STUDY OF PERIPARTUM CARDIOMYOPATHY AT A TERTIARY CARE HOSPITAL

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ORIGINAL ARTICLE

BACKGROUND
Peripartum cardiomyopathy is an uncommon form of life-threatening, but potentially treatable heart failure affecting women during peripartum period with devastating consequences. Often missed its early diagnosis and appropriate management can improve the outcome of such patients.

OBJECTIVES
To study the clinical profile, electrocardiographic and echocardiographic changes in clinically proven cases of peripartum cardiomyopathy.

SETTING
Women in peripartum period admitted to the Departments of General Medicine and Obstetrics and Gynaecology at Karnataka Institute of Medical Sciences, Hubli.

PARTICIPANTS
24 patients, diagnosed to have PPCM, based on the inclusion and exclusion criteria, selected over a period of one and a half year.

METHODS
Detailed history clinical features and investigations including ECG and Echocardiogram of selected patients at presentation and follow-ups, up to six months were recorded in prestructured proforma and data analysed.

RESULTS
Results revealed to be 1 per 944 deliveries, mean age 29±5.4 years, mean parity 2.12+0.95. 87.5% (21) of patients presented in post-partum and just 12.5% (3) in ante-partum period. All patients presented with dyspnoea. Major ECG finding was Sinus Tachycardia (79.16%) followed by normal QRS complex (75%) and Left Ventricular Hypertrophy (50%). Ejection fraction was universally reduced. The main complications were Pulmonary Oedema 11(45.83%), Cardiogenic Shock 33.3% (8). As regards to outcome, 25% (6) of the patients with delayed diagnosis and reduced LV function died within first week of admission, the remaining 75% (18) were discharged of which 83.3% (15) recovered completely, while 16.6% (3) among the discharged patients had residual Heart Failure at the end of 6 months. Major therapeutics used were routine drugs used in the treatment of heart failure.

INTERPRETATION AND CONCLUSION
Peripartum Cardiomyopathy (PPCM) is a rare, potentially life-threatening, but treatable illness. Women presenting with Heart Failure during peripartum period should be evaluated for PPCM. Early detection and standard management of cardiac failure using a multidisciplinary approach started early carries a better prognosis.

KEYWORDS
Peripartum Cardiomyopathy, Heart Failure, ECG, Echocardiography.


INTRODUCTION
Peripartum Cardiomyopathy (PPCM), a rare but potentially life-threatening condition, is a distinct form of cardiomyopathy seen in a previously healthy women during the last month of pregnancy and up to 5-6 months postpartum.¹

Clinical and experimental data on PPCM, a disease of uncertain aetiology and pathophysiology suggests inflammation, autoimmune processes, apoptosis and endothelial dysfunction as typical pathophysiological features of PPCM, although recent observations strongly suggest the specific role of prolactin cleavage to produce a potent antiangiogenic, pro-apoptotic and pro-inflammatory 16-kDa subform as a potential patho-mechanism for the development of PPCM, secondary to unbalanced peri/postpartum oxidative stress.²,³

The incidence of this disease ranges from approximately once in every 2500 deliveries, comprises less than 1% of pregnancy associated cardiovascular abnormalities, in developed countries, to once in 300 deliveries in developing country like Haiti.¹,³,⁴
PPCM is a diagnosis of exclusion, as it shares many clinical characteristics with other forms of systolic heart failure secondary to cardiomyopathy. Possible adverse effects on the foetus mandates, a multidisciplinary approach of heart failure during pregnancy, while post-delivery the treatment is in accordance with the current guidelines of heart failure. PPCM is relatively uncommon; however, with increasing incidence and its association with lasting morbidity and mortality, its outcome may be devastating with reported mortality rates between 15% to 50%.\(^5\)\(^6\) Although associated with a high morbidity and mortality, early detection and appropriate management of PPCM carries potential of full recovery. Some novel therapies such as prolatin blockade are proposed to either prevent or treat the patients with PPCM. A critical individual counseling concerning the risks of subsequent pregnancy must be considered.

Its rare incidence, geographical differences and heterogeneous presentation makes PPCM to be incompletely characterized and understood entity; hence, a persistent challenge in clinical practice. Therefore, future epidemiological trials and national registries are needed to learn more about the disease.\(^7\) This study gains its importance as there are major discrepancies in the reported incidence and mortality rates of PPCM, which most likely arise from the lack of prospective PPCM registries worldwide and as a result optimal treatment strategies and definitive predictors of left ventricular recovery associated with PPCM remain unknown.

And as peripartum cardiomyopathy seems to affect women in different parts of the world, but with considerable differences in clinical presentation; hence, this study was conducted to understand the clinical profile and outcome in patients with peripartum cardiomyopathy.

**OBJECTIVES**

To know the clinical profile in peripartum cardiomyopathy along with the radiological features, electrocardiographic and echocardiographic changes in clinically proven cases of peripartum cardiomyopathy.

**METHODOLOGY/Source of Data**

A prospective study was conducted among 24 patients admitted with a diagnosis of PPCM in the Department of Medicine/OBG, Karnataka Institute of Medical Sciences, Hubli, during the study period of one and a half years after applying the inclusion and exclusion criteria.

**Inclusion Criteria**

The study group included all those patients admitted to our Institution with any parity and age, in peripartum period (i.e. within one month before delivery or within five months of delivery), who presented with moderate-to-severe breathlessness at rest or on exertion may or may not be associated with palpitations, ankle oedema or signs and symptoms of heart failure and/or with documented evidence of LV systolic dysfunction having echocardiographic finding of either ejection fraction of <45%, fractional shortening <30% or left ventricular end diastolic dimension > 2.7 cm/m2.

**Exclusion Criteria**

Patients with previous history of cardiac disease including valvular heart disease or with evidence of cardiac failure due to severe pre-eclampsia, fluid overload due to iatrogenic, renal or hepatic cause, amniotic fluid embolism and pulmonary embolism, normal echocardiography, sepsis and other comorbid conditions were excluded from the study group.

**Method of Collection of Data**

Qualifying patients underwent detailed history, clinical examination and investigations like complete blood count, ESR, Fasting blood sugar, Serum electrolytes, Lipid profile, Chest X-ray, Electrocardiography, Trans-thoracic echocardiography, HIV serology. Data pertaining to patient’s first examination and follow-up were recorded in a pre-designed, structured proforma. Each patient was followed up at regular intervals for up to six months during which patient’s clinical status, follow-up ECG and Echocardiographic findings were recorded. Obtained data was assessed and statistically analysed.

**OBSERVATIONS**

After applying the inclusion criteria, finally 24 patients diagnosed to be having PPCM were included in our study. The age range of our study group was from 19 to 45 years with a mean of 29±5.4 years. Majority of them (45.8%) belonged to age range of 25 to 29 years and least (4.2%) belonged to more than 40 years of age. Majority of the cases 13 (54.2%) presented in the first month of the postpartum period, while 5 cases (20.8%) presented during the second month of postpartum period. Two cases (8.3%) presented in 3rd month and 1 case (4.2%) presented in 4th month onwards; 12.5% (3) of the cases presented during ante-partum period. The mean parity of 2.12±0.95 suggested that more number of patients in our study group with multi-parity suffered from PPCM. With mean BMI of 24.05±2.65 chronic hypertension was observed in 8.3% (2) cases, pre-eclampsia in 16.6% (4) cases, long-term tocolys in 16.6% (4) cases. Other risk factors for PPCM like multiple pregnancy, smoking and alcoholism was not observed in our study group.

Figure No. 1 depicts the temporal profile of patient’s symptomatology at the time of presentation and during subsequent follow-ups up to six months. Dyspnoea was the most common presenting symptom (100%) followed by easy fatigability observed in (66.6%), orthopnoea in (58.3%), pedal oedema in (54.2%), palpitations in (45.8%), cough and syncope in (29.2%) paroxysmal nocturnal dyspnoea in (25%) and chest pain in (20.8%).
(54.2%) followed by basal crepts in 45.8%, raised JVP and systolic BP <100 in 33.3% of cases each, pansystolic murmur at apex in 16.7%, left ventricular S3 in 29.3% cases, RV5 and hepato megaly in 12.6% were observed during clinical examination. None of the patients had focal neurological deficits.

Major ECG findings observed as shown in Figure No. 1, were sinus tachycardia (79.16%) followed by normal QRS complex (75%), left ventricular hypertrophy (50%), LBBB 20.8% left axis deviation, atrial ectopics, ventricular ectopics, ST-T changes all being 16.6% each. Less frequent findings included RBBB, left atrial enlargement, supraventricular tachycardia and atrial fibrillation.

Chest radiographic profile of patients revealed Pulmonary Plethora in 54.16% of cases, Pleural Effusion in 16.6%. Cardiothoracic ratio between 50 and 60 was observed in 37.5% between 60 and 70 in 20.8% and >70 in 8.3% of cases. Table No. 2 shows echocardiographic profile. At presentation our patients showed ejection fraction between 30 and 39 in 62.5%, between 40 and 45 in 20.8% of cases, while EF of less than 30 was observed in 16.6% of cases. Other findings included LV dilatation in 79.16% with LVEDD between 5-5.9 cm seen in 41.6% of cases and >6 cm in 37.5% of cases. Mild-to-moderate Mitral Regurgitation was observed in 45.8% of cases, PAH in 41.6%, pericardial effusion in 12.5% and LV clot in 12.5% of cases. Echocardiographic parameters like EF, LVEDD, LVEF, PAH, MR showed significant improvement during follow-up evaluation among survivors of our study group.

From management point of view, all our patients required diuretics. Furosemide was administered to all (100%) the patients, while additional spironolactone was needed for 54.16% of patients. Inotropic support was required in 33.3% of cases, ACE inhibitors and β-Blockers in 75%, Digoxin in 45.83% and anticoagulation with warfarin was required in 20.8% of cases. Majority (66.66%) of our patients had normal delivery, while 16.67% of our patients had assisted vaginal delivery and rest of 16.67% underwent caesarean section.

The frequency of complications during hospital stay as observed in our study group was Pulmonary Oedema and requirement of ICU care in 45.83%, Cardiogenic shock in 33.3%, cardiopulmonary arrest in 25% of cases, while atrial fibrillation and pericardial effusion was seen in 12.5% of cases. Ventricular Tachycardia was observed in 8.3% cases. None of our patients had thromboembolic episode.

Association between survival and echocardiographic parameters like EF and LVEDD was analyzed as shown in Table No. 3. Patients with low EF and higher LVEDD had poor survival; 25% (6) of patients from our study group having mean EF of 29% and mean LVEDD of 6.4 cm expired during the first week of hospitalization; 62.5% (15) of our cases having mean EF of 52% and mean LVEDD of 4.6 cm had complete recovery, while remaining 12.5% of our cases were having mean EF of 43% and mean LVEDD of 4.9 cm, improved with residual heart failure.
While analysing in our study the association of outcome with the time of diagnosis and initiation of treatment, it was observed that all the 25% of cases in whom there was delay in diagnosing the PPCM by more than one week expired, while 75% of those patients who were diagnosed and treated early had better prognosis with zero mortality attributable to PPCM. Among survivors, 83.3% of patients had complete recovery and remaining 16.7% improved with residual heart failure as shown in Table No. 2.

### DISCUSSION
Peripartum cardiomyopathy is an uncommon form of congestive heart failure affecting women in the last months of pregnancy or early puerperium with potentially devastating consequences. Little is known about the incidence of PPCM. Available literature has reported varied incidence from different geographical locations. It is around 1 in 2500–4000 in the USA, 1 in 1000 in South Africa and 1 in 300 in Haiti, and about 1 in 1000 in South Asian Countries like Pakistan and India. In an another Indian study, the incidence of PPCM was reported as one case per 1374 live births. These differences could be attributed to the availability, accessibility of medical facilities and awareness regarding PPCM, different nutritional status, lack of proper reporting of cases and use of different diagnostic criteria. Our institution being a tertiary care referral centre receives cases from local population as well as from surrounding districts from the states of Karnataka and Maharashtra, making it difficult to predict the exact incidence due to number of unreported deliveries, especially from rural areas for these cases. We got only 24 cases from our hospital during our study period of one and a half years, where on an average 10000 deliveries occur annually. Using this number, the estimated incidence was 1 per 944 deliveries, which corresponded to reported incidence of 1 in 960 by Ibrahim Shah et al in 2012.

Common reported risk factors for PPCM are advanced maternal age, multiparity, multiple gestations, black race, obesity, malnutrition, gestational hypertension, pre-eclampsia, poor antenatal care, alcohol and tobacco abuse, low socioeconomic conditions and long-term tocolysis as found in various studies.

PPCM has been reported mostly in women older than 30 years. In our study the mean age noted was 29±5.46 years; 33.4% (8) of our patients were above thirty years of age, which was similar to the study group of Shah et al having mean age of 30.94±6.63 years, while that of Elkayam et al had mean age of 29±6.

Multiparity, described as an important risk factor for PPCM in various studies, showed incremental trend in the incidence with increase in parity. In studies done by Elkayam et al, parity ranged from 1 to 9 (Mean 1.9±1.5), while that of Shah et al had mean parity of 3.66±1.41. In our study too, parity ranged from 1 to 4 with mean parity being 2.12±0.95 and the incidence showed similar incremental correlation with parity.

Various studies observed Multiple Gestations to be associated with increased incidence of PPCM; however, our study group did not have any patient with multiple gestations. Ethnicity too influences the incidence, as reported incidence among African women is 1 in 1000 compared to 1 in 300 in Haiti. Since all the patients in our study were of Indian origin, hence a comparative study of incidence among various ethnic groups was not possible.

Pre-eclampsia and chronic hypertension have been associated with a significant number of PPCM cases in various studies. Our study showed an association of 16.6% (4) cases with pre-eclampsia and 8.3% (2) cases with hypertension. This difference in frequency of risk factors can be attributed to small sample size and other factors like race.

Long term tocolysis with oral salbutamol and terbutaline in women with preterm labour, especially if combined with antenatal steroid administration for foetal lung maturation as a risk factor for PPCM. A study done by Memon et al and Shareif et al reported the mean duration of delay in arriving at diagnosis to be from weeks to months in around 30% of cases. This difference in frequency of risk factors can be attributed to small sample size and other factors like race.

In our study too, delay of more than a week was observed in 25% (6) of cases. The delay may be attributed to its clinical picture that can be mistaken for other disorders, such as respiratory tract infections like pneumonia or asthma or other systemic illness like anaemia, heart failure, depression, etc. An echocardiogram should be considered in all women presenting with such symptoms and clinical findings, especially during peripartum period. Misinterpretation of the clinical picture, delay in diagnosis and
treatment of heart failure can have detrimental consequences. Observational data suggest that potential specific treatments are only effective if started early.\(^8\)

ECG is seldom normal in patients with PPCM. Most frequent ECG findings reported were Sinus Tachycardia (68.4%), Chamber Hypertrophy (78.8%) and T-Wave Inversion (47.3%).\(^24-26\) Tibazarwa et al found that 90% (n=70) of cases in their study group presented in sinus rhythm with tachycardia (Mean heart rate being 100±21 beats/min). They also observed that at baseline, at least one ECG abnormality/variant was detected in 96% of cases. Major ECG abnormalities and minor changes were detected in 49% and 62% of cases respectively; the most common being T-wave changes (59%), p-wave abnormality (29%) and QRS-axis deviation (25%).\(^27\) Shah et al found the frequency of Sinus Tachycardia to be 63.9%, while LV Hypertrophy and T-Wave Inversion were 68.9% and 45.9% respectively.\(^9\) In our study Sinus Tachycardia was observed in 79.16% cases, while LV Hypertrophy and T-Wave had a frequency of 50% and 16.6%, respectively.

The echocardiographic features frequently associated with PPCM are reduced Ejection Fraction, Chamber Dilatation, moderate-to-severe Mitral Regurgitation, Left Ventricular Thrombus and raised Pulmonary Artery Pressure.\(^24,27\) The study group of Shah et al had mean ejection fraction of 29.2±10.06 and it was universally reduced. Other echocardiographic findings included Chamber Dilatation in 78.7% (48), moderate-to-severe Mitral Regurgitation 24.6% (15) Left Ventricular Thrombus in 19.7% (12) and Pulmonary Artery Hypertension in 24.6% (15) of cases.\(^9\)

Lori A Blauwet et al did a follow up study in 176 patients and they found that with treatment Mean LV End Systolic Dimension (LVESD) decreased significantly from 51.3±7.6 mm to 42.3±9.5 mm, while mean LV Ejection Fraction (LVEF) increased significantly from 27.3±8.1% to 43.3±12.5%, as compared from baseline to at the end of 6 months. They also reported that 21% (30) of the 141 surviving patients had fully recovered LV function (LVEF ≥55%) at 6 months. They observed that the predictors of LV Recovery included Older Age, Decreased LV End Diastolic Dimension (LVEDD) and Decreased LV End Systolic Dimension (LVESD).\(^28\) In our study too, the mean EF was 35.08±5.34, mean LVESD 5.79±0.88, mean LVEDS 4.83±0.96 at baseline, which improved to EF of 52.1±5.92, LVESD 4.93±0.51, LVEDS 4.2±0.57. The other findings at presentation were LV clot in 12.5% (3) cases, PAH in 41.6% (10) patients and MR in 45.8% (11). During follow-up, at the end of six months only one patient had MR and 12.5% (3) patients had PAH. These findings which were in accordance with the studies quoted above,\(^8,27\) indicate that baseline EF, LVESD, LVEDD and PAH could be used as the predictors of prognosis in PPCM.

Various complications described in patients with PPCM include Pulmonary Oedema, Cardiogenic Shock, Thromboembolic Events, Ventricular Tachycardia, Cardiopulmonary Arrest and Atrial Fibrillation. The main complications reported by Shah et al in their study were Thromboembolism 21.3% (13), Cardiogenic Shock 13.1% (8) Atrial Fibrillation 13.1% (8), Ventricular Tachycardias 13.1% (8), Pulmonary Oedema 11.5% (7), Pericardial Effusion 8.2% (5) and Cardiopulmonary Arrest 8.2% (5).\(^9\) We in our study observed Pulmonary Oedema in 45.83% (11), requirement of ICU care in 45.83% (11) followed by Cardiogenic Shock in 33.3% (8) cases, Cardiopulmonary Arrest in 25% (6) cases, Atrial Fibrillation and Pericardial Effusion in 12.5% (3) cases, each. Ventricular Tachycardia was seen in 8.3% (2) cases. None of our patients had Thromboembolic event. All these complications were seen at first presentation.

Many studies have described the correlation of PPCM with the mode of delivery and neonatal outcome. In study by Hasan Jahan Ara et al, 68.75% of patients had normal Vaginal Delivery, 6.2% Assisted Vaginal Delivery and 31.6% Caesarean Section; however, the association between PPCM and mode of delivery remained inconclusive.\(^29\) In our study 66.6% of patients had normal Vaginal Delivery, 16.6% Assisted Vaginal Delivery and 16.6% required Caesarean Section mainly due to obstetric reasons, thus the correlation between PPCM and mode of delivery and fetal outcome in our study too remained inconclusive in our study too. The principles of managing a acute HF due to PPCM are no different than those applying to Acute HF arising from any other cause and are summarized in the recent ESC/ESICM guidelines.\(^28\)

Since reduced Ejection Fraction being one of the diagnostic criteria for PPCM, all such patients are expected to have varying degree of Heart Failure. In our study too, reduced EF was seen in all the patients, of which 45.83% (11) of patients needed Intensive Care treatment due to pulmonary oedema and 33.33% (8) needed due to cardiogenic shock, an observation similar to that of Shah et al 37.7% (23) patients required ICU care.\(^9\)

Prognosis, in women with PPCM, is related to left ventricular dysfunction at presentation and its recovery with normalization of left ventricular size and function. Recovery usually occurs in first 2 months, but at times it may take up to 6-12 months after delivery. In a pioneering study done by Demakis et al, approximately half of 27 women studied had persistent Left Ventricular Dysfunction with the Cardiac Mortality Rate of 85% over 5 years compared to the group in whom cardiac size returned to normal with no reported cardiac mortality in the same time interval.\(^16\) A more recent study by Sutton M.S. et al corroborates these results: 50% (7/14) of their patients had dramatic improvement soon after delivery, but 85.71% (6) of the remaining 50% (7) patients died. Survivors were found to have a Higher Mean Ejection Fraction (23% vs. 11%) and Smaller Mean Left Ventricular Cavity Size (5.8 vs. 6.9 cm) at diagnosis suggesting persistence of reduced cardiac function carries higher mortality.\(^30\) In our study group, all of the 25% of the patients having EF of <35% and LVEDD of >5.5 cms at the time of presentation died within first week of presentation. Among the remaining 18 cases, 83.3% of the patients had complete recovery. (Fig 3) Their mean baseline EF of 36.7% at diagnosis improved to 52.1%, while the mean baseline LVEDD of 5.7 was improved to 4.9 at the end of six months. The remaining 16.6% cases had varying degree of symptomatic residual heart failure. As the follow-up period in these patients was 6 months, long-term outcome could not be ascertained.
Family-planning counseling is very important as women with PPCM are usually in the middle of family building. Only a few studies have reported on subsequent pregnancies of women with a history of PPCM, 31-34 Elkayam et al studied 44 women with PPCM and a subsequent pregnancy and found that LVEF increased after the index pregnancy but decreased again during the subsequent pregnancy, irrespective of earlier values. Developments of HF symptoms were more frequent in the group, where LVEF had not normalized before the subsequent pregnancy (44 vs. 21%). In addition, three of the women with a persistently low LVEF entering the subsequent pregnancy died, whereas none with normalized LVEF died. There was no perinatal mortality. 31 In a retrospective study Habli et al compared 70 patients with PPCM, where 21 had a successful subsequent pregnancy, 16 terminated the pregnancy and the remaining 33 had no subsequent pregnancy. Ejection fraction at diagnosis was higher in those who had a successful subsequent pregnancy, but had no relation to worsening clinical symptoms, which developed in nearly one-third of those patients. 35 Due to limited study period and smaller study groups, no patients with recurrent pregnancy could be recruited in our study.

Limitations of the Study
- Small sample size.
- Time limited study, so the patients could not be followed for longer period.
- Effect of recurrent pregnancy could not be studied, as it was a time limited study.

CONCLUSION
Peripartum cardiomyopathy (PPCM) is a rare and potentially life-threatening, but treatable illness. Better understanding of its clinical profile may improve rate of early diagnosis and in turn may increase the positive outcome in such cases; hence, all women having clinical features suggestive of heart failure should be evaluated for PPCM using echocardiography and modern diagnostic tools applying appropriate criteria. Standard management of cardiac failure with a multidisciplinary approach started early carries better prognosis. Follow-up is equally essential during recovery and those with persistent ventricular dysfunction should be counselled for contraception and avoidance of future pregnancy.

REFERENCES