

Peripartum cardiomyopathy: experience in an Asian tertiary centre

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INTRODUCTION Peripartum cardiomyopathy (PPCM) is a rare but life-threatening condition. We report 11 patients admitted to the National Heart Centre Singapore with a diagnosis of PPCM over a period of 14 months.

METHODS Baseline demographics, pregnancy history, haematology, serum biochemistry and echocardiographic findings of women admitted with a diagnosis of PPCM were analysed.

RESULTS The incidence of PPCM was 0.89 per 1,000 live births in our cohort. 63.6% of the patients were Malay and 27.3% were Chinese. 45.5% of the patients were smokers and 45.5% had a history of pregnancy-induced hypertension or preeclampsia. There was no maternal mortality. Mean left ventricular ejection fractions at diagnosis and at six months were $26.9\% \pm 9.1\%$ and $51.9\% \pm 10.6\%$, respectively. Mean left ventricular internal diameters in end-diastole at diagnosis and at six months were 5.5 ± 0.5 cm and 5.1 ± 0.6 cm, respectively. All patients were treated successfully for the acute episode and all but one patient had returned to New York Heart Association functional class I status at six months.

CONCLUSION PPCM remains a rare condition and appears to occur more commonly in Malay patients. Smoking and pregnancy-induced hypertension appear to be significant risk factors. While short-term outcome remains excellent, collaborative studies with other tertiary centres will help enhance our understanding of the long-term management of and clinical outcomes in these patients.

Keywords: cardiomyopathy, heart failure, peripartum, pregnancy
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INTRODUCTION

Peripartum cardiomyopathy (PPCM) is a rare but life-threatening condition that may complicate a pregnancy. The mortality rate, previously reported to be 4%–80% in the 1980s and 1990s, has dropped steadily with advancements in modern therapy.^(1–3) We report 11 patients who presented with PPCM to the National Heart Centre Singapore over a period of 14 months.

METHODS

A retrospective analysis was performed on all patients admitted to our centre with a diagnosis of PPCM between October 2009 and November 2010. The diagnosis of PPCM was based on the following four criteria described by the National Heart, Lung and Blood Institute: (a) development of cardiac failure in the last month of pregnancy or within five months of delivery; (b) absence of an identifiable cause of cardiac failure; (c) absence of recognisable heart disease prior to the last month of pregnancy; and (d) left ventricular systolic dysfunction demonstrated by echocardiographic criteria such as depressed left ventricular ejection fraction (LVEF).⁽⁴⁾

Baseline demographics, pregnancy history, haematology, serum biochemistry and echocardiographic findings were analysed for all patients. These women were followed up in the heart failure outpatient clinic upon discharge. Echocardiographic findings and status at the six-month follow-up were described according to the New York Heart Association (NYHA) functional classification.

RESULTS

The incidence of PPCM in our study was 0.89 per 1,000 live births. The mean age of patients was 32.3 ± 5.7 years. There were seven (63.6%) Malay, three (27.3%) Chinese and one (9.1%) Japanese women in the study group (Table I). Eight (72.7%) women were in their first pregnancies, two were in their second pregnancies and one patient had delivered her fifth child. One patient had a twin pregnancy. 45.5% of the women were smokers, and 45.5% had a history of pregnancy-induced hypertension or preeclampsia. The mean white blood cell count was $15.6 \pm 5.1 \times 10^9/L$ and the mean haemoglobin level was 10.8 ± 2.2 g/L in our group. The mean serum creatinine was 71.8 ± 21.3 $\mu\text{mol/L}$, troponin T was 0.044 ± 0.042 $\mu\text{g/L}$ and N-terminal prohormone of b-type natriuretic peptide (NT-proBNP) was $6,764 \pm 3,887$ pg/mL.

A majority of the patients (72.8%) developed symptoms postpartum. In our cohort, symptoms presented two days before delivery to 55 days after delivery (mean 12.8 days postpartum). Six (54.5%) patients presented with mild-to-moderate heart failure, while five (45.5%) patients presented with frank acute pulmonary oedema. Four patients among the five with pulmonary oedema needed mechanical ventilation. Only one patient required intravenous dobutamine for inotropic support. All patients received conventional treatment with angiotensin-converting enzyme inhibitor (ACE-I) or angiotensin II receptor blockers (ARBs) and β -blockers, unless contraindicated. All 11 patients were successfully treated for the acute episode and discharged well.

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Table I. Clinical characteristics and outcomes of the patients diagnosed with peripartum cardiomyopathy (n = 11).

Patient no.	Demographics	Onset of PPCM post delivery (days)	Smoking history	Comorbidities	Initial presentation/treatment	Mechanical ventilation	Echocardiographic findings		Functional status at six months
							Initial	At six months	
1	40 yrs/ Malay/ G2P2	51	No	PIH	Mild CCF/IV diuretics, β -blocker, ACE-I	No	LVEF 25%, LVIDd 6.37 cm, moderate MR	LVEF 46%, LVIDd 5.8 cm, trivial MR	NYHA I
2	21 yrs/ Malay/ G2P1	3	Yes	NA	APO requiring mechanical ventilation/ β -blocker, ACE-I	Yes	LVEF 35%, LVIDd 5.14 cm, no MR	Lost to follow-up	Lost to follow-up
3	31 yrs/ Malay/ G2P2	-2	Yes	PIH	Moderate CCF/IV diuretics, β -blocker, ACE-I	No	LVEF 28%, LVIDd 5.7 cm, mild-to-moderate MR	LVEF 55%, LVIDd 4.7 cm, trivial MR	NYHA I
4	34 yrs/ Chinese/ G2P1	6	No	PIH	Moderate CCF/IV diuretics, β -blocker, ACE-I	No	LVEF 30%, LVIDd 4.85 cm, mild MR	LVEF 57%, LVIDd 4.6 cm, no MR	NYHA I
5	32 yrs/ Malay/ G5P5	9	Yes	PIH	Mild CCF/IV diuretics, ACE-I	No	LVEF 33%, LVIDd 6.2 cm, mild-to-moderate MR	Lost to follow-up	Lost to follow-up
6	27 yrs/ Malay/ G1P1	7	Yes	Preeclampsia	APO/IV diuretics, β -blocker, ACE-I	No	LVEF 35%, LVIDd 5.3 cm, trivial MR	Lost to follow-up	Lost to follow-up
7	36 yrs/ Chinese/ G1P1	55	Yes	NA	Mild CCF/IV diuretics, ARB	No	LVEF 10%, LVIDd 6.2 cm, moderate MR	LVEF 40%, LVIDd 5.6 cm, trivial MR	NYHA I
8	31 yrs/ Malay/ G1P2	0	No	NA	APO requiring mechanical ventilation/ β -blocker, ACE-I	Yes	LVEF 35%, LVIDd 5.3 cm, no MR	LVEF 55%, LVIDd 5 cm, no MR	NYHA I
9	31 yrs/ Malay/ G2P1	0	No	NA	APO requiring mechanical ventilation/ β -blocker, ACE-I	Yes	LVEF 25%, LVIDd 4.8 cm, no MR	LVEF 35%, LVIDd 5.5 cm, trivial MR	NYHA II
10	42 yrs/ Japanese/ G1P1	7	No	NA	Moderate CCF/IV diuretics, β -blocker, ARB	No	LVEF 10%, LVIDd 5.4 cm, mild MR	LVEF 62%, LVIDd 4.9 cm, no MR	NYHA I
11	31 yrs/ Chinese/ G1P1	5	No	NA	APO requiring mechanical ventilation/ dobutamine infusion, β -blocker, ACE-I	Yes	LVEF 30%, LVIDd 5.4 cm, no MR	LVEF 65%, LVIDd 4.4 cm, no MR	NYHA I

ACE-I: angiotensin-converting enzyme inhibitor; APO: acute pulmonary oedema; ARB: angiotensin II receptor blocker; CCF: congestive cardiac failure; G: gravida; IV: intravenous; LVEF: left ventricular ejection fraction; LVIDd: left ventricular internal diameter in end-diastole; MR: mitral regurgitation; NA: not available; NYHA: New York Heart Association functional classification; P: para; PIH: pregnancy-induced hypertension; PPCM: peripartum cardiomyopathy

One patient had a subsequent pregnancy, which was terminated three months after the diagnosis of cardiomyopathy.

Mean LVEF at diagnosis was $26.9\% \pm 9.1\%$ and the mean left ventricular internal diameter in end-diastole (LVIDd) was 5.5 ± 0.5 cm. Eight patients underwent echocardiographic re-evaluation at the six-month follow-up. Of these, five patients had normal LVEF. Three patients were lost to follow-up. At six months, the mean LVEF was $51.9\% \pm 10.6\%$ and LVIDd was 5.1 ± 0.6 cm. All patients with at least mild-to-moderate grade mitral regurgitation showed improvement on echocardiography during follow-up. All patients were of NYHA functional class I status on review, except for one patient who was found to be NYHA functional class II.

DISCUSSION

The incidence of PPCM varies across geographical regions. For instance, it ranges from 1 in 3,000–4,000 live births in the United States, 1 in 1,000 live births in South Africa and 1 in 6,000 live births in Japan.^(5,6) In a study from Southern California, Asian populations were found to have the second highest incidence of PPCM, closely following people of African descent.⁽⁷⁾ Notwithstanding these wide variations in reported incidence, the real prevalence of PPCM is likely to vary, depending on factors such as accessibility to specialist care as well as the experience of each centre in diagnosing and managing the condition. Moreover, it may be difficult to differentiate PPCM from other conditions associated with heart failure in puerperium, such as

infectious, toxic or metabolic disorders and underlying valvular or ischaemic heart disease.⁽⁸⁾

In our cohort, a majority of the patients presenting with PPCM were ethnically Malay (63.6%), which translated to 4.62 women with PPCM per 1,000 live births in the Malay population, compared to 0.32 women per 1,000 live births in the Chinese population and 0.84 women per 1,000 live births in women of other races in our series. In spite of the small size of our study population, our findings may hint at the likelihood of PPCM being more prevalent among Malay women. The authors therefore propose that a heightened index of suspicion should be maintained when pregnant Malay women present with symptoms of fluid overload, prompting an early referral for a cardiology assessment.

The risk factors reported for PPCM include women over 30 years of age, multiparity, pregnancies with multiple gestations, African descent, long-term tocolytic therapy (with β -adrenergic agonists), toxemia of pregnancy, maternal cocaine abuse and nutritional deficiencies.^(5,9,10) A history of preeclampsia, eclampsia or gestational hypertension is also thought to be associated with PPCM.⁽¹¹⁾ In contrast to the above reports, we found that 72.7% of the women in our cohort were in their first pregnancies, with all but one patient having a singleton pregnancy. 45.5% of the women were smokers, an indication that tobacco smoking may increase the risk of developing PPCM. Equally, 45.5% of our patients had a history of pregnancy-induced hypertension or preeclampsia. Interestingly, in spite of the increased risk of developing PPCM in women with gestational hypertension, Kamiya et al suggested that hypertensive disorders complicating pregnancy were independently associated with a shorter hospital stay and a higher LVEF on follow-up.⁽¹²⁾

Reports have shown that patients who are more critically ill may benefit from intra-aortic balloon pump, left ventricular assist device or heart transplantation, even if they do not respond to earlier treatment.⁽¹³⁾ Biteker et al recently demonstrated that intravenous infusion of levosimendan did not improve the outcome in 24 patients with PPCM.⁽¹⁴⁾ There may be potential for the future use of bromocriptine in the treatment of PPCM. Hilfiker-Kleiner et al reported that prolactin, in its antiangiogenic and proapoptotic 16-kDa form, is associated with endothelial inflammation, impaired cardiomyocyte metabolism and reduced myocardial contraction, suggesting that oxidative stress, inflammation and prolactin may be interconnected and responsible for initiating PPCM.⁽¹⁵⁾ These authors subsequently conducted a prospective, single-centre, randomised, open-label, proof-of-concept pilot study of 20 women with newly diagnosed PPCM receiving standard care versus standard care plus bromocriptine for eight weeks.⁽¹⁶⁾ In this trial, the addition of bromocriptine to standard heart failure therapy appeared to improve LVEF and a composite clinical outcome of death, NYHA functional class III/IV or LVEF < 35% at six months in women with acute severe PPCM.

Patients may present with varying degrees of symptoms of heart failure. 54.5% of our patients presented with mild-to-

moderate heart failure and 45.5% of our patients presented with frank acute pulmonary oedema. Four from the latter group required mechanical ventilation. Only one patient required intravenous dobutamine for inotropic support. The short-term outcome at six months appeared to be excellent in our cohort, as there was no mortality and all patients were successfully treated and discharged well. The treatment of patients with mild-to-moderate heart failure required conventional management with intravenous loop diuretics and β -blockers when they were out of overt heart failure. ACE-I was initiated after delivery. None of the patients in our cohort received bromocriptine as part of their treatment.

PPCM was associated with dilatation of the left ventricle and depression of LVEF at diagnosis in our series, with improvement seen in both parameters following treatment. In our patients, the mean LVEF was $26.9\% \pm 9.1\%$ at diagnosis, which improved to $51.9\% \pm 10.6\%$ at six months. Five of eight patients (62.5%) who were assessed at six months had LVEF > 50%. This result is comparable to a previous report by Amos et al, who found improved left ventricular function in two-thirds of their patients, with 45% of patients returning to a normal ejection fraction (EF > 50%).⁽¹⁷⁾ Goland et al recently reported that recovery to LVEF > 50% at six months was significantly related to the degree of myocardial insult at the time of diagnosis.⁽¹⁸⁾ However, this was not evident in our study group, perhaps owing to its limited sample size.

There were some limitations to our study. Due to the rarity of the condition, we could only recruit a small number of patients for our study; thus, the limited sample size may constrain the statistical significance of our findings. Also, as our cohort was limited to patients from a single tertiary referral centre, whether our findings would be representative of other Asian populations remains uncertain.

In summary, PPCM remains a rare condition but appears to occur more commonly in Malay patients. Smoking and pregnancy-induced hypertension may be significant risk factors associated with the development of PPCM. Short-term outcome was excellent in our cohort. However, the long-term management and outcomes of these patients remain unclear due to the rarity of PPCM. The overall prognosis of PPCM may improve with the development of newer treatment modalities such as bromocriptine, as well as with increased awareness, prompt detection and earlier initiation of appropriate therapy for at-risk women, especially among high-risk groups. Collaborative studies with other tertiary centres would help to better understand the condition.

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