Peripartum cardiomyopathy searching for a better understanding

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ABSTRACT

Congestive heart failure is an uncommon complication of pregnancy with potentially life-threatening consequences. Peripartum cardiomyopathy (PPCM) is a disease of unknown cause in which severe left ventricular dysfunction occurs during late pregnancy or the early puerperium. In the past, the diagnosis of this entity was made on clinical grounds; however, modern echocardiographic techniques have allowed more accurate diagnoses by excluding cases of diseases that mimic the clinical symptoms and signs of heart failure. Risk factors for peripartum cardiomyopathy include advanced maternal age, multiparity, African descent, twinning, and long-term tocolysis. An extensive search for the causes of peripartum cardiomyopathy has been unrevealing. Treatment does not differ from treatment of idiopathic cardiomyopathy. The prognosis of peripartum cardiomyopathy is related to the recovery of ventricular function. Caution is advised in recommending subsequent pregnancy, especially if left ventricular dysfunction is persistent. In this review, we will discuss different aspects of PPCM as the initial patient contact, obstetricians and family practitioners must recognize this malady early and rapidly institute the proper medical therapy directed towards the congestive state.

Saudi Med J 2003; Vol. 24 (10): 1048-1051

Peripartum cardiomyopathy (PPCM) was initially defined as left ventricular dilatation and failure, first developing during the third trimester of pregnancy or during the first 6 months postpartum.[1] However, the definition has been reviewed recently based upon previous works of Demakis et al.[3,4] The recent definition is summarized as follows.

Classic criteria. 1. Development of cardiac failure in the last month of pregnancy or within 5 months of delivery. 2. Absence of an identifiable cause for the cardiac failure. 3. Absence of recognizable heart disease prior to the last month of pregnancy.

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

Historical background. A relationship between pregnancy and dilated cardiomyopathy (DCM) was first noted in the 19th century.[5] They first reported autopsy evidence of myocardial degeneration in patients who died in the puerperium[5] till 1937 when Gouley et al,[6] characterized the disease by describing the clinical and pathological features of 7 pregnant women who had severe and often fatal heart failure secondary to non-ischemic dilated cardiomyopathy in the later months of their pregnancies, which persisted after delivery.

In 1971 Demakis and Rahimatoola[4] established standard clinical criteria for the Diagnosis of peripartum cardiomyopathy (PPCM). In 1995 Lampert and Lang[7] added the forth criteria for the definition of peripartum cardiomyopathy, which includes echocardiographic demonstration of impairment in left ventricular systolic function.

Epidemiology. The incidence of PPCM varies from one in 1300 to one in 15000 pregnancies in United States of America (USA).[4,8] In Nigeria, the incidence is estimated to be as high as 1%.[9] The majority of these cases are likely to be the result of pure volume overload

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caused by the Hausa tradition of ingesting Kanw, a dried lake salt, while lying on heated mud beds for 40 postpartum days.[10] However, these incidences may be overestimated because of inadequate strict criteria for the diagnosis. The currently accepted estimate of incidence of peripartum cardiomyopathy is approximately one per 3000 to one per 4000 live births, which would translated to between 1000 to 1300 women affected each year in the USA.[11]

Etiology. The etiology of the disease is largely unknown[12-14] although some investigators question whether PPCM is indeed a distinct entity.[15] However, it is a distinct entity based on a cluster of PPCM cases found in young women (among whom idiopathic dilated cardiomyopathy is rare) in the peripartum period[12] whereas patients with underlying cardiac disease (for example valvular, ischemia) usually have symptoms and signs of heart failure during the second trimester of gestation, coinciding with the maximal hemodynamic burden imposed by pregnancy. Hemodynamic data suggest that changes in the cardiovascular system induced by pregnancy usually resolve within 1-3 months postpartum.[16] The onset of PPCM usually occurs well after delivery when the hemodynamic stress associated with pregnancy is resolving.[17] In the workshop organized by National Institute of Health.[2] The participants concurred that PPCM is a distinct entity, rather than a clinically silent underlying cardiomyopathy unmasked by hemodynamic stress of pregnancy, because the reported incidence is higher than the incidence of idiopathic cardiomyopathy.[18] In the literature so many factors have been accused as an etiology of PPCM including, myocarditis[19,20] an abnormal immune response to pregnancy[21-24] a maladaptive response to hemodynamic stresses of pregnancy[25] stress activated cytokines,[26] prolonged tocolytic treatment,[27,28] familial PPCM,[29-31] seletium deficiency[32] cocaine abuse[33] and enterovirus and coxackiviruses infection.[34,35]

Risk factors for development of peripartum cardiomyopathy. The syndrome is more prevalent in women more than 30 years old and the mean age was significantly older in patient with PPCM in comparison with the general obstetric population.[28] However, patients who were diagnosed to have PPCM were significantly younger than idiopathic dilated cardiomyopathy group.[36] This syndrome has been reported in patients of a wide range of age.[3,37] Multiparity is a risk factor for PPCM, though it has been reported in primiparous women, but the incidence is higher in women with multiple pregnancies.[13,23,28] Peripartum cardiomyopathy has been reported in white, Chinese, Korean and Asian women, however, the majority of affected patients in USA are of African origin.[8,13] Twin pregnancies at higher risk of developing PPCM and 7-10% of published cases of PPCM were twin pregnancies.[4,10,37]

Hypertension and pre-eclampsia. Elevated blood pressure is frequently demonstrated although blood pressure may be either normal or decreased.[12] Cunningham et al[8] reported 14 patients out of 21 were hypertensive. The incidence of pre-eclampsia and chronic hypertension was significantly higher among PPCM patients than the general obstetric population.[28] Pre-eclampsia is associated with PPCM and pre-eclampsia causes significant changes in hemodynamic balance and vascular re-activity in pregnancy. However, cardiomyopathy is an infrequent complication of pre-eclampsia.[28] Conversely, pre-eclampsia rarely causes heart failure in young women, but in older women with underlying vascular disease pre-eclampsia may cause after load cardiac failure.[8]

Clinical presentation. Veille's literature survey of 329 PPCM cases indicates that 37% of patients had symptoms during the first postpartum month and an additional 60% during the second postpartum month.[13] Only 3.5% of PPCM occurred during the last 8 weeks of pregnancy and 4.3% found beyond 6 months postpartum. The presentation of patients with PPCM is similar to that of patients with left ventricular systolic dysfunction. Usual presenting complaints consist of dyspnea, cough, chest pain and fatigue.[28]

Diagnosis of peripostpartum cardiomyopathy. The chest x-ray is non-specific and not sensitive for the diagnosis of PPCM.[28] The electrocardiogram has no significant contribution to the diagnosis.[3,9,38]

Echocardiography previously, the long-term prognosis correlated well with the degree of cardiomegaly persisting at 6 months after initial presentation.[39] Nowadays, echocardiography is considered the cornerstone for the diagnosis of peripartum cardiomyopathy.[28,40]

It has been proposed that echocardiography has implications not only for modifying the diagnostic criteria of PPCM, but also to stratifying the prognosis.[41] Usually it shows a dilated left ventricular cavity with marked impairment of overall systolic performance, heterogeneities in systolic wall thickness, mitral regurgitation, biatrial enlargement and small hemodynamically insignificant pericardial effusion.

Hemodynamic data. Usually demonstrated elevated right heart and left heart filling pressures, with diminished cardiac output in addition to increase total systemic vascular resistance.[25] It is indistinguishable from idiopathic dilated cardiomyopathy,[36] but Marin-Neto et al[42] found that cardiac output is high and systemic vascular resistant is low, and this provided a better level of after load and implying a more favorable prognosis. However, a hemodynamic study may require to guide the treatment during delivery in presence of heart failure and pulmonary edema.

Coronary angiogram. The yield of coronary angiography in PPCM is low; risk factor analysis should guide the clinician in requesting this study.[43]

Myocardial biopsy. Biopsy results usually is non-specific, but the picture of myocarditis may be seen if biopsy is performed early after the diagnosis. Four patients out of 14 patients (29%) with PPCM had

myocarditis compared to only 5 of the 55 patients (9%) with idiopathic dilated cardiomyopathy.[36] Therefore, biopsy is not recommended particularly if it is late after the onset of the symptoms as the incidence of myocarditis is low;[44] the link between immune suppossive treatment and resolution of myocarditis cannot be established because of spontaneous recovery.[43]

Treatment of peripartum myocardiopathy. Treatment as in any other heart failure except to consider contraindications to drugs use during pregnancy; such as angiotensin converting enzymes inhibitor. Oral anticoagulation is indicated in patients with severe left ventricular dysfunction, as thromboembolic phenomena may complicate up to 53% of cases.[3] Immuno suppressive therapy can be considered if an endomyocardial biopsy indicates myocarditis, and if there is no improvement after 2 weeks of standard heart failure therapy.[2] In the treatment of patients with persistent heart failure unresponsive to conventional medical therapy, cardiac transplantation is a valuable option, which can successfully be performed in PPCM. Favorable outcome is attributed to the young age of recipients, to the onset of the heart failure and the consequently, minimal amount of end organ damage. Aggressive measures, such as temporary support in the form of cardiopulmonary bypass or ventricular assist device, have been advocated as a bridge to cardiac transplantation.[45]

Natural history and prognosis. In the USA reported mortality from PPCM range from 25-50%[3,36] and death usually is caused by chronic progressive congestive heart failure, arrhythmia, or thromboembolic complication. Some reports suggest that the prognosis as in other form of heart failure, is related to left ventricular size[46] or the severity of left ventricular dysfunction at the time of presentation.[41]

Survivors of PPCM compared with non-survivors had significantly higher left a ventricular ejection fraction (22.8% versus 10.6%) and a small left ventricular end diastolic diameter (5.8 cm versus 6.9 cm) at the time of diagnosis.[36] Apparently, heart destined to recover normal function do so within 6 months from the time of initial diagnosis. The long term prognosis correlates well with the degree of cardiomegaly persisting by 6 months after initial presentation.[3] Recently, we reported a King Khalid University Hospital experience.[47] We identified 14 patients who satisfied the diagnostic criteria of PPCM. The average age of the patient was 32 years (range 22=40 years, SD=6.1 year). The majority of patients presented in the postpartum period, 10 (71.4%) within 3 months of delivery, and 3 patients (21.4%) between 4-6 months of delivery, with only one presenting in the last month of pregnancy.

All the women had spontaneous vaginal delivery except 2 who had cesarean section, one of them with a twin pregnancy. The duration of follow up was variable between 3-58 months. The echocardiographic finding in this study demonstrated 3 groups of patients at admission: 1. Patients with ejection fraction of more than 30% where complete recovery occurred. 2. Patients with ejection fraction of 15-30%. These patients had persistent cardiac failure. 1. Patients with ejection fraction of 15% or less died.

Subsequent pregnancies. Relapse of PPCM with subsequent pregnancies occurs as a result of persistence of left ventricular dysfunction, or by reactivation of the underlying disease process.[48] Recurrence after an intervening normal pregnancy had also been reported,[13,49] particularly in patients with persistent heart failure or those who do not attain heart size within 6-12 months after the initial episodes.[8,13] Therefore, most experts agree that patients with PPCM and persistent left ventricular dysfunction should not get pregnant again as there will be a high complication rate.

Subsequent pregnancy is controversial in patients who recover left ventricular function at rest. Dobutamine stress echo may be required to assess the contractile reserve before allowing pregnancy.[7] The rate of cesarean section reported to be 43%.[36]

Peripartum cardiomyopathy and the outcome of the fetus. There is an increase incidence of premature and low birth weight among babies of mothers with PPCM. These finding suggest that the underlying disease process may begin much earlier than the clinical signs and symptoms are manifested. The development of PPCM in the mother may be a marker of high risk for this baby.[50] The fetal growth and development were normal.[36] Fetal cardiac deceleration occurs during labor, it requires shortening the second stage of labour by either forceps or may be a caesarean section. Delivery should be under monitoring with a teamwork and multidiscipline. The risk for the fetus is not dismal compared to the risk to the mothers.

In conclusion PPCM is a rare disease of unknown etiology which occurs more commonly in older multiparous and hypertensive women. The prognosis is related to the recovery of left ventricular function. Patients with severe myocardial dysfunction are unlikely to regain normal cardiac function on follow up. Caution is advised when recommending subsequent pregnancy, especially if left ventricular dysfunction persists. Multicenter study or registry is recommended to characterize this entity in more details and provide particular search for the underlying etiology.

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