REVIEW ARTICLE

Peripartum Cardiomyopathy: A Review

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Introduction:

Peripartum cardiomyopathy (PPCM) is a rare disorder of heart muscle of unknown aetiology, and presents clinically with the onset of cardiac failure in the last month of pregnancy or in the first five post-partum months. The first description of idiopathic myocardial failure with onset in the puerperium has been attributed to Ritchie in 1849[1]. Since some of the reported patients developed cardiac failure in the first month of pregnancy, it is probably more appropriate to use the term "peripartum cardiomyopathy" rather than post-partum cardiomyopathy [2]. The early diagnosis and treatment of this form of cardiomyopathy is critical to reduce the morbidity and mortality.

Incidence:

The incidence of PPCM is not known because population based estimates are still not available [3]. Although the reported incidence and rate ranges from one per 1485 to one per 15000 live births [4], the currently accepted estimate of incidence is approximately one per 3000 to one per 4000 live births [3], with a higher incidence rate in Africa [5].

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Definition:

It is a form of dilated cardiomyopathy of unknown aetiology having following criterias[2,3]:

a) Development of cardiac failure in the last month of pregnancy or within five months of delivery;

b) Absence of identifiable cause for the cardiac failure;

c) Absence of recognizable heart diseases prior to the last month of pregnancy; and

d) Left ventricular systolic dysfunction demonstrated by classic echocardiographic criteria such as depressed shortening fraction or ejection fraction.

Risk factors:

Risk factors essentially identified include multiparity, advanced maternal age, multifoetal pregnancy, pre-eclampsia, gestational hypertension and African-American race [3].

Aetiopathogenesis:

The aetiopathogenesis of PPCM still remains unknown and many hypothesis have been proposed including myocarditis, maladaptive response to haemodynamic stresses of pregnancy, cytokine production and prolonged tocolysis[3]. Some familial cases of PPCM have been reported [8], raising the possibility that PPCM is a familial dilated cardiomyopathy unmasked by the pregnancy [6], (Fig.- 1).

In the light of the presence of dense lymphocytic infiltrate, myocyte oedema, necrosis and fibrosis revealed in vetricular biopsies of patients with PPCM, Melvin et al[7] proposed myocarditis as the cause of PPCM. Another important factor, which may cause PPCM, is the abnormal immune response to pregnancy, associated with high titers of autoandibodies against particular cardiac tissue proteins[8]. The haemodynamic stresses of pregnancy are also considered a possible cause of PPCM. The increase in blood volume and cardiac output during pregnancy causes transient and reversible hypertrophy of left ventricle. During third trimester, a reversible decrease in left ventricular systolic function occurs. It is possible that PPCM is due to the exaggeration of this decrease in the systolic function[9]. Other possibilities include, prolonged tocolysis[10], proinflammatory cytokines[11] (TNF, IL 1, IL 2), deficiency of selenium which may increase heart muscle susceptibility to viral infection, hypertension and hypocalcaemia[12]. A viral trigger for the development of PPCM has also been postulated. Bultman and colleagues[13] identified viral genomic material in endomyocardial biopsy tissue from patients with PPCM.

Clinical description:

The patients with PPCM present with the typical signs and symptoms of left ventricular failure. The majority of failure occurs after delivery and the immediate post-partum period. However, when it occurs during last month of pregnancy, the diagnosis of cardiac failure is difficult because some of the signs and symptoms such as, fatigue, orthopnoea, paedal oedema are also common during late pregnancy. Symptoms and signs that are

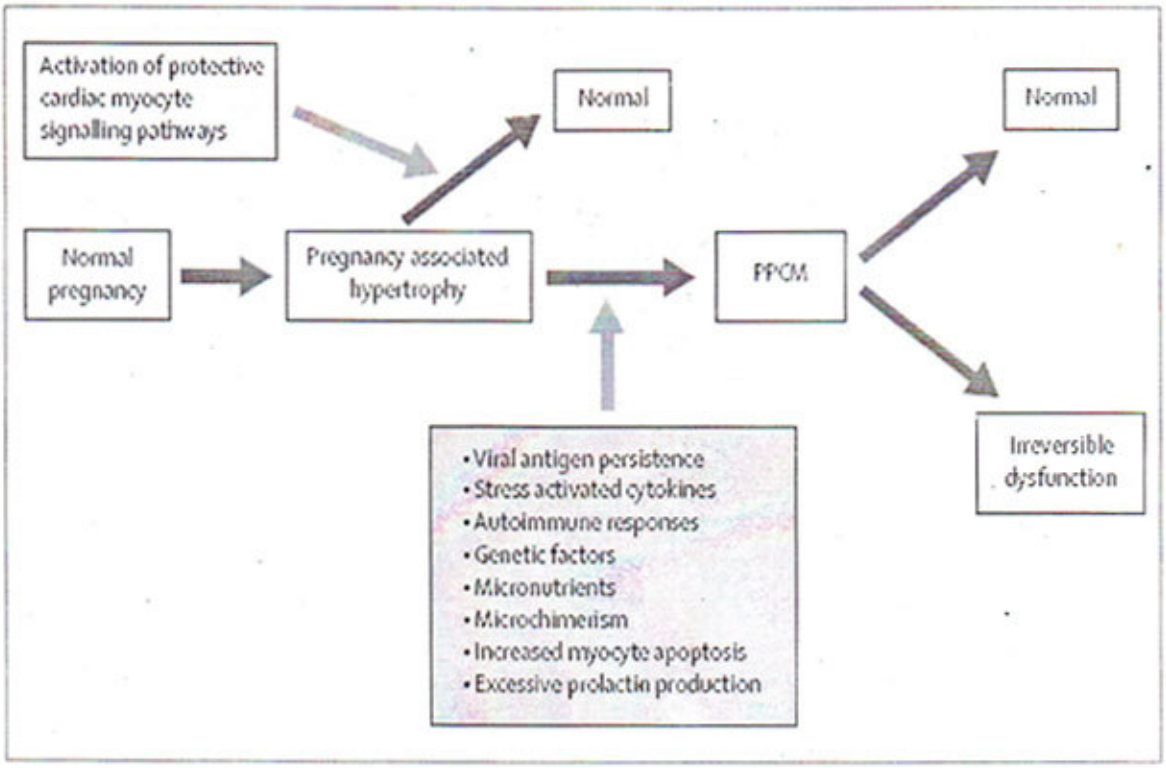

Figure-1: Proposed factors investigated to be contributing to the pathogenesis for PPCM [14]

commonly revealed include shortness of breath, orthopnoea, cough, fatigue, chest pain, palpitation, paedal oedema, jugular venous distention, tachycardia with or without third heart sound, hepatomegaly, abdominal discomfort, new murmurs and pulmonary crackles. Left ventricular thrombus is common in PPCM with a left ventricular ejection fraction less than 35%. Peripheral thromboembolism then becomes possible to any part of the body. Cerebral embolism, mesenteric artery occlusion, myocardial infarction and haemoptysis may be the sequelae[14].

Diagnostic methods:

The criteria for diagnosis of PPCM have already been described in definition. The heart failure must become manifest in the last month of pregnancy or within five months of delivery and no other aetiology for heart failure should be found. PPCM remains a diagnosis of exclusion. Therefore, all other causes of dilated cardiomyopathy with heart failure must be systemically excluded before accepting the designation of PPCM [14].

ECG, chest X-ray, and echocardiographic studies should be routinely performed. The ECG may be normal, but usually demonstrates sinus tachycardia. There may be atrial fibrillation, ventricular premature beats, non-specific ST and T changes or bundle branch blocks[15]. Chest X-ray usually shows cardiomegaly with pulmonary venous congestion and small bilateral pleural effusion[16]. Echocardiography is very important to exclude other causes of heart failure. It usually shows dilated left ventricle with impairment of overall systolic performance[17]. Haemodynamic examinations are usually not performed, but may show an elevated right and left heart filling pressure with diminished cardiac output, left ventriculography demonstrates a global reduction in the left ventricular systolic performance, and coronary angiography are generally normal[18]. The endomyocardial biopsy may be considered to confirm the diagnosis if the nature of PPCM remains unclear[19]. Finally, to rule out infective causes, blood samples to be tested by bacterial and viral culture and for Coxsackie's B virus titres.

Medical management:

The medical management of peripartum cardiomyopathy is similar to other forms of heart failure due to systolic dysfunction with exception that potential effects of drugs to the foetus must be considered. In general, the goal is to reduce the amount of volume returning to the heart (preload reduction), decrease the resistance against which heart must pump (after load reduction) and increase the contractile force (inotrophy)[20]. The corner-stone of pharmacological therapy begins with after load reduction with the use of angiotensin converting enzyme inhibitors or angiotensin II receptor blockers[21], but its use is contraindicated in pregnancy [22]. In this circumstance, the combination of hydralazine and nitroglycerine or amlodipine can be safely used[23,24]. Pre-load reduction can be accomplished with diuretics especially when sodium restriction alone is therapeutically unsuccessful[25]. In pregnancy, diuretics must be used with caution. Beta-blockers have been shown to improve mortality by reducing deleterious effects of excessive stimulation of sympathetic nervous system and delays progression of myocardial dysfunction[26]. Vasodilating beta blockers such as carvedilol also reduces afterload through alpha-1

adrenergic blockade and have clinical benefit including mortality reduction[27]. A reasonable approach is to use beta blockers in patients who continue to have symptoms despite standard heart failure management[3]. It is necessary to remember that long term use of beta blockers during pregnancy may be associated with low birth weight babies, neonatal hypotension and bradycardia[28]. Digoxin is found beneficial, especially if atrial fibrillation is present[3]. Patients with evidence of systemic embolism, with severe left ventricular dysfunction or documented intracardiac thrombus should receive anticoagulant[29]. Before delivery, heparin is the drug of choice, which can be switched to warfarin after delivery for a period of six months[3]. Immunosuppressive therapy can be considered for them who do not improve after anti-coagulant treatment[3]. One retrospective study suggested that women with PPCM when treated with intravenous immunoglobulin improve in ejection fraction of LV[30]. Patients with severe heart failure may require hospitalization and need more aggressive support including intravenous inotropic agents, oxygen and invasive monitoring[3]. Given the potential inflammatory nature of PPCM there may also be a role of other immuno-modulatory therapy such as pentoxifylline in addition to conventional therapy [31].

The non-pharmacological treatment includes low sodium diet (<4 gm/day), fluid restriction (<2 L/day) and modest daily exercise (e.g. walking). In addition to the treatment of cardiac failure, an obstetric plan of care is also needed when it occurs in pregnancy. Collaboration among the obstetrician, cardiologist and anaesthesiologist is essential to optimize the care. If the parturient's cardiac status can be stabilized with medical therapy, induction of labour is usually recommended and caesarian section is reserved for obstetric indications. However, in parturients who experience acute cardiac decompression, caesarian delivery is required because of an inability of the mother to tolerate the prolonged stresses of labour [32].

Natural history and prognosis:

Too few patients with PPCM have been studied to fully analyze the natural history of this disease[20]. The overall prognosis depends on normalization of left ventricular size and function within six months of delivery[33] and probable mortality rate ranges from 7% to 60%[4]. In a study of patients with various types of cardiomyopathy, those with peripartum cardiomyopathy had a substantially better prognosis with a 94% survival rate at five years [34].

Subsequent pregnancies:

There is concern that patients with PPCM are at risk of recurrence of their cardiomyopathy in future pregnancies. In a long term follow up study reported by Demarkis et al[32], eight of 14 patients whose heart size returned to normal after the first episode of PPCM had subsequent pregnancies. Of the eight patients, two developed PPCM with pregnancies. A study in Haiti followed 99 patients, 15 of whom became pregnant again, and eight of them again experienced worsening heart failure and long term systolic dysfunction[35]. Therefore, women with history of PPCM need extensive counseling about future pregnancies. Currently there is no consensus regarding recommendations for future pregnancy after an episode of PPCM[3]. Patients whose left ventricular size or function does not return to

normal should be counselled strongly to avoid subsequent pregnancy[32]. Patients whose cardiomyopathy apparently resolves, counselling is still recommended regarding the risk of recurrence in future pregnancies[36]. However, many women who have fully recovered from PPCM have gone to have successful pregnancies[37]. As may be expected, the cardiomyopathy can also affect the foetus. In a study by Witlin et al[8], there were no foetal deaths but there was an increased incidence of premature and low birth weight infants. Therefore, subsequent pregnancies, if they can not be avoided, should be managed in collaboration with a high risk perinatal centre[3].

Conclusion:

Peripartum cardiomyopathy is a rare disease of unknown cause that strikes women in the child bearing years, may recur in the subsequent pregnancies, and is associated with a high morbidity and mortality. Hypothesis about the cause centre on interactions of peripartum physiology with infectious, inflammatory, genetic, hormonal or metabolic factors. Many women in the last month of pregnancy or early post-partum period experience dyspnoea, fatigue, pedal oedema like symptoms identical to early congestive heart failure. Therefore, the diagnosis of PPCM is challenging and requires vigilance[38]. Clinical presentations include usual signs and symptoms of heart failure. Diagnosis of PPCM requires exclusion of other causes of cardiomyopathy and heart failure and the criteria proposed by Demarkis et al[2]. The primary goal of therapy is to alleviate symptoms of congestive heart failure. These patients need regular follow-up. Ascertainment of cardiovascular risks of subsequent pregnancies should be evaluated and active counselling is mainstay to avoid morbidity and mortality. Areas for future research includes immune dysfunction, the role of viruses, non-conventional treatment such as immunosuppression, immune adsorption, aphaeresis, antiviral treatment ,suppression of pro-inflammatory cytokines, and strategies for control and prevention[14] .

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