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Review

Peripartum cardiomyopathy: A review article

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ABSTRACT

Peripartum cardiomyopathy (PPCM) is a disease with significant morbidity and mortality. It has a global spread but with important geographic variation. The aetiology and pathogenesis of PPCM is unknown, but several hypotheses have been proposed over the years. These include myocarditis, oxidised prolactin, autoimmunity, malnutrition, genetic susceptibility and apoptosis. This review discusses the epidemiology, risk factors, aetiology, clinical features, diagnosis, treatment and prognosis of PPCM. The possible role of novel echocardiographic techniques in the study of PPCM was also discussed.

1. Introduction

Peripartum cardiomyopathy (PPCM) was described in 1880 by Virchow and Porak, who were the first to establish an association between cardiac failure and the puerperium [1,2]. In 1937, Gouley et al. described the clinical and pathological features of seven pregnant women who had severe and fatal heart failure (HF); establishing the syndrome as a distinct clinical entity [3]. These women had a dilated heart in the last months of pregnancy, which persisted after delivery. An autopsy on the four out of the seven patients who died demonstrated enlarged hearts with distinct widespread severe focal areas of necrosis and fibrosis [3]. Hull and Hidden then described 80 patients with this condition in New Orleans in 1938, and called it 'Postpartal Heart Failure' [4].

Over the years, research on PPCM had dragged on, but at a slow pace with little funding, perhaps because it has been a disease that is rare in economically advanced countries, but common among the less-privileged populations.

2. Definitions

In 1971, Demakis et al. were the first to define and describe the diagnostic criteria of PPCM. They defined PPCM as the development of HF within the last month of pregnancy or first 5 months postpartum, in the absence of any identifiable cause for HF, and any recognisable heart disease before the last month of pregnancy [5,6]. Since then, the definition of PPCM has undergone several modifications.

In April 1997, the National Heart, Lung, and Blood Institute (NHLBI) and the Office of Rare Diseases of the National Institutes of Health (NIH) of the United States convened a Workshop on PPCM, to foster a systematic review of information and to develop recommendations for research and education. The agreed definition of PPCM, was based on the definition by Demakis et al. of 1971, but including left ventricular (LV) systolic dysfunction demonstrated by classic echocardiographic criteria, such as depressed LV shortening fraction (LVSF) (<30%) or ejection fraction (LVEF) (<45%) [7].

In 2007, the European Society of Cardiology (ESC) working group on myocardial and pericardial diseases redefined cardiomyopathies including PPCM, which they defined as a form of dilated cardiomyopathy (DCM) that presents with signs of cardiac failure during the last month of pregnancy or within 5 months of delivery [8]. DCM itself was defined by the presence of LV dilatation and systolic dysfunction in the absence of abnormal loading conditions (hypertension, valve disease) or coronary artery disease (CAD) sufficient to cause global systolic impairment. Right ventricular (RV) dilatation and dysfunction may be present but is not a diagnostic criterion [8]. In this classification, the focus was mainly on the concept of morphology and function of the heart, and away from that of diagnosis by exclusion. The aim was to promote a greater appreciation of the broad spectrum of diseases that can cause cardiomyopathies in everyday clinical practice [8].

The most recent definition of PPCM was by the HF Association of ESC Working Group on PPCM, who believed that the time frame along with

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the echocardiographic cut-offs in the definition by NHLBI group is arbitrary and may lead to under-diagnosis of PPCM [7,9]. They therefore proposed the following simplified definition: "Peripartum cardiomyopathy is an idiopathic cardiomyopathy presenting with HF secondary to LV systolic dysfunction towards the end of pregnancy or in the months following delivery, where no other cause of HF is found. It is a diagnosis of exclusion. The LV may not be dilated but the LVEF is nearly always reduced below 45%" [9]. The decision by this group to expand the definition to include women who present earlier in pregnancy was informed by the results of studies which have confirmed that such presentation was not uncommon, although most of PPCM patients present in the last month of the pregnancy and puerperium [10]. Elkayam et al. have demonstrated that the clinical presentation and outcome of patients with pregnancy-associated cardiomyopathy, diagnosed between the 17th–36th weeks of gestation, were indistinguishable from those of patients meeting classic criteria for PPCM, and therefore concluded that the pregnancy-associated cardiomyopathy and PPCM represent a continuum of the same disease [10].

In general, experts now concur that PPCM is now considered to be a distinct disease, and not a clinically silent idiopathic DCM unmasked by the stresses of pregnancy [7,9]. This is mainly because the reported incidence is higher than the incidence of idiopathic DCM, its prognosis is better than that of idiopathic DCM, and because the high frequency of myocarditis would not be expected in a population presenting with decompensation of pre-existing heart disease due to hemodynamic stress [7].

3. Epidemiology

The true incidence or prevalence of PPCM is unknown. This is largely because there have been only very few population-based studies on PPCM worldwide. PPCM is rare in some parts of the world and more common in others. For example, PPCM is very rare in Europe, but common in West Africa [11,12]. Recent studies suggest an estimated incidence of one case per 299 live births in Haiti, one case per 1000 live births in South Africa, and one case per 2289–4000 live births in the USA [7,13,14,15]. The reasons for this variation in incidence between and within countries remain unknown, but probably reflect an overestimation of the disorder in earlier studies that relied upon clinical criteria alone for the diagnosis. The Hausa tribe of northern Nigeria appears to have the highest known incidence in the world of HF within the time frame of PPCM, peripartum cardiac failure (PPCF); the incidence reported to be as high as 1:100. This is probably related to some local Hausa–Fulani customs, such as ingestion of a form of lake salt in the immediate postpartum period, a practice that can produce significant volume overload [16,17].

PPCM was recently described as the most prevalent type of cardiomyopathy in Kano, north-western Nigeria, found in 55 out of 1296 patients (4.2%) referred for echocardiography over a period of 7 months, representing 52.4% of all cardiomyopathies [18]. The prevalence of PPCM is still very high, despite the fact that the cultural practices identified decades ago to be important in the aetiology of PPCF in Zaria, a city about 120 km from Kano, are no longer popular. These cultural practices include frequent hot baths by breastfeeding mothers during the puerperal period, together with regular ingestion of a thick drink made from millet and rich in dry lake salt, 'Kunun Kanwa', and lying on heated mud beds [16,17]. Some of the customs are still being practised by the Hausa and Fulani women across northern Nigeria, although with lesser frequency, for shorter duration of time within the puerperal period, or even abandoned (as in the case of lying on heated mud beds) by most women in the present day northern Nigeria [19,20]. The disease is less common among other ethnic groups in the country.

PPCM has been associated with several risk factors over the years, but there is significant inconsistency between studies of their association with the disease. These risk factors include increased age, gravidity or parity, African origin, toxaemia or hypertension of pregnancy, use of tocolytics, twin pregnancy, obesity and low socioeconomic status [21,22,23]. Although PPCM is thought to be more prevalent in the upper and lower extremes of childbearing age, and in older women of high parity, it is important to note that 24–37% of cases may occur in young primigravid patients [13,14,24]. Several case series reports from Nigeria, Haiti and South Africa did not show a disproportionate role for older age, multiparity, and long-term use of tocolytic agents in the development of PPCM [13,18,24,25]. In addition, Elkayam et al. clearly showed that PPCM in the United States is not limited to black women, and their study did not support a strong association between multiparity and development of PPCM because almost 40% of the cases occurred in association with the first pregnancy and >50% with the first 2 pregnancies [10]. However, there is a significantly higher incidence in African American women as compared with other races [26]. Gentry et al. conducted a case–control study in Augusta, Georgia, and Memphis Tennessee, and found almost a 16-fold higher incidence of PPCM in African American compared with non-African American women [26].

What is the relationship between hypertension and PPCM? Firstly, the answer(s) to this question would be debatable. The Zaria syndrome of PPCF was significantly found to be related to raised blood pressure during the acute phase of the HF, which was secondary to volume expansion following intake of large quantities of 'kanwa', but in which 22% of the patients developed sustained hypertension during 2–5 years of follow up [16,19]. However, it is important to note that this Zaria syndrome was actually defined by its authors to be "a high-output HF with well preserved ventricular function" [16]. For this reason therefore, PPCF is an entity different from what we know today as PPCM, going by the current definitions [7–9]. A recent review by ElKayam described 'hypertension' as an 'associated condition', and not an aetiologic factor [27]. In societies where both PPCM and sustained hypertension are common in women, differentiating PPCM from hypertensive heart disease could be difficult if high blood pressure is considered a clinical feature of PPCM. In support of this point, we found hypertensive eccentric left ventricular hypertrophy, irrespective of gender, to be the most common type of abnormal LV geometry in hypertensive subjects in Kano, Nigeria [28]. These patients tend to present in HF with similar clinical and echocardiographic features to PPCM, except for the high blood pressure or history of hypertension [28]. PPCM registries have shown that high blood pressure in PPCM is rare, as reported by Sliwa et al. from South Africa (seen 2%) and Fett et al. from Haiti (4%) [13,24].

4. Aetiology

The aetiology and pathogenesis of PPCM is unknown, but several hypotheses have been proposed over the years.

4.1. Myocarditis hypothesis

For a long time, this hypothesis had enjoyed greater evidence and acceptance for myocarditis as a cause of PPCM than any other proposed aetiological factor. It is believed that the absent or muted immune response during pregnancy allows for unchecked viral replication and thus a greater likelihood of myocarditis in the setting of a viral infection [7]. However, the prevalence of myocarditis in PPCM is highly variable between the different studies, ranging from none to 100% [29]. The reasons for this variability include: (a) the difficulty in defining PPCM clinically; (b) the inclusion of patients outside the accepted time frame of PPCM; (c) the difficulty in establishing the diagnosis by endomyocardial biopsy; (d) the variability in the inclusion of patients with borderline myocarditis together with those with histologic myocarditis as defined by the Dallas histological criteria; (e) the potential geographic variability of patient populations affected; and (f) the variable interval between presentation and the performance of endomyocardial biopsy [7].