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ORIGINAL RESEARCH ARTICLE

Clinical presentation and outcomes of peripartum cardiomyopathy in the Middle East: a cohort from seven Arab countries

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Abstract

Aims Published data on the clinical presentation of peripartum cardiomyopathy (PPCM) are very limited particularly from the Middle East. The aim of this study was to examine the clinical presentation, management, and outcomes of patients with PPCM using data from a large multicentre heart failure (HF) registry from the Middle East.

Methods and results From February to November 2012, a total of 5005 consecutive patients with HF were enrolled from 47 hospitals in 7 Middle East countries. From this cohort, patients with PPCM were identified and included in this study. Clinical features, in-hospital, and 12 months outcomes were examined. During the study period, 64 patients with PPCM were enrolled with a mean age of 32.5 ± 5.8 years. Family history was identified in 11 patients (17.2%) and hypertension in 7 patients (10.9%). The predominant presenting symptom was dyspnoea New York Heart Association class IV in 51.6%, class III in 31.3%, and class II in 17.2%. Basal lung crepitations and peripheral oedema were the predominant signs on clinical examination (98.2% and 84.4%, respectively). Most patients received evidence-based HF therapies. Inotropic support and mechanical ventilation were required in 16% and 5% of patients, respectively. There was one in-hospital death (1.6%), and after 1 year of follow-up, nine patients were rehospitalized with HF (15%), and one patient died (1.6%).

Conclusions A high index of suspicion of PPCM is required to make the diagnosis especially in the presence of family history of HF or cardiomyopathy. Further studies are warranted on the genetic basis of PPCM.

Keywords Cardiomyopathy; Heart failure; Outcomes; Peripartum; Registry; Symptoms

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Introduction

Most of the available literature on peripartum cardiomyopathy (PPCM) was based on either small case series or larger registry-based administrative data, focusing on incidence, risk factors, and short-term outcomes.[1,2] Published data on the clinical presentation of PPCM are very limited particularly from the Middle East. In the current study, we used prospectively collected data from a real-world cohort of consecutive patients with PPCM hospitalized with acute heart failure (HF) with two specific aims: firstly, to examine in detail the clinical presentation of patients with PPCM and, secondly, to report the management, and in-hospital and 1 year clinical outcomes of PPCM in seven Arab countries in the Middle East.

Methods

Study design

Data were extracted from the Gulf CARE registry (Gulf aCute heArt failuRe rEgistry). Details of the Gulf CARE design were previously published.[3] In summary, Gulf CARE was a multicentre, multinational, prospective, observational study that recruited patients who were admitted with the final diagnosis of acute HF from 47 hospitals in 7 Middle Eastern countries in the Arabian Gulf (Oman, Saudi Arabia, United Arab Emirates, Qatar, Bahrain, Yemen, and Kuwait) from February 2012 until November 2012. Study ethical approval was obtained from all concerned authorities in the recruiting centres, and informed consent was obtained from all patients. The study was registered at clinicaltrials.gov with the number NCT01467973. PPCM was defined as HF in the last month of pregnancy and up to 5 months postpartum with left ventricular systolic dysfunction (left ventricular ejection fraction $<$45%), where no other cause of HF was found.

Statistical analysis

Baseline and outcome data were presented as percentages for categorical variables and for continuous variables as means and standard deviations (and median and interquartile range for non-normally distributed variables) as appropriate. The Statistical Package for Social Sciences Version 22.0 (SPSS Inc., USA) was used for the analysis.

Results

Baseline characteristics

The study included 64 patients hospitalized with acute HF with the diagnosis of PPCM. Most of the patients were Arabs (96.9%) with a mean age of 32.5 ± 5.8 years. A family history of cardiomyopathy/HF was present in 11 patients (17.2%), and 12 patients (18.8%) had a past history of HF. Hypertension was present in seven patients (10.9%) and diabetes mellitus in three patients (4.7%).

Symptoms

All patients presented with dyspnoea (100%). The majority (51.6%) of patients were in New York Heart Association (NYHA) class IV, followed by NYHA class III (31.3%) and NYHA class II (17.2%). Other important symptoms were orthopnoea (90.6%), easy fatigability (81.3%), abdominal/lower limb swelling (79.7%), and weight gain (68.8%).

Signs

Common physical signs included basal lung crepitations (98.2%), peripheral oedema (84.4%), a raised jugular venous pressure (76.6%), and an enlarged tender liver (67.2%).

Investigations

The mean left ventricular ejection fraction by transthoracic echocardiography was 35% (±9). Electrocardiogram in all patients showed sinus rhythm with no reported significant arrhythmia. One patient was hospitalized after resuscitation from cardiac arrest. Only seven patients had results for HF biomarkers; B-type natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP) were elevated in all (*Table 1*).

In-hospital course

Three patients (4.7%) underwent tracheal intubation and mechanical ventilation. Inotropes were used in 10 patients (15.6%), blood transfusion in 9 patients (14.1%), and antibiotics were administered to 16 patients (25%). The median length of stay was 7 days (interquartile range 6–11). There was one case of in-hospital mortality (1.6%) that occurred in the patient that presented with cardiac arrest.

Discharge medications

Most patients were discharged on diuretics (98.4%), beta-blockers (75%), angiotensin-converting enzyme inhibitors (76.6%), and aldosterone antagonists (68.8%).

One-year follow-up

At 1 year, rehospitalization for HF had occurred in nine patients (14.8%) with one new death reported (1.6%) (*Table 2*).

Discussion

The current study examined in detail the clinical features of patients with PPCM admitted with acute HF in seven Middle Eastern countries. The striking observation in our study was that a significant number of PPCM patients presented with only mild to moderate dyspnoea (17.2% NYHA class II and 31.3% NYHA class III). Dyspnoea is commonly seen in normal pregnancy, affecting up to 60% of healthy women during exercise and 20% of women at rest.[4] Physiological dyspnoea of pregnancy is thought to be induced by sex hormone-related hyperventilation and the increased metabolism in normal

Table 1 Baseline characteristics, clinical presentation, and investigations

Variable Presented as *n* (%), unless expressed otherwise	PPCM (*N* = 64)
Patients' characteristics	
Age in years, mean ± SD	32.5 ± 5.8
Ethnicity: Arab	62 (96.9%)
Family history of cardiomyopathy/heart failure	11 (17.2%)
Past history of systolic LV dysfunction	12 (18.8%)
Hypertension	7 (10.9%)
Diabetes mellitus	3 (4.7%)
Hyperlipidaemia	1 (1.6%)
Asthma/COPD	1 (1.6%)
Thyroid disease	1 (1.6%)
Atrial fibrillation	1 (1.6%)
Current smoker	3 (4.7%)
Clinical presentation	
Dyspnoea NYHA class	
NYHA II	11 (17.2%)
NYHA III	20 (31.3%)
NYHA IV	33 (51.6%)
Orthopnoea	58 (90.6%)
Easy fatigability	52 (81.3%)
Abdominal/lower limb swelling	51 (79.7%)
Chest pain	12 (18.8%)
Palpitation	27 (42.2%)
Weight gain	44 (68.8%)
HR (b.p.m.), mean ± SD	79.7 ± 10.8
RR, mean ± SD	27.5 ± 4.7
BMI (kg/m^2), mean ± SD	27.2 ± 5
Systolic blood pressure (mmHg), mean ± SD	125.5 ± 28.8
Diastolic blood pressure (mmHg), mean ± SD	83.4 ± 21
Raised JVP ≥ 6	49 (76.6%)
Signs of pleural effusion	21 (32.8%)
Gallop	45 (70.3%)
Basal lung crepitations	63 (98.2%)
Enlarged tender liver	43 (67.2%)
Ascites	15 (23.4%)
Peripheral oedema	54 (84.4%)
Investigations	
LVEF (%), mean ± SD	35 ± 9
LVEF (%), median (IQR)	36 (29–39)
BNP value (pg/mL), median (IQR) (*n* = 5)	1000 (918–1250)
NT-proBNP value (pg/mL), median (IQR) (*n* = 2)	5043 (3637–5043)
Creatinine (μmol/L), mean ± SD	90.5 ± 29.6
First haemoglobin, mean ± SD	11 ± 2
Presentation with cardiac arrest	1 (1.6%)

BMI, body mass index; BNP, B-type natriuretic peptide; COPD, chronic obstructive pulmonary disease; HR, heart rate; IQR, interquartile range; JVP, jugular venous pressure; LV, left ventricular; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; PPCM, peripartum cardiomyopathy; RR, respiratory rate; SD, standard deviation.

Table 2 Management and outcomes

	PPCM, *N* (%)
In-hospital course	
Inotropes	10 (15.6%)
NIV	2 (3.1%)
Intubation/ventilation	3 (4.7%)
IABP	1 (1.6%)
Acute dialysis/ultrafiltration	1 (1.6%)
Major bleeding	2 (3.1%)
Blood transfusion	9 (14.1%)
Systemic infection requiring antibiotics	16 (25.0%)
Discharge medications	
Diuretics	63 (98.4%)
Beta-blockers	48 (75.0%)
ACE inhibitors	49 (76.6%)
ARBs	6 (9.4%)
Aldosterone antagonists	44 (68.8%)
Digoxin	40 (62.5%)
Oral nitrates	9 (14.1%)
Hydralazine	4 (6.3%)
Ivabradine	5 (7.8%)
Aspirin	37 (57.8%)
Clopidogrel	1 (1.6%)
Oral anticoagulants	8 (12.5%)
CCB	1 (1.6%)
Antiarrhythmics	37 (57.8%)
Length of stay (days), median (IQR)	7 (6–12)
In-hospital mortality	1 (1.6%)
Mortality (new) at 1 year	1 (1.6%)
Rehospitalization for HF at 1 year	9 (14.8%)

ACE, angiotensin-converting enzyme; ARBs, angiotensin II receptor blockers; CCB, calcium channel blocker; HF, heart failure; IABP, intra-aortic balloon pump; IQR, interquartile range; NIV, non-invasive ventilation; PPCM, peripartum cardiomyopathy.

pregnancy.[5] In addition, several other symptoms and clinical signs observed may also be seen in normal pregnancy. Weight gain and lower limb oedema, observed in most of our cases, may also be misinterpreted as consequences of changes in pregnancy. Because PPCM is an uncommon disease, many women and their physicians may consider these symptoms and signs to be normal. It is therefore essential to have a high index of suspicion when evaluating patients with dyspnoea in pregnancy so as not to miss the diagnosis because both survival and recovery of PPCM are improved by early detection.[6] Moreover, the physical signs specific to HF that were observed in most of our patients were signs of pulmonary oedema, namely, basal lung crepitations. As lung crepitations are not considered part of the physiological signs associated with pregnancy,[7] lung bases should be carefully examined in pregnant patients presenting with dyspnoea.

A family history of cardiomyopathy or HF was present in 17.2% of our patients. This is consistent with previous reports that suggested, at least in some cases, a hereditary or genetic component of PPCM. A family history of cardiomyopathy (imprecisely defined as PPCM, idiopathic cardiomyopathy, sudden death, or arrhythmias in first-degree relatives) was noted in 15% of patients in one German cohort.[8] In addition, a genome-wide association study in 79 patients identified a single-nucleotide polymorphism near the parathyroid hormone-like hormone gene as being associated with PPCM.[9] Furthermore, variants in genes encoding myofibrillar proteins including the gene encoding the sarcomere protein titin have been identified in rare pedigrees of patients affected by both PPCM and dilated cardiomyopathy (DCM).[10] Genetic mutations surrounding dystrophin have also been proposed.[11] Moreover, a retrospective study investigated the association of familial DCM and PPCM[12] and found that a subset of PPCM patients with certain genes had an initial manifestation of

familial DCM. It is not easy to distinguish sporadic PPCM from other genetic forms, and therefore, careful familial history should be taken in these patients as well as counselling of affected families.

Results for HF biomarkers, BNP and NNT-proBNP, were measured in seven patients in our cohort (10.9%) and in all were increased. Levels of BNP or NT-proBNP do not fluctuate during pregnancy or postpartum period and are only mildly elevated in women with pre-eclampsia.[13,14] Natriuretic peptides have therefore been suggested as useful tools to evaluate pregnant and postpartum women with suspected HF to distinguish between physiologic symptoms of pregnancy and early signs of HF owing to their high sensitivity and negative predictive value.[15] Combined with a transthoracic echocardiogram, BNP or NT-proBNP could be useful non-invasive screening tests when PPCM is suspected.

Conclusions

A high index of suspicion of PPCM is required to make the diagnosis as associated symptoms and signs can be indistinguishable from those related to normal pregnancy. Transthoracic echocardiography and BNP biomarkers are useful screening tests to aid in an early diagnosis to limit life-threatening complications. Future HF registries should include variables specific to pregnancy and foetal outcomes, when PPCM is the aetiology of HF, which would enable detailed study of this uncommon condition.

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Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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