Peripartum cardiomyopathy: Implications for WHNPs and midwives

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Peripartum cardiomyopathy (PPCM) is one of the most severe cardiovascular complications in previously healthy childbearing women during, or within the weeks immediately following, pregnancy. The exact etiology of PPCM remains unknown. Prompt recognition of actual or impending heart failure, and rapid access to further diagnostic testing and appropriate treatment, is essential to promote survival, recovery, and minimize potential recurrence in future pregnancies. Thus, the role of the women's health nurse practitioner or midwife is integral to the identification, diagnosis, treatment, and, most importantly, the support and education of women and their families with this elusive phenomenon.

KEY WORDS: **Peripartum cardiomyopathy, heart failure, heart failure and pregnancy, postpartum heart failure, cardiovascular complications and pregnancy, PPCM**

Peripartum cardiomyopathy (PPCM) is one of the most severe cardiovascular complications in previously healthy childbearing women during, or within 5 to 8 weeks following, pregnancy. It is a form of an acquired systolic heart failure that develops because of pregnancy and is not like any other form of heart failure that develops because of pregnancy.[1–4] This condition has been described as an idiopathic, nonischemic cardiomyopathy that is almost always associated with a reduced left ventricular ejection fraction (LVEF) less than 45%.[1,5,6] Although PPCM resembles dilated cardiomyopathy, it is considered an independent entity.[5,7] The causes of PPCM are not fully understood, but it is believed that it is possibly related to conditions like chronic hypertension, undiagnosed mitral stenosis, obesity, preeclampsia, anemia, and other complications of pregnancy.[8] It is a diagnosis of exclusion and considered when no other cause is evident. This article explores the phenomenon of PPCM and summarizes its clinical presentation, treatments, and implications to inform women's health nurse practitioners (WHNPs) and midwives about this pervasive, and potentially fatal, condition.

Incidence

Because many cases of PPCM go unrecognized, its true incidence

may not be known. Considerable regional and ethnic differences exist, however, with global estimates of the incidence of PPCM varying by region. A disproportionately high incidence exists in certain ethnic groups like those of African descent. The highest prevalence is identified among Nigerian women, possibly due to the cultural tradition of ingesting kanwa (dried lake salt) for 40 days postpartum leading to fluid overload.[9] Further, the incidence of PPCM in Nigerian and Haitian women has been reported as 1 in 100 women (or 1 in 300 pregnancies) compared to 1 in 1,500 women in the United States.[6,10] In contrast, PPCM among Hispanic women is low.[3] Thus, high variations between countries and continents suggests environmental factors may contribute to the development of PPCM.[6] In the US, the incidence of PPCM is rising, possibly due to advanced maternal age, an increased rate of multifetal pregnancies secondary to modern fertility techniques, and increased recognition and awareness of the disease.[4,11] Mortality rates in the US have not been well documented but range from 11% to 16%.[10]

Pathophysiology

The pathophysiology of PPCM is not fully understood but is likely multifactorial. What is currently understood is that maximal cardiovascular changes occur in the second trimester when most women with any preexisting cardiac disease will likely begin to develop symptomatic heart failure.[1,12] However, the majority of women with PPCM develop symptoms during late pregnancy or after delivery.[1]

Several mechanisms have been proposed to explain the genesis of PPCM. The extant literature supports a predominant hypothesis that the high levels of the hormone prolactin combined with the oxidative stress of pregnancy is a key implication for the development of PPCM.[3,6,13] The literature also identifies an association between nutritional deficiency and the development of PPCM. Specifically, a deficiency in the essential trace element selenium is hypothesized to interfere with proper thyroid hormone metabolism and DNA synthesis, and to minimize the body's protection against oxidative damage.[1,3,14] Immune system changes, an autoimmune process, viral myocarditis, and increased cardiomyocyte death have also been suggested.[1,3]

Genetics have been explored as a contributing factor in the development of PPCM. The hemodynamic changes and stress of pregnancy (ie, increased heart rate, cardiac stroke volume, volume overload with a decline in peripheral vascular resistance) are believed to unmask previously undiagnosed cardiomyopathy. Thus, an association between PPCM and a familial dilated cardiomyopathy, or from fetal genetic abnormalities, has been proposed.[15–17] Most women with PPCM do not have a family history of cardiomyopathy and PPCM does not always recur in subsequent pregnancies, however, which indicates that any genetic origin is inconclusive and that additional risk factors, or a combination of risk factors, may be more directly implicated in the development of the disease (*Box 1*).[1]

Signs and symptoms

Most cases of PPCM go unrecognized. A woman may experience symptoms in the last month of pregnancy or earlier or as late as 5 months, and possibly 1 year, after delivery.[2,18] Confounding the scenario, a supposedly healthy woman often presents complaining of nonspecific symptoms like general discomfort, fatigue, or peripheral edema that are also common complaints toward the end of pregnancy or in the first weeks' postpartum. The severity of symptoms, however, is related to the severity of heart failure.

Box 1. Risk factors for PPCM

- Advanced maternal age
- African ancestry
- Genetics
- HELLP syndrome
- Hypertensive disorders
- In vitro fertilization
- Multigestational pregnancy
- Multiparity
- Preeclampsia

HELLP, hemolysis, elevated liver enzymes, low platelets; PPCM, peripartum cardiomyopathy.

Most women will present initially with subtle symptoms that progressively worsen to lethargy, increasing peripheral edema, palpitations, dry cough, and breathlessness.[9,11] Women with PPCM may report, "I can't catch my breath."[2] Indeed, shortness of breath is the most common presenting symptom, and reports of difficulty catching breath are common.[19] Further, women are more likely to develop these symptoms if they are also diagnosed with other risk factors like hypertension or preeclampsia.[20]

Other symptoms of heart failure may be present. These include dizziness, dyspnea, orthopnea, paroxysmal nocturnal dyspnea, chest tightness or pain, and agitation.[1,2] If heart failure is severe, a woman may have signs of cardiogenic shock, peripheral hypotension and hemodynamic instability, acute pulmonary edema, severe arrhythmias, or thromboembolic events.[5]

On physical examination, the WHNP or midwife may identify tachypnea, tachycardia, signs of increased jugular venous pressure (ie, jugular vein distention), pulmonary rales, and pitting peripheral edema.[5] Peripheral oxygen saturation may be normal or low, with the latter a late finding and a critical stage of the disease presentation.[3]

Box 2. Differential diagnoses for PPCM

- Myocardial infarction
- Severe preeclampsia
- Myocarditis
- Pericarditis
- Amniotic fluid embolism
- Pulmonary embolism
- Sepsis
- Drug toxicity

PPCM, peripartum cardiomyopathy.

Diagnosis

The diagnosis of PPCM relies on awareness and appreciation that subtle, progressively worsening symptoms may be red flags for PPCM. Because there is considerable overlap with other conditions, all other possible causes of heart failure (eg, myocardial infarction, congenital heart disease, myocarditis) must be excluded before a diagnosis is made. Prompt diagnostic testing and subsequent referral to a cardiologist are warranted.

The number of differential diagnoses possible given the clinical presentation complicates the diagnosis of PPCM (*Box 2*). A thorough history and physical examination that includes uncovering when the symptoms began, the duration, severity, and relieving factors, if any, is imperative. Diagnostic testing is always indicated.

The electrocardiogram (ECG), although not specific for PPCM, is a first-line noninvasive diagnostic modality. The ECG may show nonspecific abnormalities, with the most common including ST-T wave abnormalities, sinus tachycardia, and left ventricular hypertrophy.[3] A normal ECG, however, does not rule out PPCM.[1]

A chest x-ray is also a convenient, noninvasive diagnostic tool. A chest x-ray should be normal in PPCM but may reveal the presence of pulmonary venous congestion, increased cardiac size, the presence of any pleural effusion, fluid in the lungs, or interstitial alveolar edema indicative of pulmonary edema.[1–3] A chest x-ray is considered safe in pregnancy because the dose of radiation is negligible.[3]

The echocardiogram, however, can provide detailed information to assist in the diagnosis of PPCM, specifically because it determines the LVEF. In PPCM, the LVEF is typically less than 45%, signifying global impairment of the left ventricle.[1,3,4] If the LVEF is severely reduced, the left ventricular apex should be clearly visualized to explore for the presence of intracardiac thrombus.[1] An echocardiogram may also reveal systolic dysfunction in addition to left or right ventricular dilatation and dysfunction or identify concomitant right ventricular involvement, functional mitral and/or tricuspid regurgitation, pulmonary hypertension, left atrial or biatrial enlargement.[4]

Laboratory blood work is indicated in diagnosing PPCM, specifically brain naturietic peptide (BNP) and N-terminal pro-BNP. These two lab tests do not change significantly in normal pregnancy but may be mildly elevated. Normal values can rapidly rule out acute heart failure. Elevated BNP is a marker of acute heart failure and its severity, especially when the values are 200 pg/mL or more.[1,2] N-terminal pro-BNP is a nonspecific marker for pregnancy complications like preeclampsia, heart failure, or other diseases that is markedly elevated in PPCM.[21] Additional lab tests to help support diagnosing PPCM include measuring troponin to rule out any myocardial ischemia or infarction, thyroid function tests, and inflammatory markers like erythrocyte sedimentation rate and C-reactive protein.[3]

Although not routinely performed, a cardiac magnetic resonance imaging (MRI) can be useful to provide accurate ejection fraction and chamber measurements to assess biventricular systolic function when echocardiography is inadequate or inconclusive. It can also determine myocardial contractility and the presence of cardiac damage.[1,2,22] However, gadolinium, the contrast media commonly used for MRI, although safe to use in the postpartum period without interruption of breastfeeding, is avoided in pregnancy because it crosses the placenta.[3,23] An endomyocardial biopsy may be considered if there is suspicion of an alternative diagnosis (eg, giant cell myocarditis) that would require a different customized management plan.[1]

Treatment

Treatment for PPCM is similar to that used in heart failure. The focus is on treating the woman, not the fetus. A team approach is necessary and is likely to include cardiology, obstetrics, and neonatology. Treatment varies depending on two factors: if a woman is still pregnant at the time of diagnosis and if the woman is hemodynamically stable or unstable (*Table*). Because a woman may become critically ill within an unpredictable timeframe, she is likely to be admitted to the hospital for close cardiac monitoring and to receive supplemental oxygenation.

Severe PPCM with hemodynamic instability requires immediate intervention. A rapid review of vital signs and a targeted physical assessment are used to determine initial stability/instability. Continuous cardiac and blood pressure monitoring will be needed with supplemental oxygen provided to maintain an oxygen saturation greater than 95%. Admission to an acute care or critical care unit is common so

that strict intake and output, daily weights, and the intravenous (IV) administration of powerful vasoactive drugs can occur.[3] IV vasodilators like nitroglycerin are commonly used for decompensated heart failure during pregnancy. Inotropic support may be needed with dobutamine, dopamine, or milrinone to maintain systolic blood pressure and tissue perfusion in the critically ill woman.[24] If the heart failure continues to deteriorate and a woman develops cardiogenic shock, more aggressive therapies are indicated. Temporary mechanical circulatory support with an intra-aortic balloon pump (IABP), percutaneous ventricular assist device, or extracorporeal membrane oxygenation have been used successfully in PPCM with hemodynamic instability despite inotropic support.[24] Circulatory support is continued until the underlying heart function is improved or if heart transplantation is considered.[3] If the woman is antepartum, fetal monitoring will be employed to detect abnormalities in the fetal heart rate that could indicate poor oxygenation and circulatory compromise. In that case, prompt surgical delivery may be necessary.[3]

The goal of therapy for a hemodynamically stable woman with PPCM is to optimize maternal hemodynamics with careful observation of the fetus if pregnant. Pharmacotherapy is limited to beta blockers, vasodilators (preferably hydralazine), diuretics for fluid overload, and inotropes like digoxin if necessary.[8] Maternal hypotension is avoided to prevent decreased uterine perfusion if pregnant.[4] Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers improve survival in heart failure, but, along with spironolactone, are avoided in pregnancy.[1]

Women with PPCM are at high risk for the development of thrombosis and thromboembolism secondary to pregnancy-related hypercoagulability and likely blood stasis associated with varying degrees of systolic dysfunction. Anticoagulants must be considered.[8] Anticoagulants should be used when LVEF is less than 30% during late pregnancy or within 6 to 8 weeks postpartum.[10,25,26] To date, no published data are available to guide the decision of prophylactic versus therapeutic anticoagulation.

Heparin is preferred for use during pregnancy. Warfarin crosses the placenta and is avoided during

Table. Treatment overview for PPCM[1,3,4,8,23]

	Hemodynamically unstable (SBP < 90 mm Hg, SpO2 < 90%, lactate > 2.0 mmol/L)	Hemodynamically stable
Referral	Admit to acute care or critical care unit Goal: optimize preload with fluids or diuretics	Monitor as outpatient Goal: optimize maternal hemodynamics Careful observation of fetus if pregnant
Medication considerations	If SBP > 110 mm Hg: improve afterload with vasodilators (if pregnant, use hydralazine) If SBP < 90 mm Hg, consider inotropes or vasopressors Anticoagulation: heparin or low-molecular-weight heparin (eg, enoxaparin) preferred Avoid dobutamine in PPCM	Limited to: Beta blockers Vasodilators (hydralazine if pregnant) Diuretics for overload Anticoagulation: heparin or low-molecular-weight heparin (eg, enoxaparin) preferred
Other interventions	Consider mechanical circulatory support: percutaneous devices like a heart pump or ECMO	
Fetal considerations	Consider terminating pregnancy or early delivery Steroids for fetal lung maturity up to 34 weeks' gestation Operative delivery preferred Regional anesthesia for delivery preferred	Induce fetal lung maturity before 34 weeks' gestation Vaginal delivery preferred Regional anesthesia for delivery preferred
Postpartum considerations	Careful weaning and management from invasive modalities and medications Echocardiographic follow-up as indicated	Introduce standard heart failure therapy: ACE inhibitors and ARBs Beta blockers Echocardiographic follow-up as indicated

ACE, angiotensin-converting enzyme; ARBs, angiotensin receptor blockers; ECMO, extracorporeal membrane oxygenation; PPMC, peripartum cardiomyopathy; SBP, systolic blood pressure.

pregnancy.[22] Low-molecular-weight heparins (eg, enoxaparin) have gained favor because they do not cross the placenta and are considered safe during pregnancy and lactation.[1,3] The newer generation of anticoagulants, however, require more investigation for their use in pregnancy and lactation. To date, these are avoided.

ACE inhibitors should be started postpartum along with other medications to improve the prognosis of heart failure, including beta blockers. Pharmacotherapy will be continued indefinitely in the presence of persistent cardiac dysfunction, with most heart failure medications compatible with breastfeeding during the postpartum period.[27] If a woman is free from congestive symptoms, diuretic medications can be stopped first. Additional heart failure medications, if stopped, should be weaned off in a stepwise fashion with frequent clinical reassessments and echocardiographic monitoring of the LVEF every 3 to 6 months.[1] Left ventricular function will need to be reassessed after every drug discontinuation followed by annual clinical and echocardiographic assessments as indicated.

Delivery considerations

A pregnant woman with PPCM should continue her pregnancy until fetal viability and/or good fetal outcome can be achieved, but not at the expense of maternal health.[3] The goal of treatment is to stabilize the mother to avoid potential fetal complications of prematurity. Vaginal delivery is preferred if the mother is stable. Surgical delivery via cesarean section is associated with an increased incidence of hemorrhage, thromboembolic complications, and infection.[1] Hemodynamic instability despite medical therapy will prompt an early delivery or possible termination if the fetus is not viable. In the presence of severe heart failure, pulmonary edema, or an extremely preterm baby, operative delivery is preferred. Regional anesthesia for either vaginal or cesarean delivery is preferred.[28]

Timing and mode of delivery for a pregnant woman with PPCM should be discussed with her and coordinated with a combined team of cardiology and obstetrics with input from anesthesiology, nursing, pharmacy, and social work.[28] If vaginal delivery is being attempted, mothers with PPCM may tire faster and require additional support during the first and second stages of labor.[2] Regional anesthesia is preferred to decrease preload and afterload, and sudden drops in maternal blood pressure are avoided.[3]

Future pregnancy

Safety is a concern for women who had PPCM during, or in the weeks following, pregnancy. Consecutive pregnancies carry a recurrence risk of 30% to 50%.[8] Preconception counseling should include a discussion of the potential risks of recurrent myocardial dysfunction, which can persist after pregnancy. Recurrence, however, is unpredictable. Prepregnancy LVEF is the strongest indicator of outcomes, and a prepregnancy LVEF of 55% or greater is an important determinant for freedom from relapse in a future pregnancy.[29] If evidence of persistent myocardial dysfunction is present, a woman should be advised regarding the reported high risk of recurrent heart failure, further deterioration of cardiac function, and mortality.[1] If echocardiography demonstrates incomplete recovery of cardiac function after treatment, future pregnancy should be deferred while further treatment is attempted.[15] Contraceptive options for a woman with a history of PPCM to consider are limited. Estrogen-containing methods are contraindicated because of potential serious adverse effects. Progestin-releasing subcutaneous implants and progesterone-containing intrauterine devices or nonhormonal intrauterine devices are safe, reliable, and recommended.[3,5] Although barrier methods like a diaphragm remain an option, the use of such methods could be inconsistent and render the method ineffective. Sterilization eliminates the possibility of pregnancy and may be a viable option for women with persistent, severe heart failure.[1,3]

Conclusion

Peripartum cardiomyopathy is poorly understood and elusive. The pathophysiology of PPCM displays similar demographic and genetic characteristics like other forms of cardiomyopathy. It results in a decline in LV function and the onset of heart failure. The condition may be a mild or self-limiting illness or it can lead to severe heart failure and death. PPCM, however, continues to be underdiagnosed and incompletely characterized. The WHNP or midwife may be the primary source of healthcare along the continuum of prenatal, postpartum, and interconception care. Thus, PPCM should be considered in any pregnant or postpartum woman presenting with symptoms of heart failure.

Symptoms of heart failure, especially those related to shortness of breath or dyspnea, should be investigated with lab and imaging studies to assess LVEF. Prompt treatment with medications tailored to pregnancy and lactation may prevent adverse outcomes. Acutely ill women should be managed collaboratively by a specialized team. A woman may require advanced heart failure

therapies. Women considering subsequent pregnancies after a diagnosis of PPCM should be counselled and monitored by physicians or WHNPs and midwives familiar with PPCM. Thus, the role of the WHNP or midwife is integral to the identification, diagnosis, treatment, and, most importantly, the support and education of women with this puzzling and potentially lethal phenomenon. ■

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