has introduced new complexities in the diagnosis and management of PPCM. As we noted a sudden rise and devastating outcome in peripartum cardiomyopathy cases, several questions arised - can these cases of cardiomyopathy be COVID-19 related? Could further investigations like Cardiac Magnetic Resonance, cardiac enzymes, COVID IgG IgM antibody testing yield a favorable result? Enhanced awareness and surveillance are crucial for early identification and intervention, ensuring better outcomes for pregnant and postpartum women during and beyond the pandemic.

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