International Clinical and Medical Case Reports Journal
Review Article (ISSN: 2832-5788)

A Review Article on Peripartum Cardiomyopathy

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Citation: *Samreen AF. A Review Article on Peripartum Cardiomyopathy. Int Clinc Med Case Rep Jour. 2023;2(3):1-12.* DOI: https://doi.org/10.5281/zenodo.7598365

Received Date: 27 January, 2023**; Accepted Date:** 30 January, 2023**; Published Date:** 02 February, 2023

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ABSTRACT

Peripartum cardiomyopathy (PPCM) is an uncommon, dilated cardiomyopathy with left ventricular systolic failure that can occur during late pregnancy or within five months of delivery. Although the condition is widespread, it appears to be most prevalent in black, Nigerian, and Haiti women. Although the exact pathogenesis of peripartum cardiomyopathy is unknown, genetic, inflammatory, and pregnancy-related hemodynamic alterations are thought to be contributory causes. Typically, the patient presents with classic symptoms of heart failure, such as exertional dyspnea, lower extremity edema, and signs and symptoms of hypervolemia (such as rales, S3 gallop and edema). The risk of thromboembolism and tachyarrhythmias is increased with PPCM. Generally, echocardiography is diagnostic; in some circumstances, cardiac magnetic resonance may be required. Salt restriction, loop diuretics, and if blood pressure permits, cardio selective beta blockers may be used. Due to teratogenicity, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, and mineralocorticoid receptor antagonists should be avoided. A multidisciplinary team strategy comprised of obstetricians, cardiologist, and maternal fetal medicine specialists should be adopted to enhance the outcome.

Keywords: Peripartum cardiomyopathy; Hypervolemia; Thromboembolism; Tachyarrhythmias

INTRODUCTION AND BACKGROUND

Peripartum cardiomyopathy (PPCM) is a rare, idiopathic, dilated cardiomyopathy that manifests in late pregnancy or early postpartum and is characterized by systolic failure. It was first documented in 1849 [1]. In 2010, the European Society of Cardiology defined peripartum cardiomyopathy as the onset of heart failure with a left ventricular ejection fraction of less than 45% during the last month of pregnancy or within five months after birth in the absence of an identifiable cause for the HF. Myocardial ischemia, stress cardiomyopathy, and substance abuse are notable causes of systolic heart failure. This review highlights current literature on the epidemiology, etiology, pathophysiology, presentation and management of PPCM.

Epidemiology

PPCM affects women of all racial and geographical backgrounds. Its incidence in the United States is believed to be between one in 900 and one in 4000 live births [3]. According to a recent study employing the US Nationwide Inpatient Sample, its prevalence climbed from one in every 1181 live births in 2004 to one in every 849 live births in 2011 [4]. Possible explanations for this trend include the rising incidence of PPCM risk factors such as advanced maternal age, pre-eclampsia, and multiple gestation (caused in part by assisted reproductive technologies), the increased prevalence of cardiovascular risk factors such as hypertension, diabetes, and obesity among women of reproductive age [4]. Given the rising incidence of polycystic ovarian syndrome (PCOS), which is partly attributable to the worsening obesity epidemic [5], assisted reproductive technology has gained popularity. Various pharmacological medications have been used in the treatment of PCOS [6], not only to aid in weight loss but also to stabilize and improve the hormonal profile and insulin resistance. For efficient weight loss and weight management strategies, a healthy balanced diet [7] and regular physical activity are considered indispensable.

The incidence appears to be highest in Nigeria (1 per 100 live births) and Haiti (One in 300 live births) [8]. There may be a genetic predisposition to this, as well as a high incidence of selenium deficiency [9] and, in Haiti, a high frequency of zinc deficiency [10] and pre-eclampsia. These are all potential reasons for this phenomenon. Incidence is three to four times greater among black women than among white women [11] and is the lowest score for Hispanic women [12]. A well-documented independent risk factor for PPCM is maternal age of 30 years or more, with an adjusted odds ratio of 1.7-1.8 compared to women under 30 [12]. PPCM is associated with pre-eclampsia and eclampsia. Other risk factors include substance abuse (cocaine use), diabetes, and multiparity (Table 1). Through a spectrum of physiological and biochemical alterations, it has been established that diabetics are at a very high risk for cardiovascular disorders [13-15].

Table 1: Risk Factors of PPCM

Non modifiable risk factors	Modifiable risk factors
Genetics	Obesity
Race- black, Nigerian and Haiti women	Diabetes mellitus
Pre-eclampsia	Hypertension
Age	Substance abuse (Cocaine use)
	Multiparity

Pathogenesis

Multiple pathogenic variables have been discovered despite the absence of a clear, unifying cause for PPCM. In the context of pregnancy-related cardiovascular alterations in the mother, these various factors result in a single final pathway with increased oxidative stress, breakdown of prolactin to angiostatic N-terminal 16 kDA prolactin fragment, and decreased vascular endothelial growth factor (VEGF) signaling due to elevated soluble FMS-like tyrosine kinas [2,16,17]. The pathophysiology of PPCM may entail abnormal prolactin processing. The 16 kDa prolactin cleavage fragment (16K PRL) promotes endothelial damage and cardiac dysfunction [17].

Hemodynamic changes in pregnancy: Several maternal cardiovascular physiologic abnormalities have been implicated in the pathogenesis of PPCM, including increased plasma volume, higher heart rate, and increased left ventricle volume and mass to accommodate the increased plasma volume and augment cardiac output [18].

Genetic predisposition: Evidence from numerous studies lends credence to the idea that genetic susceptibility and pregnancy-related variables may interact to cause PPCM. Variations in sarcomere-encoding proteins, such as TTN, have been associated with dilated cardiomyopathy [19].

Inflammatory cytokines: Tumor necrosis factor-alpha, interleukin-6, Fas/Apo-1, an apoptotic signaling receptor, and C-reactive protein are all linked to PPCM [20,21]. It has been proposed that PPCM can be caused by a maternal immunologic response to a fetal antigen (also known as fetal microchimerism). Fetal cells may enter the maternal circulation and become lodged in heart tissue, triggering a pathogenic immunological response [22]. Myocarditis has also been proposed as a factor in the development of PPCM [23].

Clinical features

Dyspnea with exertion, orthopnea, paroxysmal nocturnal dyspnea, and lower extremity edema. 6 Uncommon manifestations include symptomatic or even unstable arrhythmias [24] and arterial thromboembolism [25]. Although pregnancy may increase the risk of thromboembolism due to changes in the coagulation cascade caused by pregnancy, preexisting risk factors such as obesity may also play a role [26,27]. Lung crackles, S3 heart sound, high Jugular venous pressure, abdominal distention, and lower extremities edema are among the physical examination findings.

Diagnosis

Chest radiography may show pulmonary edema as well as an enlarged heart silhouette. BNP and N-terminal pro-BNP are frequently higher than in normal pregnancy [28]. Troponin may rise modestly. A diagnosis of PPCM necessitates echocardiographic evidence of left ventricular failure with LVEF 45% or greater, with or without left ventricular dilatation. Pulmonary hypertension, left atrial or biatrial enlargement, functional mitral and tricuspid regurgitation, and intracardiac thrombus can all be seen with echocardiography [29]. When echocardiography is technically constrained, cardiac magnetic resonance imaging may help diagnose. Although 1.5 Tesla magnetic resonance imaging is regarded to be safe in pregnancy, recommendations advise against using gadolinium, which penetrates the placenta and may be teratogenic [30]. Abdominal shielding is advised in pregnant women to reduce fetal radiation exposure [18]. Endomyocardial biopsy is not recommended and has no diagnostic histologic results.

Differential diagnosis

The differential diagnosis includes pre-existing cardiomyopathy, including familial dilated cardiomyopathy, Takotsubo/stress cardiomyopathy [31,32], prior myocarditis, valve abnormalities from infective endocarditis [33,34], ischemic cardiomyopathy, and drug [35] or toxin-induced cardiomyopathy; mitral stenosis and aortic stenosis, congenital heart disease, such as shunt lesions; and pulmonary arterial hypertension [36].

Management

In general, management recommendations are drawn from other heart failures with lower ejection fraction recommendations. Volume management comprises salt restriction, loop diuretics, and if hemodynamics allow cardio selective beta blockers to prevent uterine contraction via B2 innervation. Due to the risk of maternal hypotension and uterine hypoperfusion, it is prudent to avoid over-diuresis. Due to its teratogenicity, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are contraindicated during pregnancy. Sacubitril-valsartan, an angiotensin receptor, and neprilysin inhibitor is also contraindicated during pregnancy and has not been investigated during breastfeeding. As a vasodilator therapy, hydralazine and nitrates can be employed. Based on the RALES and EMPHASIS-HF studies [37], mineralocorticoid receptor antagonists are recommended for patients with NYHA II-IV heart failure and an LVEF 35%114; the use of mineralocorticoid receptor antagonists has been associated with a reduction in mortality in heart failure with preserved ejection fraction [38]. Due to their anti-androgenic effects, these agents should be avoided during pregnancy, but may be used throughout breastfeeding [39]. Digoxin is safe during pregnancy. In PPCM, the use of the B agonist dobutamine has been contentious. Thromboembolism is a relatively frequent PPCM complication. Following ESC guidelines, patients with PPCM and LVEF 35%, as well as those who have received bromocriptine, should be anticoagulated [40]. Warfarin is not recommended due to its teratogenic effects. Due to a lack of human data, the newer directly acting oral anticoagulants are not approved during pregnancy. Unfractionated heparin and heparin with a low molecular weight do not pass the placenta and are the anticoagulants of choice for pregnant women with PPCM. Women with PPCM complicated by arrhythmias may require acute or chronic antiarrhythmic medication therapy, or both. Cardioversion and defibrillation are deemed safe during pregnancy and should be administered immediately in emergencies, just as they would be for non-pregnant individuals [41]. Due to reports of subsequent fetal arrhythmias in cases of non-emergent cardioversion, fetal monitoring may be recommended. The ESC and AHA advocate considering wearable cardioverter defibrillation devices as a bridge to left ventricular recovery or ICD implantation after three to six months in women with PPCM and LVEF 35% [29]. A multidisciplinary team comprised of obstetrics, anesthesia, maternal-fetal medicine, and cardiology should individualize patient management, including follow-up intervals and mode of delivery [42] (Figure 1).

Figure 1: A Multidisciplinary Patient Management Team comprised of obstetrics, anesthesia, maternal-fetal medicine and cardiology.

According to ESC [43], cesarean birth should be considered in cases of acute heart failure but is otherwise reserved for obstetric purposes. Hemodynamic labor changes may be minimized by epidural anesthetic and aided second-stage delivery (use of vacuum or forceps) [44].

CONCLUSION

Peripartum cardiomyopathy is a rare but fatal cardiovascular disorder defined by reduced left ventricular systolic function affecting women in late pregnancy or early puerperium. In addition to advanced maternal age, multiparity, obesity, diabetes, and preeclampsia are major risk factors. Although the actual cause is unknown, the occurrence is particularly common among black women and women from Nigeria and Haiti. There appears to be a genetic predisposition as well. To prevent catastrophic consequences, timely assessment and evaluation using imaging techniques such as echocardiography, specialist referral, and management with loop diuretics and beta blockers are crucial. A multidisciplinary strategy comprising maternal-fetal medicine, cardiologist, and obstetricians is critical in enhancing both maternal and fetal outcomes.

CONFLICT OF INTEREST

Author reports that there are no conflicts of interest.

FUNDING

This research did not receive any specific grant from funding agencies in the public, commercial, or not for profit sectors.

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