STUDY OF CLINICAL PROFILE, DISEASE COURSE AND OUTCOME OF PERIPARTUM CARDIOMYOPATHY: SINGLE CENTER STUDY
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ABSTRACT: OBJECTIVES: To study the clinical profile, course of disease and outcome of peripartum cardiomyopathy (PPCM). METHODS: A prospective study was conducted at Mahatma Gandhi Medical College and Hospital, Rajasthan, India from May 2012 to June 2014. 18 cases were included in the study. Data included age distribution, parity, symptoms and risk factors. Medical management and pregnancy outcome were documented. Serial echocardiography was done for a period of one year. RESULTS: In our study 8/18 (44%) were primigravidae, 3/18 (16%) had pre-eclampsia and 4/18 (22%) had co-existing hypertension, 7(38.89%) patients underwent Caesarean section and no complication happen during delivery in all. The difference in Echocardiography parameters observed between recovered and non-recovered patients was significant; Left Ventricular End diastolic dimension (5.0 cm vs 6.0 cm) Left ventricular Ejection fraction (28% vs 22%) and left ventricular fractional shortening (19% vs 12%). 14 out of 18 patients were followed up for a period of one year out of which 64% (9/14) patients recovered completely. There was no mortality and two patients waiting for cardiac transplant due to refractory symptoms. CONCLUSION: Majority were young primigravidae presenting postnatally. Pre-eclampsisa and hypertension were risk factors. ECHO parameters were reliable predictors of recovery. KEYWORDS: Peripartum Cardiomyopathy, Pregnancy, Heart Failure.

INTRODUCTION: Peripartum cardiomyopathy (PPCM) is a life threatening disease. No definition has been universally accepted, but European society of Cardiology Working Group, stressing that PPCM is a diagnosis of exclusion, has defined it as idiopathic cardiomyopathy presenting with heart failure secondary to left ventricular dysfunction occurring during the last month of pregnancy or within 5 months of delivery in previously healthy women.¹

Common causes of congestive heart failure in peripartum period are listed in table 1. Uncertainty exists about whether cases fulfill diagnostic criteria or whether the disorder represents a pre-existent cardiomyopathy that became apparent during pregnancy. Echocardiography is essential to establish the diagnosis. The precise incidence of PPCM is unknown but appears to be approximately 1 in 2500 to 1 in 4000 in US and around 1 in 300 in Haiti ¹. Known risk factors include multiparity, black race, older maternal age and preeclampsia.
Table 1: Causes of new or exacerbated heart failure in Peripartum Period.

PPCM.
Preexisting familial or idiopathic dilated cardiomyopathy.
HIV related cardiomyopathy.
Cocaine-induced heart disease.
Pre-existing valve disease.
Hypertensive heart disease.
Pregnancy associated myocardial infarction.
Pulmonary embolism.
Preeclampsia.
Tachycardia associated cardiomyopathy.

MATERIALS AND METHODS: A prospective study of PPCM was conducted at Mahatma Gandhi medical college and Hospital Rajasthan India between May 2012 to June 2014. A total of eighteen patients were indentified during the study period that fulfilled the inclusion criteria. PPCM definition criteria included: 1. Heart failure in the last month of pregnancy and up to five months postpartum. 2. Absence of other known causes of heart failure. 3. Left ventricular systolic dysfunction demonstrated by classic echocardiography criteria such as depressed shortening fraction (Less than 30%), ejection fraction (Less than 45%) and a left ventricular end diastolic dimension of more than 2.7 cm/m² of body surface area.

Clinical data, including age distribution, gestational age at presentation, parity, presenting symptoms and identifiable risk factors was collected. Other causes of heart failure were ruled out by detailed clinical examination, and investigations. ECHO equipment used was Philips HD11 (2D, M-mode and Doppler) and data was analyzed by proper software. ECHO parameters measured were LV end diastolic dimension, LV fraction shortening and LV ejection fraction.

Echocardiography was repeated at six months and one year by the same cardiologist. A multidisciplinary team of intensivists, obstetricians and cardiologists were involved in the management.

Management goals included preload optimization, after load reduction and increasing the cardiac contractility. In other respects, the treatment of PPCM is the same as for other forms of congestive heart failure except that ACE inhibitors and angiotensin receptor blocking agents are contraindicated in pregnancy.

This study was conducted in conformity with the ethical guidelines and approval of hospital Ethics Committee with respect to clinical care, informed consent of all patients, laboratory investigation, study protocol and even submission of manuscripts for publication.

RESULTS: Our study revealed that a majority were young primigravidae and were at a higher risk for developing PPCM, mean age being 22.06 yrs. Out of 18 patients 11(61.11%) underwent normal vaginal delivery and 7 (38.89%) underwent caesarean section, no complication happen during delivery of all. Mean Apgar score was 8 which was done in all newborn after one minute of delivery for assessment of neonatal wellbeing.
The initial occurrence of symptoms of heart failure was predominantly during the postpartum period 12/18 (66%) All of them had dyspnoea (100%) at presentation, followed by cough (33%) shock (22%) chest pain (11%), and haemoptysis (11%). According to NYHA (New York Heart association) 1/8 (05%) were in class II, 5/18 (27%), were in class III and 12/18 (66%) were in class IV. 14 cases were available for further follow up, all of whom underwent serial 2 D Echo at six months and one year interval. No patients expired and two patients were in waiting list of cardiac transplant in our center due to refractory symptoms. Mean LV end diastolic dimension (cm), Mean LV Ejection fraction (%) and Mean LV fractional shortening (%) at diagnosis, six months and one year were tabulated (table 3 & 4).

| Mean age (Yrs) | 22.6 |
| Mean parity | 1.5 |
| Mean time of presentation (Days postpartum) | 12.8 |
| Mean gestation (Weeks) | 36.4 |
| Primigravida | 8 |
| Average Apgar score | 8 |
| Mode of delivery | | |
| Normal | 11 |
| Caesarean section | 7 |
| Co-existing pre-eclampsia | 3 |
| Co-existing hypertension at diagnosis | 4 |
| NYHA | | |
| II | 1 |
| III | 5 |
| IV | 12 |

Table 2- Clinical data of 18 study patients

Table 3: Serial echocardiography record of study patients (14 patients):

| At Diagnosis | After 6 months | After1 year |
| Mean LV End diastolic dimension (cm) | 5.6 | 5.4 | 5.3 |
| Mean LV fractional shortening (%) 14.9 | 18.1 | 23.6 |
| Mean LV Ejection fraction (%) | 26.3 | 32 | 43 |

Echocardiography values of recovered and non-recovered patients were compared (table 4) using unpaired-T test with Welch correction.
Table 4: Comparison of serial echocardiography data for recovered and non-recovered study patients:

|                                | Recovered (9 Patients) | Non-recovered (5 Patients) | P Value |
|--------------------------------|------------------------|-----------------------------|---------|
| Mean LV End diastolic dimension (cm) | 5.04+0.24 (5.3-5.9)    | 6.06+0.13 (5.9-6.2)         | 0.0008  |
| Mean LV Ejection fractional (%)  | 28.7+1.90 (26-32)      | 22.4+1.51 (22-24)           | <0.0001 |
| Mean LV fractional shortening    | 19.5+1.58 (14-19)      | 12.4+1.30 (12-15)           | <0.0007 |

**At Diagnosis**

**After 6 months**

|                                | Recovered (9 Patients) | Non-recovered (5 Patients) | P Value |
|--------------------------------|------------------------|-----------------------------|---------|
| Mean LV End diastolic dimension (cm) | 5.2+0.075 (5.2-5.6)    | 5.94 +0.11 (5.8-6.1)        | <0.0001 |
| Mean LV Ejection fractional (%)  | 44.1+0.26 (45.8-46.4)  | 29.4 +0.26 (25-32)          | 0.0001  |
| Mean LV fractional shortening    | 20.6+2.66 (16-24)      | 16.8+0.83 (16-18)           | <0.0055 |

**After 1 year**

|                                | Recovered (9 Patients) | Non-recovered (5 Patients) | P Value |
|--------------------------------|------------------------|-----------------------------|---------|
| Mean LV End diastolic dimension (cm) | 4.01+0.13 (4.8-5.0)    | 5.86+0.13 (5.7-6.0)         | <0.0001 |
| Mean LV Ejection fractional (%)  | 52+0.91 (45-48)        | 32.6 +3.0 (29-37)           | <0.0004 |
| Mean LV fractional shortening    | 24.3 +1.99 (20-25)     | 20 + 1.58 (18-22)           | <0.0014 |

Prognosis based on 2D Echo at diagnosis; Echocardiography parameters in our study like LV size, ejection fraction and fractional shortening at diagnosis differed significantly between those who recovered and those who did not.

**DISCUSSION:** PPCM is a form of idiopathic primary myocardial disease associated with the pregnant state. The etiology and pathophysiology are poorly understood, but inflammation may play a role, because serum marker of inflammation (C-reactive protein, interferon-Y {IFN-Y} and interleukin-6) are elevated in many patients. Autoimmune processes, apoptosis, and endothelial dysfunction also play a role.

Recent studies suggest that PPCM is a vascular disease, with cardiac angiogenic imbalance and an excess of antiangiogenic signaling that is accentuated by preeclampsia. The placenta in late pregnancy secretes vascular endothelial growth factor (VEGF) inhibitors such as soluble Flt1 (sFlt1), and plasma levels of sFlt1 have been shown to be abnormally high in women with PPCM.

PPCM remains a diagnosis of exclusion. In contrary to published literature where increasing age and multiparty were considered as high risk factors for development of PPCM,3,4 our study revealed that a majority of patients were young primigravidae. Although our study failed to establish the reason for high prevalence in primigravidae, the Myo clinic study which was conducted over a period of 5 year hints that multiparity and increasing age are not as important risk factors as seen in western population5 and similarly another large study6 shown nearly similar large percentage of women with primigravidae.
PPCM in south Asian population may have preponderance towards a younger age group due to earlier age of marriage. Pre-eclampsia was seen in 16% of patients and co-existing hypertension was diagnosed at presentation in 22% patients.

A high index of suspicion is essential in detecting early signs of heart failure, thus aiding early recognition and intervention. Diagnosis of PPCM as previously mentioned, rests on the echocardiography identification of new left ventricular systolic dysfunction, depressed fractional shortening, and ejection fraction during a limited period surrounding parturition.\(^2\)

In our study, 2D Echo findings of recovered and non-recovered patients varied significantly at diagnosis (LVED 5.0 cm vs 6.06 cm, LVFS: 19% vs 12 %, LVEF: 28.7% vs 22.4%) and were statistically significant (P value <0.01). The above Echo parameters at six months and one year were also statistically significant. Echo remains the single best tool in prognosis; however prediction of recovery eludes Echo.

Medical therapy used was similar as in other forms of heart failure. Diuretics, vasodilators, digoxin, ACE inhibitors, inotropes formed the mainstay of treatment. Subsequently, after initial stabilization, β-blockers were added. All our patients required supplemental oxygen. Six of our patients required non-invasive ventilation while three patients were intubated and ventilated. Two patients required amiodarone, indication being atrial fibrillation with fast ventricular rate. LMWH (Low molecular weight heparin) was routinely used for DVT prophylaxis. Patients who did not recover or even those with mild LV dysfunction were continued with long term medical management including ACE inhibitors and diuretics. Three patients presented intra-natally and six patients were postnatal at the time of initial presentation.

We can summarise that the stress of delivery may play a significant role in unmasking probable underlying LV dysfunction. Eight patients had a vaginal delivery and caesarean section was done for obstetric indication only. Presence of PPCM or its severity has minimal effect on foetal outcome if timely obstetric care is in tandem with aggressive medical management. Prognosis for women with peripartum Cardiomyopathy depends on normalization of LV size and function within six months of delivery. Normalisation of ventricular function occurs in approx 23% to 54% of patient with PPCM,\(^6\) and appear to be more likely if the ejection fraction is greater than 30 % at the time of diagnosis. Recurrence of PPCM in next pregnancy is 30%.\(^7\) Such recurrence may result in significant clinical deterioration and even in death. Hence we strongly counseled our patients to avoid future pregnancies.

**CONCLUSION:** PPCM is a diagnosis of exclusion. Majority were young primiparae presenting postnatally. Pre-eclampsia and co-existing hypertension appears to be strong associations. Echo parameters were sensitive predictors of recovery. Aggressive medical and obstetric management is crucial for a good outcome. Future pregnancies are better avoided.

**Study Limitations:** Exact incidence of PPCM could not be determined in view of tertiary high-risk referral care centers, and the relatively small number of cases studied.
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