Incidence, risk factors, and clinical outcomes of peripartum cardiomyopathy in Hong Kong

Liliana SK Law *, LT Kwong, KH Siong, Sani TK Wong, WL Chan, KY Tse, Yannie YY Chan, KS Eu, CY Chow, Joan KO Wai, HC Mok, PL So

ABSTRACT

Introduction: Peripartum cardiomyopathy (PPCM) is an uncommon but serious form of heart failure affecting women during late pregnancy or early postpartum. This territory-wide multicentre retrospective study aimed to evaluate the local incidence, risk factors, and clinical outcomes, including subsequent pregnancies, in Hong Kong.

Methods: Medical records were retrospectively reviewed for women who delivered at all public hospitals between 1 January 2013 and 31 December 2022 and met the 2010 European Society of Cardiology Working Group criteria for PPCM. Regression analysis was performed to investigate maternal risk factors.

Results: Thirty Asian women were diagnosed with PPCM, corresponding to an incidence of 1 in 11 179 live births. Eleven (36.7%) had antepartum onset of symptoms, and 25 (83.3%) were diagnosed after childbirth, most presenting with severe symptoms (90%). The median left ventricular ejection fraction was 30% (range, 10%-44%). Notable complications included cardiogenic shock (10%), respiratory failure (23.3%), acute renal failure (23.3%), and thromboembolism (23.3%). Most women received guideline-directed heart failure therapy. At 12 months, all-cause mortality was 6.7%, and cardiac recovery occurred in 60%. Eleven women had 13 subsequent pregnancies (three miscarriages, five terminations, and five live births). There were no maternal deaths or cases of recurrent PPCM. Genetic testing identified potentially pathogenic variants in at least 10% of women. Antenatal anaemia (adjusted odds ratio [OR]=13.04; 95% confidence interval [95% CI]=3.72-45.70) and hypertensive disorders of pregnancy (adjusted OR=38.00; 95% CI=9.66-149.52) were associated with higher odds of PPCM.

Conclusion: This study highlights the substantial morbidity and mortality associated with PPCM. Genetic testing may aid in risk stratification and prognostication.

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New knowledge added by this study

- Peripartum cardiomyopathy (PPCM) is an uncommon but potentially fatal disease in Hong Kong.
- Genetic testing by next-generation sequencing identified 10% of women with PPCM as carriers of potential genetic variants associated with cardiomyopathy.
- Antenatal anaemia and hypertensive disorders of pregnancy are independent clinical risk factors for PPCM.

Implications for clinical practice or policy

- Screening for and prevention of anaemia during pregnancy and pre-eclampsia may help reduce the incidence of PPCM.
- The integration of genetic testing in PPCM management may support personalised medical care.

香港產婦周產期心肌病變的發病率、風險因素及臨床結果

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引言：周產期心肌病是罕見但嚴重的心力衰竭形式，主要影響妊娠晚期或產後早期的女性。這項全港性多中心回顧性研究旨在評估香港的本地發病率、風險因素及臨床結果，包括後續妊娠情況。

方法：我們對2013年1月1日至2022年12月31日期間在所有公立醫院分娩並符合2010年歐洲心臟學會工作小組所訂周產期心肌病診斷準則的女性病歷進行回顧分析，並透過迴歸分析探討母體相關風險因素。

結果：共30名亞洲女性被確診周產期心肌病，發病率相當於每11 179例活產中有1例，其中11例（36.7%）於產前出現症狀，25例（83.3%）在產後確診，大多數出現嚴重症狀（90%）。左心室射血分率中位數為30%（範圍：10%-44%）。主要併發症包括心因性休克（10%）、呼吸衰竭（23.3%）、急性腎衰竭（23.3%）和血栓栓塞（23.3%）。大多數患者接受指引導向的心衰治療。12個月追蹤時，全因死亡率為6.7%；60%患者心臟功能恢復。11名患者其後共有13次妊娠（3例流產、5例人工中止妊娠、5例活產），未出現孕產婦死亡或周產期心肌病復發病例。基因檢測發現至少10%患者帶有潛在致病性基因變異。產前貧血（經調整勝算比=13.04；95%置信區間=3.72-45.70）及妊娠高血壓疾患（經調整勝算比=38.00；95%置信區間=9.66-149.52）與周產期心肌病發生風險顯著相關。

結論：本研究揭示周產期心肌病相關的高發病率與死亡率。基因檢測可能有助於風險分層和預後評估。

Introduction

Peripartum cardiomyopathy (PPCM) is a rare form of heart failure that occurs in relation to pregnancy, resulting in substantial morbidity and mortality.[1] In 2010, the Heart Failure Association of the European Society of Cardiology (ESC) defined PPCM as "an idiopathic cardiomyopathy presenting with heart failure secondary to left ventricular systolic dysfunction towards the end of pregnancy or in the months following delivery, where no other cause of heart failure is found".[2] Globally, its incidence varies widely, ranging from 1 in 100 live births in Nigeria[3] to 1 in 20 000 live births in Japan.[4]

The exact pathogenesis of PPCM is not yet fully understood; the current hypothesis proposes a 'two-hit' model involving an initial vascular insult caused by vasculotoxic hormonal effects, including soluble FMS-like tyrosine kinase-1 and prolactin, followed by a second hit of underlying predisposition—such as genetic susceptibility and other risk factors—that limits some women's ability to withstand this vasculotoxic insult.[1] Genetic or familial predisposition to PPCM has been supported by multiple reports.[5-8] Additionally, well-recognised risk factors for PPCM include advanced maternal age, African American ancestry, multiple pregnancies, hypertension, and pre-eclampsia.[9]

Peripartum cardiomyopathy is a potentially life-threatening myocardial disease that affects women of all ethnic groups[10] and can have long-term health consequences.[11] Until now, there has been a lack of information regarding the clinical phenotype and outcomes of this disease in Hong Kong. The present population-based study was conducted to evaluate the local incidence, clinical presentation, management, complications, 12-month outcomes, and subsequent pregnancies in women with PPCM. Additionally, we examined potential risk factors by comparing the clinical characteristics of women with and without PPCM to provide a basis for future preventive strategies.

Methods

Study design

This was a population-based retrospective study of all women with PPCM who delivered in public hospitals in Hong Kong between 1 January 2013 and 31 December 2022. Cases were identified through the Clinical Data Analysis and Reporting System, which captures obstetric data and hospitalisation diagnoses from eight public hospitals providing obstetric services. First, all women who delivered during the study period and had a diagnosis code for heart failure from the third trimester to 6 months postpartum were identified. Each woman's medical record was systematically reviewed by two authors to determine whether the following criteria for PPCM were met: development of cardiac failure (with left ventricular ejection fraction [LVEF] <45% on echocardiography) during the third trimester or within 6 months postpartum without an identifiable cause. Women were excluded if LVEF was ≥45%, a recognised cause of heart failure was identified, or there was no physician-confirmed diagnosis of PPCM.

Clinical variable collection

Baseline characteristics (including socio-demographics, preexisting health conditions, and obstetric history) at the time of PPCM diagnosis were obtained from medical records. Clinical presentation and initial investigations, including electrocardiography, chest radiography, echocardiography, and laboratory results, were collected. All in-hospital complications and reported outcomes during follow-up were recorded, including all-cause mortality and cardiac recovery determined by echocardiography at 12 months. Management strategies were documented, including admission to the intensive care unit or cardiac care unit, use of mechanical ventilation or circulatory support, medications prescribed at hospital discharge, pacemaker insertion, and heart transplantation. Complete recovery of cardiac function was defined

as LVEF ≥50%. Some patients underwent genetic evaluation, and their reports were analysed.

Obstetric outcomes at the time of the PPCM event were assessed, including hypertensive disorders of pregnancy; gestational diabetes; thyroid disease; antenatal anaemia (defined as a haemoglobin level <10.5 g/dL); use of tocolytics; placenta accreta spectrum; placental abruption; fetal growth restriction; preterm delivery; assisted vaginal delivery or caesarean section; primary postpartum haemorrhage (blood loss ≥500 mL); and caesarean hysterectomy. Neonatal outcomes were examined, including stillbirth, sex, birth weight, small for gestational age, Apgar scores, admission to the neonatal intensive care unit, and death within 28 days of life. Data from the territory-wide electronic healthcare database were also extracted regarding outcomes of subsequent pregnancies, including LVEF before, during, and after pregnancy. The interval between the PPCM pregnancy and the first subsequent pregnancy was recorded.

To investigate risk factors for PPCM, women who gave birth during the same period but did not develop heart failure were selected as the control group, with a PPCM-to-control ratio of 1:4. Demographic and clinical characteristics were compared between women with and without PPCM.

Statistical analysis

Data analysis was conducted using SPSS (Windows version 26.0; IBM Corp, Armonk [NY], United States). The incidence rate was calculated by dividing the total number of PPCM cases by the total number of live births during the study period. Descriptive data for continuous variables were presented as mean ± standard deviation or median (range or interquartile range), and categorical data were presented as numbers with percentages. Comparisons between women with and without PPCM were performed using Student's *t* test or the Mann-Whitney *U* test for continuous variables, and the Chi squared test or Fisher's exact test for categorical variables. Risk factors associated with PPCM were assessed using univariable and multivariable logistic regression analyses, with results expressed as odds ratios (ORs) and 95% confidence intervals (95% CIs). A P value of <0.05 was considered statistically significant. The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines were followed in the preparation of this article.

Results

Incidence of peripartum cardiomyopathy in Hong Kong

During the 10-year study period, 30 women with PPCM delivered in public hospitals (Fig 1). Over the same period, there were 335 376 live births, yielding an estimated PPCM incidence of 1 in 11 179 live births in Hong Kong.

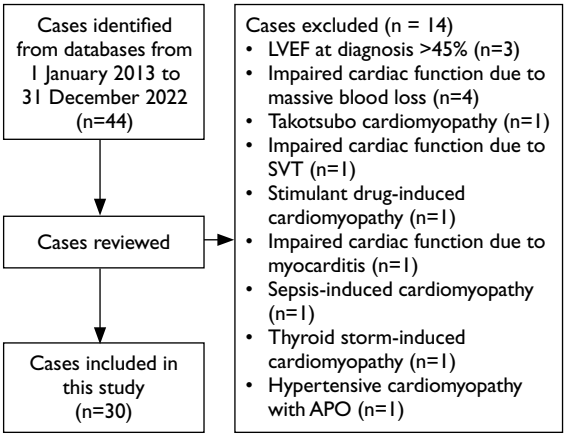

FIG 1. Identification of study population
Abbreviations: APO = acute pulmonary oedema; LVEF = left ventricular ejection fraction; SVT = supraventricular tachycardia

Demographics, clinical characteristics, and investigations

Detailed characteristics are listed in Table 1. All women in this study were Asian. The mean age was 33.5 years and the median body mass index was 22.0 kg/m^2. One woman had a positive family history of heart failure of unknown cause; no women had a previous history of PPCM or cardiac disease.

Symptoms began antepartum in 36.7% of women and postpartum in 63.3%; PPCM was predominantly diagnosed postpartum (83.3%). The median time from symptom onset to diagnosis was 3.5 days (range, 0-107). At diagnosis, 90% of women had severe symptoms (New York Heart Association functional class III/IV), most commonly comprising shortness of breath, peripheral oedema, and desaturation. Common electrocardiographic findings included sinus tachycardia and prolonged QTc interval. At the first echocardiographic assessment, the median LVEF was 30% (range, 10-44). More than half of the women had abnormal chest radiographs showing congestive lung fields, cardiomegaly, and pleural effusion (Table 2).

Complications, management, and cardiac recovery

Detailed results are presented in Table 3. Of the 30 women with PPCM, 19 (63.3%) were managed in the intensive care unit or cardiac care unit. Cardiogenic shock, respiratory failure, and acute renal failure occurred in 10% to 20% of cases. Inotropic support, mechanical ventilation, extracorporeal membrane oxygenation, and renal replacement therapy were used during acute treatment.

TABLE 1. Maternal socio-demographic characteristics, medical history, and obstetric history (n=30)*

Socio-demographic characteristics	
Age at diagnosis, y	33.5 ± 5.1
Advanced maternal age (≥40 y)	5 (16.7%)
Marital status	
Single	2 (6.7%)
Married	28 (93.3%)
Education	
Primary	1 (3.3%)
Secondary	22 (73.3%)
Tertiary or above	7 (23.3%)
Ethnicity	
Chinese	27 (90%)
Other: Filipino, Nepalese	3 (10%)
BMI at first antenatal visit, kg/m^2	22.0 (17.0-33.2)
Obesity (BMI ≥25 kg/m^2)	8 (26.7%)
Current smoker	6 (20%)
Current drinker	1 (3.3%)
Drug abuse	
Ex-abuser	2 (6.7%)
Current abuser	2 (6.7%)
Family history of heart failure	1 (3.3%)
Medical history	
History of PPCM	0
Congenital heart disease	0
Chronic hypertension	4 (13.3%)
Preexisting diabetes	0
Preexisting thyroid disease	1 (3.3%)
HBV carrier	6 (20%)
HIV carrier	0
Thalassaemia carrier	0
Asthma	1 (3.3%)
Chronic renal disease	2 (6.7%)
Psychiatric disorders	4 (13.3%)
Obstetric history	
Gravidity	2.5 (1-9)
Parity	1 (0-4)
Nulliparity	14 (46.7%)
Previous caesarean section	2 (6.7%)

Abbreviations: BMI = body mass index; HBV = hepatitis B virus; HIV = human immunodeficiency virus; PPCM = peripartum cardiomyopathy

* Data are shown as mean ± standard deviation, No. (%), or median (range)

At hospital discharge, most women were prescribed angiotensin-converting enzyme inhibitors (ACEis) or angiotensin receptor blockers (ARBs) and beta-blockers. Four women received prophylactic low–molecular-weight heparin for venous thromboembolism prevention after the event; another four required warfarin for the treatment of cerebral venous thrombosis, brachial artery thromboembolism, pulmonary embolism, or deep vein thrombosis (Table 3).

One woman experienced decompensated heart failure requiring an intra-aortic balloon pump and a left ventricular assist device 9 months after diagnosis, followed by heart transplantation 1 year after the event. Two women underwent implantable cardioverter-defibrillator insertion due to symptomatic premature ventricular contractions and poor LVEF recovery. Seven women (23.3%) experienced nine thromboembolic events within 1 year of the PPCM episode, including left ventricular thrombi, ischaemic stroke, and pulmonary embolism. The median follow-up duration after PPCM was 47 months (range, 3-140). At 12 months, all-cause in-hospital mortality was 6.7%; causes of death were myocardial infarction and pulmonary embolism. Overall, recovery of left ventricular function (LVEF ≥50%) occurred in 60% of women (Table 3).

Antenatal co-morbidities, obstetric outcomes, and neonatal outcomes

Prior to PPCM, 80% of women received antenatal care. Four women (13.3%) had twin pregnancies. Antenatal anaemia was present in 50% of women. Hypertensive disorders of pregnancy occurred in 56.7%, whereas gestational diabetes was noted in 13.3%. Complications related to pre-eclampsia included haemolysis, elevated liver enzymes, and low platelets syndrome in 3.3%; eclampsia in 3.3%; and placental abruption in 6.7%. No women received tocolytics during pregnancy. The median gestational age at delivery was 37 weeks (range, 28-41). The caesarean section rate was 53.3%, and the most frequent indication was unstable maternal condition (31.3%). Primary postpartum haemorrhage occurred in 30% of cases; one woman required hysterectomy for placenta accreta spectrum. Among the 34 newborns, 32 (94.1%) were born alive; two were stillborn in the third trimester (5.9%) due to placental abruption and trisomy 18. The median birth weight was 2745 g, and 11.8% of newborns were small for gestational age. Four newborns (11.8%) had an Apgar score below 7 at 5 minutes, and nine (26.5%) required admission to a neonatal intensive care unit. There were no cases of early neonatal death (Table 4).

Outcomes of subsequent pregnancies

The obstetric and cardiac outcomes of the 11 women with subsequent pregnancies are shown in Figure 2. The median interval between the PPCM-affected pregnancy and the next pregnancy was 17 months

TABLE 2. Clinical presentation and investigations (n=30)*

Clinical presentation	
Timing of PPCM onset	
Antepartum, wk	11 (36.7%)
<34	5 (16.7%)
34-36	3 (10%)
≥37	3 (10%)
Postpartum, mo	19 (63.3%)
1	14 (46.7%)
1-2	3 (10%)
2-3	2 (6.7%)
Timing of PPCM diagnosis	
Antepartum	5 (16.7%)
Postpartum	25 (83.3%)
Antenatal diagnosis to delivery interval (n=5)	
<24 hours	3 (60%)
1-7 days	1 (20%)
>7 days	1 (20%)
Time between symptom onset and diagnosis, d (median [range])	3.5 (0-107)
>7	9 (30%)
NYHA functional class	
I/II	3 (10%)
III	16 (53.3%)
IV	11 (36.7%)
Signs and symptoms	
Chest pain	7 (23.3%)
Palpitations	13 (43.3%)
Dizziness	9 (30%)
Peripheral oedema	20 (66.7%)
Shortness of breath	27 (90%)
Cough	12 (40%)
Tachypnoea	13 (43.3%)
Elevated jugular venous pressure	7 (23.3%)
Heart murmur	1 (3.3%)
Pulmonary crepitations	15 (50%)
Third heart sound	0
Desaturation	20 (66.7%)
Systolic BP, mm Hg (median [range])	140 (100-192)
Diastolic BP, mm Hg (median [range])	90 (58-135)
Electrocardiogram	
Heart rate, beats per minute (median [range])	113 (56-159)
Tachycardia	22 (73.3%)
Atrial fibrillation or flutter	1 (3.3%)
Long QTc duration	16 (53.3%)
LBBB	2 (6.7%)
Left ventricular hypertrophy	4 (13.3%)

Abbreviations: BP = blood pressure; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PPCM = peripartum cardiomyopathy

* Data are shown as median (interquartile range) or No. (%), unless otherwise specified

TABLE 2. (cont'd)

Echocardiogram	
LVEF, % (median [range])	30 (10-44)
Mitral regurgitation	
Mild	16 (53.3%)
Moderate	7 (23.3%)
Severe	4 (13.3%)
Left ventricular dilatation	16 (53.3%)
Right ventricular impairment	5 (16.7%)
Pericardial effusion	9 (30%)
Chest radiography	
Cardiomegaly	23 (76.7%)
Pulmonary congestion	27 (90%)
Pleural effusion	20 (66.7%)
Laboratory test results	
Haemoglobin, g/dL	11.4 (10.1-12.5)
White blood cells, $\times 10^9$/L	12.8 (7.6-17.9)
Platelets, $\times 10^9$/L	273.5 (193.0-422.8)
Albumin, g/L	27.5 (23.8-33.3)
Alanine transaminase, U/L	24.5 (14.0-79.3)
Bilirubin, μmol/L	8.0 (4.8-17.0)
Serum creatinine, μmol/L	64.5 (51.8-86.8)
Serum urea, mmol/L	5.2 (3.1-6.4)
Elevated cardiac troponin	22 (73.3%)
Deranged liver function test	9 (30%)
Deranged renal function test	8 (26.7%)

(range, 4-60). There were 13 subsequent pregnancies (three miscarriages, five terminations, and five live births). Of the five terminations, two were advised due to poor cardiac condition; the remaining three were elective for maternal anxiety or social reasons. There were no maternal deaths or cases of recurrent PPCM.

Cases with genetic testing

Genetic analysis using a dilated cardiomyopathy (DCM) panel by next-generation sequencing was requested by physicians in three cases (online supplementary Table 1). Case 1, involving a woman with a family history of heart failure, revealed a pathogenic variant in the *FLNC* gene. Case 2, concerning a patient with a history of cancer-related chemotherapy who developed refractory postpartum heart failure requiring heart transplantation 1 year after PPCM diagnosis, had no prior signs of heart failure before pregnancy. A genetic test identified two pathogenic variants in the *TTN* and *MYBPC3*

TABLE 3. Management, complications, and cardiac recovery during hospitalisation and follow-up (n=30)*

All-cause mortality at 12 months	2 (6.7%)
Death due to myocardial infarction	1 (3.3%)
Death due to pulmonary embolism	1 (3.3%)
Cardiac outcomes	
Cardiogenic shock	3 (10%)
Inotropic support	4 (13.3%)
Intra-aortic balloon pump	1 (3.3%)
Left ventricular assist device	1 (3.3%)
Extracorporeal membrane oxygenation	1 (3.3%)
Heart transplant	1 (3.3%)
Arrhythmia	3 (10%)
Defibrillator/pacemaker insertion	2 (6.7%)
Respiratory outcomes	
Respiratory failure	7 (23.3%)
Mechanical ventilation	8 (26.7%)
Renal outcomes	
Acute renal failure	7 (23.3%)
Renal replacement therapy	2 (6.7%)
Thromboembolic events	
Left ventricular thrombosis	3 (10%)
Ischaemic stroke	1 (3.3%)
Arterial embolism	1 (3.3%)
Pulmonary embolism	2 (6.7%)
Deep vein thrombosis	2 (6.7%)
Admission to intensive care unit/cardiac care unit	19 (63.3%)
Length of stay in intensive care unit, d	3 (2-9)
Duration of PPCM admission, d	8 (1-158)
Medication on discharge	
Loop diuretic	17 (56.7%)
Spironolactone	5 (16.7%)
ACEis/ARBs	28 (93.3%)
Beta-blockers	22 (73.3%)
Digoxin	1 (3.3%)
Bromocriptine	3 (10%)
Hydralazine	4 (13.3%)
Warfarin	4 (13.3%)
Low–molecular-weight heparin	4 (13.3%)
Recovered LVEF (≥50%) at 12 mo	18 (60%)
Length of follow-up, mo	47 (3-140)

Abbreviations: ACEis = angiotensin-converting enzyme inhibitors; ARBs = angiotensin receptor blockers; LVEF = left ventricular ejection fraction; PPCM = peripartum cardiomyopathy

* Data are shown as median (range) or No. (%)

TABLE 4. Antenatal co-morbidities, obstetric outcomes, and neonatal outcomes*

Antenatal co-morbidities (n=30)	
Received antenatal care	24 (80%)
Twin pregnancy	4 (13.3%)
Pregnancy-induced hypertension	3 (10%)
Gestational proteinuria	1 (3.3%)
Pre-eclampsia	12 (40%)
HELLP syndrome	1 (3.3%)
Eclampsia	1 (3.3%)
Gestational diabetes	4 (13.3%)
Thyroid disease	1 (3.3%)
Anaemia (haemoglobin <10.5 g/dL)	15 (50%)
Use of tocolytics	0
Placenta accreta spectrum	1 (3.3%)
Placental abruption	2 (6.7%)
Fetal growth restriction	2 (6.7%)
Obstetric outcomes (n=30)	
Gestational age at delivery, wk	37 (28-41)
<32	2 (6.7%)
32-36	13 (43.3%)
≥37	15 (50%)
Mode of delivery	
Normal vaginal delivery	10 (33.3%)
Instrumental delivery	4 (13.3%)
Caesarean section	16 (53.3%)
Indications for caesarean delivery (n=16)	
Unstable maternal condition	5 (31.3%)
Pre-eclampsia	3 (18.8%)
Non-reassuring fetal heart rate tracing	2 (12.5%)
Labour dystocia	2 (12.5%)
Placental abruption	2 (12.5%)
Placenta accreta spectrum	1 (6.3%)
Twin pregnancy	1 (6.3%)
Primary postpartum haemorrhage (blood loss ≥500 mL)	9 (30%)
Caesarean hysterectomy	1 (3.3%)
Neonatal outcomes (n=34)†	
Live birth	32 (94.1%)
Stillbirth	2 (5.9%)
Male sex	16 (47.1%)
Birth weight, g	2745 (700-3665)
Low birth weight (<2500 g)	11 (32.4%)
Small for gestational age	4 (11.8%)
Apgar score <7 at 5 minutes	4 (11.8%)
Neonatal intensive care unit admission	9 (26.5%)
Neonatal death within 28 days	0

Abbreviation: HELLP syndrome = haemolysis, elevated liver enzymes, low platelets syndrome

* Data are shown as median (range) or No. (%)

† Four pairs of twins among 30 women with peripartum cardiomyopathy

genes. Case 3 involved a woman with chronic kidney disease who exhibited persistent left ventricular systolic dysfunction 4 years after PPCM diagnosis. Genetic evaluation was pursued due to her young-onset multisystem disease, revealing a variant in the *NEXN* gene. This variant, associated with autosomal dominant monogenic DCM, was absent from population databases but showed conflicting results on in silico prediction algorithms; therefore, it was classified as a variant of uncertain significance. Overall, potentially pathogenic genetic variants were identified in at least 10% of women with PPCM.

Maternal factors associated with peripartum cardiomyopathy

Compared with the control group, univariable logistic regression analysis showed that factors associated with PPCM included advanced maternal age (≥40 years), smoking, hypertensive disorders of pregnancy, and antenatal anaemia. In multivariable regression analysis, PPCM was independently associated with hypertensive disorders of pregnancy (adjusted OR=38.00; 95% CI=9.66-149.52; P<0.001) and antenatal anaemia (adjusted OR=13.04; 95% CI=3.72-45.70; P<0.001) [online supplementary Table 2].

Discussion

Time from symptom onset to diagnosis

Over the 10-year study period, we observed a PPCM incidence of 1 in 11 179 live births in Hong Kong. Worldwide variation in PPCM incidence may relate to ethnic and socio-economic factors[12]; rates are expected to increase because of advancing maternal age,[13] multiple pregnancies, and obesity. About one-third of our patients developed symptoms before delivery, a finding comparable to the Asia-Pacific group in the ESC EURObservational Research Programme registry.[10] Overall, 30% of women were diagnosed more than 7 days after symptom onset. Among those with antepartum-onset symptoms, 54.5% were diagnosed after delivery. This diagnostic delay may be attributed to the difficulty in distinguishing PPCM from normal physiological changes of pregnancy—its symptoms often mimic those of late gestation and may only be recognised postpartum when they become more pronounced. Delayed diagnosis has been associated with lower rates of left ventricular recovery.[14] Early recognition and awareness among both pregnant women and healthcare professionals are crucial to enable prompt initiation of heart failure therapy, which may improve cardiac recovery. To support early detection and facilitate timely specialist referral for diagnostic evaluation, serum biomarkers can be measured to rule out heart failure with high probability during pregnancy or the postpartum period.[15]

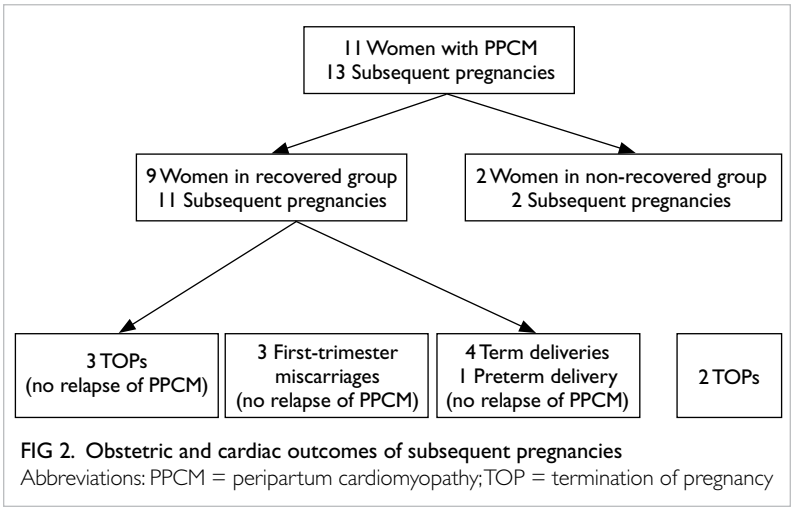

FIG 2. Obstetric and cardiac outcomes of subsequent pregnancies
Abbreviations: PPCM = peripartum cardiomyopathy; TOP = termination of pregnancy

Pre-eclampsia and peripartum cardiomyopathy

In our study, approximately half of the cases involved pre-eclampsia, a finding consistent with the Asia-Pacific cohort in the ESC EURObservational Research Programme registry.[10] A meta-analysis of 22 studies demonstrated a fourfold higher prevalence of pre-eclampsia among women with PPCM relative to the general obstetric population (22% vs 5%).[16] Our multivariable regression analysis confirmed that hypertensive disorders of pregnancy constituted an independent risk factor for PPCM. The association between pre-eclampsia and PPCM may be explained by their shared pathophysiological mechanism—systemic vascular angiogenic imbalance.[1,15,17] Pre-eclampsia and PPCM might represent a single disease spectrum with substantial overlap.[17] Low-dose aspirin is generally used for the prevention of pre-eclampsia and its associated morbidity and mortality.[18] Although aspirin use for PPCM prevention is not supported by evidence-based guidelines, it could theoretically provide benefit due to the shared vascular dysfunction pathways. Consequently, the use of aspirin for pre-eclampsia prevention may indirectly reduce the risk of PPCM in high-risk women.

Anaemia and peripartum cardiomyopathy

We found that antenatal anaemia was independently associated with PPCM. A systematic review and meta-analysis previously indicated that women with anaemia had up to fivefold higher odds of developing PPCM compared with women exhibiting normal haemoglobin levels.[19] The precise nature of this association remains unclear; iron deficiency may contribute by impairing myocardial contractile function.[20] Anaemia screening and correction during pregnancy may help reduce the risk of PPCM.

Management of peripartum cardiomyopathy

A multidisciplinary approach involving cardiologists, obstetricians, intensivists, cardiac surgeons, anaesthesiologists, neonatologists, and nurses is essential for the management of PPCM.[21] In severe cases with haemodynamic instability, acute management—including immediate resuscitation and mechanical respiratory or circulatory support—may be required.[15] Urgent caesarean section should be considered for advanced heart failure that persists despite optimal medical therapy. According to international consensus, the main treatment should follow guideline-directed medical therapy for heart failure with reduced ejection fraction in non-pregnant patients, while respecting contraindications for certain drugs during pregnancy.[6,22-25] Standard therapies include diuretics, ACEis or ARBs, mineralocorticoid receptor antagonists, vasodilators (hydralazine/nitrates), digoxin, beta-blockers, and anticoagulants. A 2022 meta-analysis of global data demonstrated that frequent prescription of beta-blockers, ACEis/ARBs, and bromocriptine or cabergoline was associated with lower all-cause mortality and better left ventricular recovery at 12 months.[26] In our study, most patients received ACEis/ARBs and beta-blockers; fewer were prescribed bromocriptine at discharge. The rationale for using dopamine agonists to inhibit prolactin secretion lies in the proposed pathophysiological mechanism involving 16-kDa prolactin, an oxidative stress-mediated cleavage product that damages cardiovascular tissue.[27] Regarding prolactin inhibition in women with PPCM, a meta-analysis reported that those treated with bromocriptine had higher odds of left ventricular recovery, without a significant difference in all-cause mortality.[28] However, bromocriptine use is associated with an increased risk of thromboembolic complications. The 2019 ESC–Heart Failure Association position statement issued a weak recommendation for bromocriptine use, advising that it should always be accompanied by at least prophylactic anticoagulation.[15] Future randomised controlled trials and registry data with longer follow-up are needed to provide stronger evidence supporting its use. For women who do not recover from PPCM within 1 year, the American College of Cardiology/American Heart Association Joint Committee and the ESC recommend implantable cardioverter-defibrillator therapy for the primary prevention of sudden cardiac death due to ventricular tachyarrhythmia.[22,29,30] Cardiac transplantation may be required for patients with refractory severe heart failure despite maximal medical therapy, as occurred in one of our cases.

Cardiac recovery and mortality

Estimates of left ventricular recovery and mortality in PPCM vary considerably across geographic regions,[26] presumably due to differences in medical therapy, access to healthcare services, and follow-up duration. A 2022 meta-analysis of 4875 patients from 60 countries reported overall 12-month rates of left ventricular recovery and all-cause mortality of 58.7% and 9.8%, respectively.[26] In our cohort, 60% of women achieved cardiac recovery; two patients (6.7%) died of myocardial infarction and pulmonary embolism within 12 months of diagnosis. Both had poor social support and did not adhere to treatment or attend follow-up visits, which likely contributed to their adverse outcomes. These findings highlight the need for greater public awareness, improved medication compliance, and stronger social support systems. We recommend enhanced nursing outreach and structured patient education, along with post-discharge monitoring, to optimise outcomes.

Prevention of thromboembolic complications

Thromboembolism, a potentially life-threatening complication of PPCM, affected 23.3% of women in our cohort. This high rate may be attributed to the hypercoagulable state of pregnancy, impaired circulation, and blood stasis from cardiac failure. Our incidence was higher than the reported global rate of 6.1% in a recent international study.[26] Therapeutic anticoagulation is recommended for patients with intracardiac thrombus or systemic embolism. In our study, 13.3% of patients received low molecular weight heparin for thromboembolism prophylaxis. Both the AHA and ESC recommend anticoagulation in PPCM cases involving severe left ventricular dysfunction (LVEF <30% to <35%) during the peripartum period and up to 8 weeks postpartum.[29,31] Despite the high thromboembolic risk in PPCM, anticoagulation remains a subject of ongoing debate.[32] Our data support prophylactic anticoagulation for all women with PPCM, given the high incidence observed. Ultimately, individual assessment of thromboembolic risk—considering the extent of left ventricular dysfunction, caesarean delivery, immobility, and ventricular dilatation—may help identify patients most likely to benefit from thromboprophylaxis.

Relapse of peripartum cardiomyopathy in subsequent pregnancies

Relapse of PPCM and associated mortality in subsequent pregnancies are not uncommon; rates range from 5.3% to 29.5% and 0% to 55.5%, respectively.[33] In our study, nine of 11 patients (81.8%) had confirmed recovery of cardiac function before conception. There were no maternal deaths or PPCM recurrences during pregnancy. A recent meta-analysis showed that women with persistent left ventricular dysfunction prior to a subsequent pregnancy had a higher risk of mortality and

worsening function compared to women whose cardiac function had recovered.[33] However, recovered left ventricular function does not guarantee an uncomplicated subsequent pregnancy.[34,35] It is crucial to monitor cardiac function throughout pregnancy—and up to 6 months postpartum—to detect subclinical left ventricular dysfunction or PPCM recurrence. Women with a history of PPCM should be counselled regarding the risks of future pregnancies, including irreversible ventricular deterioration, maternal death, and fetal loss.[36] Subsequent pregnancy is not recommended if LVEF fails to normalise. Contraceptive counselling should begin early after the acute event; reliable methods with minimal thromboembolic risk are preferred.[37]

Genetic assessment

A study has demonstrated a genetic contribution to PPCM in at least 15% of cases.[38] The most commonly affected gene is *TTN*, which encodes the large sarcomeric protein titin.[39] The relative prevalence of truncating variants in these genes is nearly identical between PPCM and DCM.[39] In our study, three of 30 patients (10%) were screened for cardiomyopathy-related genes (*TTN, FLNC, MYBPC3, NEXN*), all of whom were in the non-recovery group, indicating that at least 10% had a genetic predisposition to PPCM. The American College of Cardiology/American Heart Association Joint Committee recommends that patients with non-ischaemic cardiomyopathy undergo genetic counselling and testing for inherited cardiomyopathies to facilitate early cardiac disease detection and timely initiation of treatments that reduce heart failure progression and sudden death risk.[22] The identification of pathogenic genetic variants can provide valuable prognostic information and clarify associated risks (eg, arrhythmic complications linked to *FLNC* and *DSP* mutations), thereby guiding decisions on preventive measures, including implantable defibrillator placement and exercise recommendations. Furthermore, cascade genetic testing for relatives enables closer pregnancy monitoring, informed reproductive decisions (including prenatal or preimplantation genetic diagnosis), and lifelong cardiovascular surveillance to improve outcomes.[40] The value of routine genetic testing remains limited by low penetrance, variable clinical expression, and uncertain variant significance. It may also lead to patient anxiety, potential genetic discrimination, and substantial resource implications. Careful patient selection with thorough pre- and post-test counselling is essential. Because the clinical presentation of PPCM closely resembles that of DCM, the ESC suggests that genetic testing be considered in PPCM cases with a positive family history,[15] where clinically actionable findings are most likely to be identified.

Limitations

This study had several limitations. Because PPCM is a rare condition, a small sample size was inevitable. The retrospective nature of data collection over a 10-year period may have resulted in incomplete information. Outcomes could also have been influenced by variations in heart failure management over time and across hospitals. Furthermore, some PPCM cases managed in the private sector or outside Hong Kong might not have been captured. The long-term impact of PPCM on women's overall health was not assessed. The establishment of a local PPCM registry would facilitate a better understanding of the condition, identification of outcome determinants, and optimisation of clinical care in Hong Kong.

Conclusion

Peripartum cardiomyopathy is an uncommon but potentially life-threatening medical condition affecting women worldwide. Genetic factors contribute to disease susceptibility in at least 10% of cases. Genetic testing may offer a valuable tool to guide prognosis and management in affected women.

Author contributions

Concept or design: LSK Law, LT Kwong, PL So.
Acquisition of data: LSK Law, KH Siong, HC Mok, STK Wong, JKO Wai, CY Chow, WL Chan, KY Tse, YYY Chan, KS Eu, PL So.
Analysis or interpretation of data: LSK Law, PL So.
Drafting of the manuscript: LSK Law, PL So.
Critical revision of the manuscript for important intellectual content: All authors.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

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Ethics approval

This research was approved by the Central Institutional Review Board of Hospital Authority, Hong Kong (Ref No.: CIRB-2023-114-3). The requirement for informed patient consent was waived by the Board due to the retrospective nature of the research. All data used in the research were anomymised and unidentifiable.

Supplementary material

The supplementary material was provided by the authors and some information may not have been peer reviewed. Accepted supplementary material will be published as submitted by the authors, without any editing or formatting. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by the Hong Kong Academy of Medicine and the Hong Kong Medical Association. The Hong Kong Academy of Medicine and the Hong Kong Medical Association disclaim all liability and responsibility arising from any reliance placed on the content. To view the file, please visit the journal online (https://doi.org/10.12809/hkmj2512986).

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