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Peripartum cardiomyopathy is a rare cardiac condition, overall. However, in certain populations can be found frequently enough and the signs, symptoms, and management should be readily understood. Here we provide an updated overview of this topic.

KEYWORDS
Peripartum Cardiomyopathy, outcomes

1 | INTRODUCTION

Peripartum cardiomyopathy (PPCM) is a rare, idiopathic dilated cardiomyopathy defined by the clinical manifestation of signs and symptoms of heart failure in the last month of pregnancy through the fifth month postpartum. There must be no other identifiable cause for cardiac failure and no identified heart disease before the last month of pregnancy. Echocardiographic parameters require 1 of the following to be present: ejection fraction <45%, fractional shortening <30%, or both, with a possible additive left ventricular end diastolic dimension >2.7 cm/m² body surface area.1–3 The incidence varies by region and affects less than 0.1% of all pregnancies globally but carries devastating effects, with morbidity and mortality rates as high as 5% to 32%.4–6

Although there was significant variance with regard to socioeconomic profiles in the occurrence of PPCM worldwide, the clinical variables considered risk factors were consistent among all populations. Multiparity (mean = 3.1), twin pregnancies, as well as preeclampsia and other hypertensive disorders were commonly found among women with PPCM.10,11 Within the United States, 43% of women with PPCM had a hypertensive disorder associated with their pregnancy.11 Advanced maternal age (≥30 years of age) is a significant risk factor, with increasing risk of PPCM with increasing maternal age.12

Human immunodeficiency virus (HIV) has also emerged as a potential risk factor for peripartum cardiomyopathy and was seen most often in patients diagnosed with PPCM outside of Europe.10 This correlation may be related to the higher incidence of HIV in populations living outside of Europe, but further investigation is warranted.

2 | EPIDEMIOLOGY

Significant regional variability in the populations that present with PPCM has been found with very low rates among the Japanese (1:20 000 births) and higher rates in black populations reaching upward of 1:100 births as seen in Nigeria.7–9 A more recent assessment of global PPCM burden by Sliwa et al. indicated that the disease manifested more equally among black and Caucasian populations.10 Within countries associated with the European Society of Cardiology, the disease was prevalent among Caucasians and more commonly presented among blacks outside of Europe. Women with lower socioeconomic profiles were more likely to be afflicted by this disease outside of Europe. The human development index (HDI) evaluates longevity, education, and income to determine a nation’s social and economic ranking. HDI was significantly higher in women with PPCM within Europe compared to other nations.

3 | ETIOLOGY

Multiple etiologies have been identified as potentially leading to PPCM, making this diagnosis a broader umbrella term that includes heart failure caused by various pathologies that occur in the specified time period. However, the overarching concept of unbalanced oxidative stress and decreased angiogenesis appears to be an overlying theme with most identified etiologies. Hypertension, abnormal hemodynamic stress response, viral etiology, and nutritional deficiencies have all been identified as potential causes of oxidative stress leading to PPCM.4,13

Several dysregulated immune responses have been associated with the development of PPCM. Fetal cells often gain access to the maternal circulation but maternal immunity destroys them. These fetal chimerisms may escape weakened maternal immunity and nestle...
in maternal myocardium. After delivery, maternal immunity returns to normal, attacking the foreign pathogens. Antibodies to cardiac myosin heavy chains have been found in women with PPCM, but not in the serum of those with idiopathic dilated cardiomyopathy.\textsuperscript{14,15}

Abnormal prolactin metabolism caused by oxidative stress–related improper cleaving of the hormone into an active, antiangiogenic form disturbs cardiomyocyte angiogenesis leading to heart failure.\textsuperscript{13,16}

### 4 | MANAGEMENT

There are no clinical trials to date assessing the appropriate management of acute heart failure due to PPCM. Therefore, standard management for acute systolic heart failure is employed in these cases. In women presenting with severe acute decompensated heart failure, it is important to protect the airway, manage breathing, and maintain circulation.\textsuperscript{4} Intubation or bilevel positive airway pressure may be required to provide appropriate oxygenation, especially in the setting of acute pulmonary edema. Loop diuretics are safe antepartum and postpartum, and provide the required diuresis. Continuous infusions of vasodilators, such as nitroglycerin and nitroprusside, can provide the needed reductions in afterload and preload. If there is significant cardiac dysfunction, an inotrope such as milrinone or dobutamine may be initiated to provide support; other mechanical support (ie, intra-aortic balloon pump, left ventricular assist device, or extracorporeal membrane oxygenation) may be needed for more severe cardiogenic shock.\textsuperscript{17} If the woman presents antepartum, fetal monitoring is crucial during the decompensation period.\textsuperscript{4} If the ejection fraction is <35%, low-molecular-weight heparin may be used to prevent left ventricular thrombi in this population of patients already at high risk for clotting if antepartum and Coumadin can be used in the postpartum period.\textsuperscript{18} Treatment would continue for 3 to 6 months after delivery or until left ventricular recovery takes place.\textsuperscript{18,19}

By definition, these patients present in the last month of pregnancy at the earliest, if the patient is antepartum, delivery of the fetus may reduce hemodynamic stress on the heart with the method of delivery based on obstetric indications.\textsuperscript{18}

It has been suggested that if the heart failure remains refractory despite these extensive efforts, it may be beneficial to refrain from breastfeeding and initiate bromocriptine therapy to suppress prolactin production.\textsuperscript{4,20} A recent study by Hilfiker-Kleiner et al. revealed that patients who received bromocriptine treatment, even if only for 1 week, had higher rates of left ventricular recovery with lower morbidity and mortality compared to women with PPCM from a different study who were not treated with this drug. Unfortunately, this study did not have a placebo arm to allow for a control group within the study. However, patients who received the drug for as little as a week had improvements in ejection fraction of approximately 20%.\textsuperscript{20} To the contrary, a survey of women with a history of PPCM revealed that breastfeeding was associated with a higher rate of left ventricular function recovery.\textsuperscript{21}

Once stabilized, management of heart failure involves medications that are least teratogenic in the antepartum period. β-blockers, specifically carvedilol and metoprolol succinate, hydralazine for vasodilation, digoxin, and loop diuretics all carry acceptably low risks of fetal complications.\textsuperscript{4} In the postpartum phase, drug choice will need to be made based on the women’s desire to breastfeed. Profound hypotension in the infant may result with the use of angiotensin receptor blockers (ARBs) or angiotensin converting enzyme inhibitors (ACEIs), especially in the first few weeks of neonatal life. ARBs are not recommended in nursing women at any time for the same reason. Enalapril, captopril, and quinapril are acceptable ACEIs and are preferred for use after the infant is a few months old. All other heart failure medications are appropriate for use by new mothers (ie, loop diuretics, hydralazine, isosorbide dinitrate, and aldosterone antagonists).\textsuperscript{17,22} β-blockers are extremely important for left ventricular recovery in this cohort of heart failure patients as well. Unfortunately, they are terribly underutilized in non-European countries with significantly higher rates of symptomatic heart failure 1 month after delivery.\textsuperscript{10}

Use of an implantable cardioverter-defibrillator (ICD) should be deferred until the patient has been given a chance at recovery. A significant proportion of women with PPCM have normalization of ejection fraction within 6 months of diagnosis, with only 3% having residual deficit that warrants use of an ICD.\textsuperscript{11} While awaiting recovery of left ventricular function, an external wearable defibrillator can be utilized to protect against ventricular arrhythmias in the interim.

### 5 | OUTCOMES

With current improved understanding of heart failure management, PPCM mortality rates have decreased to as low as approximately 3% within 6 months postpartum.\textsuperscript{6,23} Fortunately, recovery of left ventricular function is markedly higher in PPCM than in other dilated cardiomyopathies. Approximately 50% of patients will recover to normal ejection fraction within 6 months to 5 years.\textsuperscript{24,25}

Despite appropriate heart failure management, transplant may be needed in up to 4% of PPCM patients.\textsuperscript{11} At times, mechanical circulatory support may be needed as well. However, given the high likelihood of recovery to normal ejection fraction within a relatively short period of time, such permanent mechanical strategies should be avoided, if possible.

### 6 | SUBSEQUENT PREGNANCIES

Approximately 50% of patients will recover to a normal or near-normal ejection fraction after developing PPCM. These women had significantly lower mortality rates and better chances of improved cardiac function.\textsuperscript{26} Of the women who continue to have diminished cardiac function, subsequent pregnancies are associated with a 25% mortality rate and further decline in cardiac function.\textsuperscript{26} When compared to standard heart failure management strategies, initiation of bromocriptine therapy immediately after delivery was associated with significant improvement in left ventricular function and 0% mortality.\textsuperscript{26} If a woman with a history of PPCM is considering a subsequent pregnancy, a care team involving cardiology, high-risk obstetrics, and perinatology will be needed to provide the best management strategy for mother and baby. There may be benefit from performing
routine assessment with brain natriuretic peptide levels and troponins to determine if the etiology of shared symptoms are due to heart failure or pregnancy. MiR-146a is a microRNA found in women with PPCM, not in unaffected women, and could be considered a novel method of identifying postpartum women with this disease. ⁷⁷ Dobutamine stress echo may provide a greater assessment of a woman’s ability to endure a subsequent pregnancy without recurrence after PPCM. ⁷⁸

7 | PREVENTION

Currently, no risk calculator exists to help determine the probability a woman with develop PPCM. In an effort to prevent the development of PPCM, women should follow a heart healthy lifestyle. Regular exercise, refraining from alcohol consumption and smoking, as well as a balanced diet all help the heart. Bromocriptine may be beneficial in reducing mortality and preventing further reduction in ejection fraction in women with a history of PPCM when presenting for a subsequent pregnancy. ²⁶

Conflicts of interest

The authors declare no potential conflicts of interest.

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