

Most Common Risk Factors Associated with Peripartum Cardiomyopathy amongst Kurdish Population

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Abstract

Background: Peripartum cardiomyopathy (PPCM) is idiopathic cardiomyopathy that presents during the last trimester or the first several months after delivery and it is a serious complication of pregnancy. **Objectives:** The aim was to assess the most common risk factors seen among pregnant women leading to PPCM and factors that are associated with better outcomes after therapy. **Materials and Methods:** A total of 20 patients who presented to the outpatient cardiology clinic and fulfilled the diagnostic criteria of the European Society of Cardiology were recruited to participate in the study. A detailed history was obtained and left ventricular measurements were evaluated using M-mode, 2-dimensional, and Simpson methods to estimate the ejection fraction. Data were analyzed using the Statistical Package for the Social Sciences. **Results:** Mean age at diagnosis was 34.7 ± 5.2 years. Multiparous women constituted 60% of the study sample. Gestational age at presentation ranged between 28 and 38 weeks, with a mean of 32.9 ± 2.6 . Being overweight was a common feature as 60% of patients had above-normal body mass index. Family history was reported in 50% of patients, followed by passive smoking (35%), hypertension (25%), thyroid disorders (30%), and type II diabetes mellitus (20%). The mean left ventricular ejection fraction at the time of diagnosis was $32.3\% \pm 6.7\%$ with an increase to $44.2\% \pm 8.9\%$ at follow-up. Younger patients were more likely to regain normal left ventricular function following diagnosis ($P = 0.005$). **Conclusion:** These preliminary results strongly demonstrate that advanced maternal age, anemia, multiparity, and family history were the most common risk factors seen among our population.

Keywords: Peripartum, dilated cardiomyopathies, Iraq

INTRODUCTION

Peripartum cardiomyopathy (PPCM) is a rare, but severe and idiopathic form of clinical heart failure with reduced left ventricular ejection fraction (LVEF) that develops toward the end of pregnancy or within 5 months after delivery.^[1]

Several factors have been associated with a higher risk of developing PPCM, these include older maternal age, multiparity, African or African American ancestry, multifetal gestations, hypertension, pre-eclampsia and eclampsia, and prolonged tocolysis with beta-adrenergic agonists.^[1,2]

The pathogenesis of PPCM is still not elucidated and likely multifactorial. Several hypotheses have been put

forward to explain the pathogenesis and have included genetic factors, increased hemodynamic demand of pregnancy, myocarditis, pathological maternal immune response to fetal antigens, nutritional imbalances, and hormonal disturbances.^[3]

The outcomes of PPCM are variable. Most studies show that the great majority of women have a complete recovery of heart function. However, a considerable number of

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Submission: 18-Aug-2023 **Accepted:** 25-Oct-2023 **Published:** 02-Aug-2023

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How to cite this article: Amen SO, Rasool BQ, Shehata DG, Al-Hadeethi BT, Maqdasy RF, Qader SM, *et al.* Most common risk factors associated with peripartum cardiomyopathy amongst Kurdish population. Med J Babylon 2023;20:249-53.

Access this article online

Quick Response Code:



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DOI:
10.4103/MJBL.MJBL_183_22

patients remain with chronic heart failure and residual left ventricular dilation.^[4]

The incidence of PPCM varies by geographical region,^[5] and exact data about the incidence and risk factors of PPCM in the Kurdistan Region of Iraq are scarce.

The aim of this study is to evaluate and explore the predisposing risk factors, clinical features, and echocardiographic measurements associated with PPCM in Iraqi Kurdistan. This study would be beneficial to our region and our results would be useful to clinicians to identify patients at higher risk of developing PPCM.

MATERIALS AND METHODS

Study design

An observational study.

Setting and duration of the study

The study was conducted in an outpatient clinic of a cardiologist in Erbil/Kurdistan, Iraq, from January 2021 to December 2021.

Sample size and sampling method

A total of 20 patients were chosen in a non-randomized manner as they were convenient to enroll due to their presentation to the outpatient clinic.

The inclusion criteria were based on diagnostic guidelines of the European Society of Cardiology (2020) for PPCM, which are the following:

- Presence of heart failure due to left ventricular systolic dysfunction with an LVEF of <45%.
- Development of the heart failure occurred toward the end of pregnancy or in the weeks following delivery.
- No other detectable cause of heart failure.

Patients not fulfilling the aforementioned criteria were excluded from the study.

Data collection

The data were collected through a detailed history taken from the patients emphasizing risk factors such as multiple pregnancies, advanced age, drug abuse, smoking, and malnutrition followed by a general physical examination. In addition, a follow-up questionnaire was prepared to assess the patients' health status posterior to their selection according to the predetermined criteria.

Echocardiography

The left ventricular function was evaluated using M. Mode 2-dimensional. and Simpson method to estimate ejection fraction. Abnormalities of the segmental wall were assessed by both long- and short-axes views. Additionally, the diameter of the left atrium during diastole has also been taken.

Statistical analysis

Statistical Package for the Social Sciences (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp) was used for data entry and analysis. Descriptive statistics as a first approach was used to determine frequencies and percentages. The second approach analytic statistics such as Chi-square and Fisher's exact tests were used for categorical variables. P -value ≤ 0.05 is regarded as statistically significant.

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients' verbal and analytical approval before the sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee according to document number Meeting Code-5, Paper Code-2 on February 20, 2022) to get this approval.

RESULTS

The total number of patients with confirmed PPCM attending our outpatient clinic from April to December 2021 was 20. The mean age was 34.7 ± 5.2 years with an age range of 26–44 years and the majority of patients (65%) were found to be in their 4th decade. Parity ranged between 1 and 9. Grand multiparous patients constituted 50% (10) of the total study sample, while multiparous patients accounted for 40% (8) and 10% (2) were primiparous [Table 1].

Time of diagnosis was established after delivery in all of our patients. Majority (65%) were diagnosed in the second and third months postpartum. However, 25% were diagnosed within the first postpartum month and 10% were diagnosed four months after delivery.

Table 1: Baseline characteristics of patients with peripartum cardiomyopathy

Age groups	
20–29 years	4 (20%)
30–39 years	13 (65%)
40–49 years	3 (15%)
Parity	
Primiparous	2 (10%)
Multiparous	8 (40%)
Grand multiparous	10 (50%)
Socioeconomic status	
Poor	4 (20%)
Fair	7 (35%)
Good	8 (40%)
Very good	1 (5%)
BMI class	
Normal	8 (40%)
Overweight	11 (55%)
Obese class I	1 (5%)

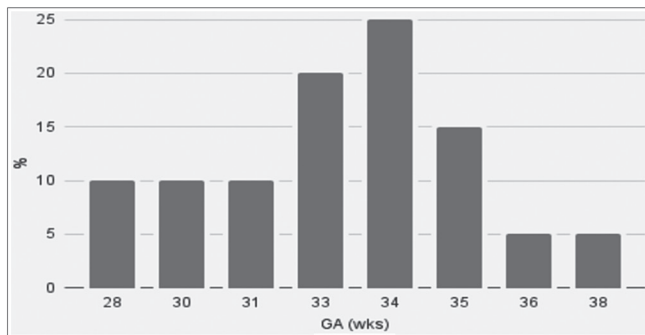


Figure 1: Gestational age at onset of symptoms

Table 2: Frequency of risk factors associated with PPCM

Risk factor	Number and percentage
Essential hypertension	5 (25%)
Hyperthyroidism	2 (10%)
Hypothyroidism	4 (20%)
Diabetes mellitus type II	4 (20%)
Family history	10 (50%)
Passive smoking	7 (35%)

Gestational age (GA) at presentation ranged between 28 and 38 weeks with a mean of 32.9 ± 2.58 weeks [Figure 1].

History of chronic hypertension was obtained in 25% of patients. Other comorbid conditions included diabetes (20%), hypothyroidism (20%), and hyperthyroidism (10%). None of our patients were smokers, yet 35% had exposure to secondhand smoking. Twin pregnancies were reported in 25% of the patients and family history was reported in 50%. According to body mass index (BMI) classification, 11 out of 20 patients (55%) were overweight, 8 (40%) had a normal BMI, and 1 (5%) was obese class I [Table 2].

The mean LVEF at the time of diagnosis was $32.3\% \pm 6.7\%$ (range, 20% and 40%) and increased to $44.2\% \pm 8.9\%$ (range, 28%–55%) at the last follow-up. Recovery of LVEF (>54%), observed in 10% of patients with 50% of patients having mildly abnormal (41%–53%) ejection fraction (EF). Moreover, moderately abnormal EF (30%–40%) was observed in 35% of the patients whereas 5% of the patients had a severely abnormal EF (<30%). Left ventricular diastolic dysfunction (LVDD) resolved in only 10% of the patients at follow-up whereas 90% had residual LVDD.

Cesarean section (CS) was the most common mode of delivery, performed for 15 (75%) patients, whereas five (25%) patients had a normal vaginal delivery.

The entirety of the study sample reported post-delivery symptoms. The most common symptoms were fatigue and dyspnea, which were reported by all 20 patients. Other symptoms included chest pain, orthopnea, pedal edema, and paroxysmal nocturnal dyspnea, which were reported in 40%, 30%, 20%, and 5% of patients, respectively [Table 3].

Table 3: Frequency of symptoms reported by patients with peripartum cardiomyopathy

Symptom	The number and percentage of patients presenting with symptoms currently
Dyspnea	20 (100%)
Orthopnea	6 (30%)
PND	1 (5%)
Chest pain	8 (40%)
Fatigue	20 (100%)
Pedal edema	4 (20%)

PND = paroxysmal nocturnal dyspnea

Table 4: Correlation between age at diagnosis and recovery of left ventricular function

		Follow-up LVEF				<i>P</i> = 0.005
		Normal	Mildly abnormal	Moderately abnormal	Severely abnormal	
Age at diagnosis	20–29	2	2	0	0	
	30–39	0	8	5	0	
	40–49	0	0	1	1	

At follow-up, and according to New York Heart Association classification, the majority of patients were in class II (70%), whereas 15% were in Class III, 10% in Class IV, and 5% in Class I.

In the presented study, age at diagnosis had no influence on the initial LV function ($P = 0.214$), but when compared with the recovery of LVEF, younger age groups were more likely to regain normal LV function compared to those in older age groups ($P = 0.005$) [Table 4].

Comparison between parity with initial and follow-up echocardiography did not yield any significance ($P = 1.0$), ($P = 0.59$), respectively. Twin pregnancy had no influence on initial and follow-up echocardiographic findings as well ($P = 0.61$), ($P = 0.15$), respectively.

When investigating other risk factors, anemia was found to be significantly related to persistence of LV dysfunction on follow-up echocardiography ($P = 0.01$). Interestingly, hypertension had no correlation with the severity of initial and follow-up LV dysfunction, ($P = 1.0$), ($P = 0.50$), respectively.

In our study sample, when compared with CS, normal vaginal delivery was associated with more severe LV dysfunction at diagnosis in the postpartum period ($P = 0.01$).

DISCUSSION

PPCM is an idiopathic dilated cardiomyopathy that presents in women during the latter part of pregnancy or the first several months after delivery and it is a serious complication of pregnancy.^[6] Studies investigating the risk factors that worsen outcomes have yielded conflicting

results, and for that reason studies like this present study are crucial to determine the possible factors associated with this unfortunate pregnancy complication. To our knowledge this is the first study in our region addressing and investigating PPCM.

This presented study sample included 20 patients. The age of our patients ranged from 26 to 44 years with a mean (standard deviation) of 34.7 ± 5.2 years which was similar to that studied by Kezerle *et al.*^[7] and Farhan and Yaseen^[8] suggesting that PPCM is more likely to be diagnosed in women in their fourth decade. Conversely, other studies showed higher prevalence in the third decade.^[9,10]

In our study sample, grand multiparous patients constituted 50% of the total study sample, whereas multiparous patients accounted for 40% and 10% were primiparous. This finding supports the existing literature that correlates multiparity with the increased risk of developing PPCM.^[11] On the contrary, multiple other studies found that primiparous women were of greater risk of developing PPCM.^[12-14]

Family history was present in 50% of our patients. This is consistent with previous reports that suggest genetic or hereditary factors might play a role in the pathogenesis of PPCM. The prevalence of family history in our study was higher than those reported in the Middle East and a German cohort study (17.2%), (16.5%), respectively.^[15,16]

The baseline mean LVEF in our patients was $32.3\% \pm 6.7\%$. This was comparable to the EORP registry ($31\% \pm 10\%$),^[17] but higher values were reported in patients from the Middle East (35 ± 9)^[15] and the Iraqi registry (34.7 ± 8.1).^[8]

The follow-up mean LVEF in our sample was comparable to findings reported by Farhan and Yaseen (44.5 ± 11.9) and the German cohort ($47 \pm 19\%$).^[8,16]

An interesting finding arose from correlating the age at presentation with recovery of LVEF.

Whereas the age at diagnosis had no influence on the initial LV function, it was of interest that with recovery of LVEF, younger age groups were more likely to regain normal LV function compared to those in older age groups. Similar findings were reported by Liang *et al.* In their study, they found that the mean age of the LVEF-recovered patients was 27.5 ± 5.9 .^[18] In addition to age, another factor affecting LVEF recovery is anemia which is consistent with existing data suggesting that anemia is a strong risk factor for developing PPCM.^[19]

Existing literature suggests a strong association between pre-existing hypertension and pregnancy-induced hypertensive disorders with the pathogenesis of PPCM.^[2] Whereas the history of pre-existing hypertension was obtained in 25% of our patient's sample, none of our patients developed pregnancy-induced hypertensive disorders. The

Iraqi registry reported a higher prevalence of pregnancy-induced hypertensive disorders (51.7%)^[8] among their study sample, whereas that of the Middle eastern^[15] study, it was 10.9%. We are uncertain why none of the patients in our study had pregnancy-induced hypertensive disorders or why these differences of the above-mentioned findings exist; perhaps, it could be attributed to the small sample size, substandard management, and suboptimal primary health care services, or other unknown reasons.

In this presented sample, when compared with cesarean section delivery, normal vaginal delivery was associated with more severe LV dysfunction at diagnosis in the postpartum period. This can be explained by the great hemodynamic changes that are expected to occur in the puerperium period. It includes autotransfusion of blood from the fetal uteroplacental bed to the maternal systemic circulation. In contrast, a study conducted by Ruys *et al.*^[20] had a different conclusion. It showed that cesarean section, planned or emergent, might have adverse effects on both fetal and maternal outcomes. It stated that when it comes to the fetal outcomes, pregnancy was shorter and fetal weight was lower in pregnancies delivered by cesarean section. In addition to that, their study showed that in the postpartum period, patients who underwent cesarean section have a higher chance of developing heart failure. This can be due to many causes, such as the antenatal steroids given to the patient to promote fetal lung maturity, which can lead to fluid retention. The difference in results seen in our study compared to this study can be due to many variables, such as the difference in population size and the inclusion criterion.

It is worth mentioning that our study lacks mortality cases compared to global literature. This is accounted for by our inclusion criteria that followed a general approach of assessing echocardiographic findings supporting a diagnosis of PPCM in otherwise healthy women and excluding patients with findings suggesting another medical diagnosis that could cause a diminished LV systolic function.

Relatively small sample size and single centered study are some of the limitations that this study results and thus our study cannot be generalizable. Also, it was obtained in a non-randomized manner.

Moreover, few patients with PPCM were referred from other clinics/hospitals, possibly introducing some bias. The collection of information was dependent on the patients' response and/or the referring physician.

CONCLUSION

This study helps to define the clinical profile of patients with pregnancy-associated cardiomyopathy diagnosed in a single outpatient clinic in Kurdistan region. PPCM is a

serious cardiac complication of pregnancy. Risk factors were: maternal age between 30 and 40, multiparity, family history, and anemia. Efforts are needed to understand its cause in some women and to address the issues with its management in our community. A national study needs to be conducted to identify the prevalence of this debilitating disease.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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