

## EXPLORING THE IMPACT: CLINICAL PRESENTATION AND OUTCOMES IN PATIENTS WITH PERIPARTUM CARDIOMYOPATHY

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### Abstract

**Background:** The study analysed the clinical profiles and outcomes of women with peripartum cardiomyopathy. **Materials and Methods:** This study was a retrospective, observational investigation. Data were extracted from patient records. **Result:** The incidence of peripartum cardiomyopathy was found rare. 26 women, with an average age of 22.3 years and an average gestational age of 35.6 weeks, were included in the study, with 15 of them being primigravidae. Maternal and fetal deaths occurred in 4 and 8 subjects, respectively. The presence of mild-to-moderate maternal anemia was found to be associated with fetal mortality. Reduced left ventricular ejection fraction and cardiogenic shock were significantly associated with adverse maternal outcomes. **Conclusion:** The study concluded that peripartum cardiomyopathy with poor left ventricular ejection fraction and shock is associated with adverse maternal outcomes, while non-severe maternal anemia predisposes to adverse fetal outcomes.

## INTRODUCTION

Peripartum cardiomyopathy (PPCM) is a potentially life-threatening condition characterized by heart failure (HF) and reduced left ventricular ejection fraction (LVEF) in previously healthy women. Despite the known risks and consequences of this condition, its exact cause remains unknown and is a topic of speculation. While PPCM shares similarities with dilated cardiomyopathy (DCM) in terms of its phenotypic characteristics, it is considered a distinct entity separate from other forms of cardiomyopathy. The diagnosis of PPCM relies on the timing of symptoms in relation to pregnancy and the exclusion of other forms of cardiomyopathy. Despite increased awareness of PPCM, there are still many unanswered questions.<sup>[1,2]</sup>

Epidemiological studies have contributed to the limited data on PPCM. Africans and African-Americans have shown a higher propensity for developing PPCM. In Caucasian populations, the incidences was higher Germany compared to Denmark. Reports of USA revealed a hospitalization rate of 0.46 per 1000 deliveries for cardiomyopathy in the postpartum period. There is a significant difference in the incidence of PPCM among different ethnic groups.<sup>[3-10]</sup>

Limited data is available on the prevalence of PPCM in Asian populations. Several risk factors for PPCM have been identified. It is important to note that the

disease process is heterogeneous, as not all women with preeclampsia develop PPCM, and a significant number of women with PPCM are young and experiencing their first pregnancy. The variations in incidence among different populations and ethnicities may be attributed to differences in estimation.<sup>[4,11-17]</sup>

Studies have also shown an increasing trend in mortality with maternal age, women with at least four live births, and black women, who are 6.4 times more likely to die compared to white women. A significant number of deaths occur within the first week and between 80-90% within six months of diagnosis, primarily due to progressive heart failure or sudden cardiac death. Mortality is higher in women with a baseline LVEF of 25% or less. Delayed diagnosis of PPCM has also been associated with increased mortality.<sup>[18,19]</sup>

Mandal et al. conducted a study on PPCM in India, focusing on the associations and outcomes of women. The lack of literature from India population has hindered the development of strategies for diagnosing, managing, and following up with women.<sup>[20,21]</sup> Therefore, our objective was to analyse the incidence of PPCM in a North Indian population and identify significant associations with maternal and foetal outcomes.

## MATERIALS AND METHODS

This study was a retrospective, observational investigation that focused on women who were admitted to the Departments of Obstetrics and Gynaecology at Government Medical College, Bettiah Bihar from October 2022 to September 2023. The study was approved by institutional research and ethical committee. Data were extracted from patient records.

### Inclusive Criteria

Women had to exhibit signs of heart failure (HF) within the last four weeks of pregnancy or up to five months postpartum. Additionally, they had to have no other identifiable causes of HF, such as valvular lesions. Women were also required to have no signs of HF prior to the last month of pregnancy and to exhibit left ventricular (LV) systolic dysfunction on echocardiography. LV systolic dysfunction was defined as having a left ventricular ejection fraction (LVEF) of less than 45%, a fractional shortening of less than 30%, or both. Furthermore, women needed to have a possible additive LV end diastolic dimension greater than 2.7 cm/m<sup>2</sup> body surface area.

### Exclusion criteria

The study included incomplete patient details at baseline, pre-existing HF, chronic obstructive pulmonary disease, valvular heart disease, blood

pressure of 170/100 mmHg or higher, or severe anemia.

The primary outcomes of interest in this study were the risk factors, disease characteristics, and predictors of poor maternal and fetal outcomes.

The data was tabulated in Microsoft excel spread sheet and the statistical analysis was evaluated using SPSS software.

## RESULTS

The analysis included a total of 26 women with PPCM and meeting the inclusion and exclusion criteria. Among them, the majority were primigravidae. The mean age at presentation was 22.3 years, with a mean gestational age of 35.9 weeks. Out of the 26 women, 2 had multiple pregnancies, all of which were twin gestations. Within the study population, maternal deaths were observed in 4 out of 26 and fetal deaths in 8 out of 18. To compare maternal and fetal outcomes, patient characteristics were tabulated and presented in [Tables 1 and 2]. Previous studies have highlighted the various causes of maternal and fetal mortality of which hemorrhage, puerperal sepsis, and hypertension together accounted for majority of maternal deaths.

**Table 1: Patient characteristics and maternal outcomes.**

Characteristics	Survivors		Non-survivors		p-Value
	n = 22	%	n = 4	%	
Mean age (years)	23.7		21.2		0.66
Parity					
Primigravida	12	54.5	3	75	0.41
Multiparous	10	45.5	1	25	
Mean gestational age (weeks)	35.5		36.1		0.18
Multiple pregnancies	2	9.1	0	0	1.00
Mode of delivery					
Normal delivery	7	31.8	1	25	0.69
Caesarean section	13	59.1	3	75	0.98
Operative vaginal delivery	2	9.1	0	0	1.00
Maternal comorbidities					
Hypertensive disorders	11	50	2	50	0.32
Anaemia	8	36.4	2	50	0.29
Hypothyroidism	3	13.6	0	0	1.00
Echocardiography findings					
Mean ejection fraction	35.4		26.2		0.03
LV thrombus	1	4.5	0	0	100
Cardiogenic shock	3	13.63	3	75	0.01
Postpartum haemorrhage	2	9.1	1	25	0.26

**Table 2: Patient characteristics and fetal outcomes.**

Characteristics	Survivors		Non-survivors		p-Value
	n = 18	%	n = 8	%	
Mean age (years)	25.9		24.6		<b>0.06</b>
Parity					
Primigravida	11	61.1	6	75	0.24
Multiparous	7	38.9	2	25	
Mean gestational age (weeks)	35.8		33.9		0.05
Echocardiographic findings					
Ejection fraction Mean ± SD	35.9	4.4	33.9	5.2	0.21
LV Thrombus	1	5.5	0	0	
Cardiogenic shock	3	16.6	2	25	
Maternal comorbidities					
Hypertensive disorders	9	50	4	50	0.58

Anaemia	1	5.6	1	12.5	0.21
Hypothyroidism	2	11.11	0	0	0.29
Gestational Diabetes	6	33.33	3	37.5	0.01

Upon presentation, the most common symptom observed was exertional dyspnea. Among the women, majority had New York Heart Association (NYHA) class III symptoms, while about a half had NYHA class IV symptoms. During clinical examination, majority women showed signs of pulmonary edema, and a few women exhibited cardiogenic shock, characterized by hypotension, cold and clammy extremities, and poor cardiac contractility. None of the women reported experiencing syncope. Significantly less women had documented episodes of thromboembolism. Sinus tachycardia was observed in all women, with an average heart rate of 103. beats per minute. Ischemic changes, such as ST-T changes and poor R wave progression, were noted in women. The baseline echocardiogram revealed a mean ejection fraction of 35.4. Out of the 12 women who underwent long-term follow-up with repeat echocardiography, the average duration of follow-up was 21.2 months.

16 women underwent a lower segment caesarean section (LSCS), while 2 women underwent operative vaginal deliveries using either a suction cup or forceps. When evaluating the primary outcome of maternal mortality, it was found that the mean EF (ejection fraction) was significantly lower in the group with poor maternal outcomes compared to the group with good maternal outcomes. The odds of experiencing a poor maternal outcome were significantly higher in individuals with cardiogenic shock. Other comorbid illnesses such as gestational hypertension, hypothyroidism, and anaemia did not have an impact on maternal outcomes. Out of the total, 9 women had gestational diabetes mellitus, but there was no significant association with maternal mortality. Factors associated with poor fetal outcomes included non-severe anaemia. The mean hemoglobin level among those with poor fetal outcomes was 103 g/l. Mild-to-moderate anemia was identified as a predictor of poor fetal outcomes. In the group with adverse maternal outcomes, left ventricular ejection fraction (LVEF) was significantly reduced, and there was a higher proportion of individuals experiencing cardiogenic shock compared to the group with good maternal outcomes.

## DISCUSSION

PPCM is a rare illness that occurs during late pregnancy or early puerperium, but its exact cause is still unknown. The incidence of PPCM varies depending on the geographic location and race. In our study, we found the incidence to be extremely low. This is similar to the findings of a study conducted by Pandit et al,<sup>[21]</sup> where they reported one case per 1374 live births. Although the cause of PPCM is not well understood, several hypotheses have been

proposed.<sup>[23]</sup> It is important to note that PPCM is different from idiopathic DCM. Some of the suggested causes include infective viral triggers, abnormal hemodynamic response due to pregnancy, myocarditis, autoimmune factors, inflammatory mediators, prolonged tocolysis, and selenium deficiency.<sup>[24,25]</sup>

Previous studies have identified certain risk factors for PPCM. These include multiparity, advanced maternal age, multiple gestation, African descent, gestational hypertension, preeclampsia, family history, smoking, and maternal habits and abuse.<sup>26</sup> Elkayam et al. have shown that PPCM can occur at any age, but it is more common in women aged 30 years or older.<sup>[27]</sup> In our study, the mean age at presentation was 23.7 years, indicating that our cohort was relatively younger. Regarding traditional risk factors, we did not find a significant association between gestational hypertension, diabetes mellitus, hypothyroidism, and PPCM. However, we did observe that anemia was associated with fetal mortality.

PPCM presents a variable clinical course and poses challenges in both diagnosis and treatment. The clinical features are similar to those seen in other forms of DCM, including exertional dyspnea, fatigue, syncope, and edema.<sup>[28]</sup> The primary method for diagnosing and predicting PPCM is through echocardiographic analysis, which demonstrates LV systolic dysfunction after ruling out other causes of heart failure such as valvular heart disease, restrictive cardiomyopathy, and hypertrophic cardiomyopathy.<sup>[29]</sup> Electrocardiography typically shows non-specific features like sinus tachycardia, non-specific ST-T changes, and signs of left atrial or ventricular enlargement. However, it is valuable in identifying and addressing aggravating factors like arrhythmias.<sup>30</sup> In our cohort, ECG features included sinus tachycardia with a mean rate of 103.8 beats per minute and ischemic changes in few women. In some cases, an endomyocardial biopsy may be necessary to confirm or rule out other types of cardiomyopathies. The management of PPCM is comparable to that of other types of HF and is dependent on the functional class, with NYHA class III and IV cases preferably being treated in a hospital.<sup>[30]</sup> Maintaining a euvolemic status involves restricting dietary sodium and fluid intake while optimizing the use of diuretics.<sup>[28]</sup> ACEIs and ARBs, which are commonly used to manage HF in non-pregnant individuals due to their effects on preload and afterload, are not recommended during pregnancy as they can cause various complications. However, they may be considered for use after childbirth, following appropriate counseling regarding potential risks in future pregnancies. In pregnancy, hydralazine and nitrates are the preferred vasodilators, while beta-blockers, calcium channel blockers, and digoxin have

shown to improve outcomes in women with HF. Ivabradine, although effective in women with reduced EF and tachycardia, is not currently used during pregnancy.<sup>[17,32-33]</sup>

Anticoagulation should be taken into consideration for patients with atrial fibrillation, a history of thromboembolism, or a left ventricular ejection fraction (LVEF) below 35%. In our cohort, none of the women had atrial fibrillation, but those with a reduced LVEF and cardiogenic shock experienced poor maternal outcomes.<sup>[32]</sup> Implantable cardioverter defibrillators may be used in women at risk of sudden cardiac death.<sup>[34]</sup> Other potential treatment options include immunosuppressive therapy, such as azathioprine and prednisolone, intravenous immunoglobulin, or cardiac transplantation.<sup>[35-37]</sup> Bromocriptine may also play a role due to its ability to inhibit prolactin secretion. Additional drugs being evaluated for the management of peripartum cardiomyopathy (PPCM) include pentoxifylline and levosimendan.<sup>[40,41]</sup> In terms of obstetric management, vaginal delivery is preferred for women with compensated heart failure, while cesarean section is reserved for those who are decompensated or in cases of fetal distress. Shortening the second stage of labor with forceps or suction devices is advisable to reduce cardiac workload. In our cohort, 59.1% of women underwent cesarean section, while 9.1% had operative vaginal deliveries.

Previous studies have documented the recovery of left ventricular (LV) function in a significant percentage of women, typically within the first six months.<sup>[42]</sup> In our study, we had access to review echocardiograms, with a significantly larger follow-up period.

It is crucial to inform women about the risk of recurrent peripartum cardiomyopathy (PPCM) in subsequent pregnancies. Both cardiologists and obstetricians should provide guidance on the safest and most effective contraceptive methods. Additionally, women planning for future pregnancies should consider undergoing baseline LV function assessment through rest and stress echocardiography. This evaluation should take place three months after discontinuing angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), as these medications are contraindicated during pregnancy. In cases where women with persistent LV dysfunction unintentionally become pregnant, early termination may be considered to prevent further deterioration of LV function and potential maternal mortality.

## CONCLUSION

The study conducted on women diagnosed with PPCM revealed that adverse maternal outcomes were linked to lower LVEF and cardiogenic shock. Mild-to-moderate anaemia was found to be associated with adverse foetal outcomes. It is crucial to counsel

women against further pregnancies due to the risk of PPCM recurrence.

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