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CARDIOMYOPATHY COMPLICATING PREGNANCY. OUTCOME OF 25 CASES AND REVIEW OF LITERATURE.

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ABSTRACT

Background: Cardiomyopathy associated with pregnancy is very rare. It can be a peripartum cardiomyopathy or other varieties like dilated and hypertrophic cardiomyopathy which either develop during pregnancy or they were existent before pregnancy. Though the incidence is very low the mortality rates and morbidity associated with this condition is very high during pregnancy. **Material and methods:** Data of 25 cases of cardiomyopathy complicating pregnancy collected in a period of 2 year duration associated with pregnancy and reviewed for clinical profile, maternal and peinatal outcome, associated etiological factor, the management and course of the disease of the women were recorded. **Result:** Mean age of the patients was- 25.92±3.22year. Commonly associated conditions were hypertension (36%), anaemia (24%). Nineteen out of 25 cases were diagnosed to be peripartum cardiomyopathy (PPCM) and 6 cases were diagnosed to be dilated cardiomyopathy (DCMP). The left ventricular ejection fraction of the patients at the time of diagnosis/ at the time of admission was 31.33±8.11 (mean ± SD) and improved during hospital stay at the time of discharge up to (45%). Maternal mortality rate was 8%. **Conclusion**: This study tries to define the clinical profile, maternal and perinatal outcomes of the pregnant women with pre-existing and peripartum cardiomyopathy.

KEYWORDS: Cardiomyopathy associated with pregnancy is very rare.

INTRODUCTION

Cardiomayopathy is a disease of heart muscle and defined as "a heterogenous group of diseases of myocardium associated with mechanical and/ or electrical dysfunction that usually exhibit inappropriate ventricular hypertrophy or dilatation and are due to a variety of causes that frequently are genetic." Based on electrocardiographic findings cardiomyopathy can be classified into dilated, restrictive and hypertrophic variety.[1]

Dilated cardiomyopathy is characterised by enlarged left ventricle with decreased systolic function or left ventricular ejection fraction. It has multiple etiologies commonly- inflammatory myocarditis associated with viral (coxsackie, adeno), bacterial(diphtheria) and other infections, toxic effect of alcohol or chemotherapeutic agents (trastuzumab), nutritional deficiency like thiamine, selenium, carnitine etc, familial cardiac myopathy and many more. But the pathogenesis is common to all like when myocardial injury is acquired some myocytes may die and remaining myocytes undergo hypertrophy in response to increased wall stress. Local and circulating factors stimulate secondary response that contribute to progression of disease and diastolic dysfunction. Mitral regurgitation commonly develops and `finally heart failure develops.[1]

Peripartum cardiomyopathy (PPCM) definition as provided by the Heart Failure Association of the European Society of Cardiology Working group as "an idiopathic cardiomyopathy presenting with heart failure secondary to left ventricular systolic dysfunction towards the end of pregnancy or in the months following delivery, where no other cause of heart failure is found. It is a diagnosis of exclusion. The left ventricle may not be dilated but the ejection fraction is nearly always reduced below 45%.[2] PPCM occurs in previously healthy women in the final month of pregnancy and up to 5 months after delivery.[3] Though the incidence is less than 0.1% of pregnancies, morbidity and mortality rates are high(5-32%).[4] The echocardiographic status may return to normal or may progress to cardiac failure and even sudden cardiac death.[5] In severe cases women may require cardiac transplantation or die of heart failure, thromboembolic events or cardiac arrhythmias.[6]

Here in this study the authors have reviewed 25 cases of cardiomyopathy associated with pregnancy to find out the maternal and perinatal outcome in a tertiary hospital.

MATERIALS AND METHODS

This is an observational study conducted in the department of Obstetrics & Gynaecology of Maulana Azad Medical College and Lok Nayak Hospital in two year duration (from 1st Feb 2014 to 31st Jan 2016). All the pregnant women who were diagnosed to have cardiomyopathy were included in the study. Informed written consent was obtained from all the cases who were participated in the study. The history regarding the duration of symptoms, family history of heart failure/ myopathy/ sudden death, history of alcohol or chemotherapeutic drug use, number of diagnostic criterias for PPCM present at diagnosis were collected. The criteria for diagnosis of PPCM used was based on National Heart Lung and Blood institute and the Office of Rare Diseases of the National Institute of Health are- 1)Development of heart failure in the last month of pregnancy or within 5 months postpartum. 2) Absence of an identifiable cause of heart failure. 3)Absence of recognizable heart disease before the last month of pregnancy.4) Left ventricular systolic dysfunction demonstrated by left ventricle ejection fraction of less than 45%.[7] Their demographic profile, the clinical course in the hospital like duration of ICU/ HDU stay, pregnancy outcomes like gestational age at delivery, development of IUGR in fetus, mode of delivery, any complications during delivery, outcome of the newborn like AGA/SGA baby, APGAR score at 1 and 5 minutes and any associated complication were noted. All patients were managed conservatively till they delivered and recovered with clinical improvement and discharged with advice to attend cardiology clinic of GB Pant hospital associated to MAMC. All patients were initially kept in HDU and were shifted to ICU if their condition deteriorated or shifted to maternity ward if their condition improved and there is shortage of bed in the HDU. Almost all patients were discharged from the maternity ward.

All cases were followed up till they discharge from the hospital. The investigations done for all cases include a complete blood count, tests for coagulation abnormalities (PT, APTT etc), ECG, Echocardiography, chest X-ray, LFT, KFT, serum electrolytes. The management aimed at optimising cardiac function with cardiac drugs like- diuretics, diltiazem and metoprolol. They were planned for vaginal delivery and Caesarean section was performed only for obstetrics indication. Elective LSCS for compromised cardiac condition were performed in patients as advised by Cardiologist. Other treatment were based on symptoms. Maternal outcome like mode of delivery, number of days of ICU/HDU stay, any complication were noted. Perinatal outcomes include live or still birth, complications like intrauterine growth restriction, birth asphyxia, etc were also noted.

RESULTS

Twenty five women out of 20,496 deliveries during the study period were found to have cardiomyopathy associated with pregnancy. The frequency being 1.2 cases per 1000 deliveries. Table-1 depicts the demographic characteristics of all the cases with cardiomyopathy associated with pregnancy. Maximum number of patients were between 25-30 yr age group (60%), 24%were <25years of age group &16%were of 30-35yr age group. Mean age of the patients were- 25.92±3.22year. Most of the patients were multigravida (72%). Most of the patients under study (80%) were from urban area. Most of the patients were from lower (80%) socioeconomic status & lower middle class were 20%. Maximum number of patients (60%) were diagnosed to have cardiomyopathy after 34 weeks of gestation. Six cases had diagnosed before 34 weeks of gestational age. One case had diagnosis of cardiomyopathy one year before pregnancy. Three cases had diagnosed cardiomyopathy in the postpartum period. These three cases had irregular antenatal visits outside this hospital but never diagnosed to have cardiomyopathy prior.

Table-2 depicts the maternal characteristics and outcome of all 25 cases diagnosed with cardiomyopathy during pregnancy. Nineteen (76%) cases were diagnosed to have peripartum cardiomyopathy, 6 cases had dilated cardiomyopathy. One out of six cases of dilated cardiomyopathy was diagnosed 1 year before pregnancy. There were no cases of Hypertrophic cardiomyopathy. Most of the cases (80%) have delivered at term gestation and 64% had vaginal delivery. Remaining 36% of cases had undergone Caesarean section, 5 cases had elective CS as per cardiologist opinion regarding cardiac status of the patient to sustain the labour pain and 4 cases had emergency CS due to obstetric complication during labour. Most of the cases (64%) had NYHA class 2/3 and 36% cases had diagnosed to have NYHA 4. Six cases required ICU stay because of their poor cardiac status and following elective caesarean section for recovery from anaesthesia and the mean±SD of ICU stay of those patients were 1.8±1.3 days. All cases stayed in HDU, 13 cases required <7days of HDU stay, 9 cases required 1-4 weeks of HDU stay and 3 cases required >4 weeks of HDU stay. Twenty three cases (92%) had no maternal complication during delivery or till discharge. Nine cases required 2 cardiac drugs, 9 cases required 3 cardiac drugs and 7 cases required 4 cardiac drugs. Seven cases had Post Partum complication, one case had heart failure and 6 cases had sudden breathlessness following delivery. Three cases had postpartum hospital stay of less than 7 days and 4 cases had to stay more than 14 days postpartum in the hospital, other cases were discharged between 7-14 days. Those cases who had developed complications required hospital stay of more number of days. There were 2 cases of maternal death. One case had death before delivery at 29 weeks of gestation and the other had died on 4th day of delivery by LSCS due to sudden heart failure.

Table-3 depicts perinatal outcome of all the cases. Ninty two percent of babies had APGAR score of 9 at 0 min and at 5 min of birth. Nine cases had premature babies.

All of the premature babies were of mothers with hypertensive disorder. Two cases had intrauterine death of the fetus associated with severe preeclampsia and they had delivered macerated stillbirth babies. Two cases had intrauterine growth restriction associated with hypertensive disorder and 1 baby had developed birth asphyxia.

TABLE 1: Demographic characteristics of the cases of cardiomyopathy complicating pregnancy.

S.NO.	Characterstic	Number	Percentage
1.	Age(years)		
	• <25y	6	24
	• 25-30	15	60
	• 30-35 • Mean±SD-25.92±3.22	4	16
2.	Gravida		
	• Primi	7	28
	• Multi	18	72
3.	Parity		
	• 1-4	17	68
	• >4	1	4
4.	Gestational age at admission		
	• <34	7	28
	• 34-37	9	36
	• >37	6	24
	• Postpartum	3	12
5.	Diagnosis		
	• Prior to pregnancy	1	4
	• Present pregnancy(GA) • GA at diagnosis • <34 • 34-37 • >37 • Mean±SD=34.95±4.88	21 6 9 6	84 24 36 24
	Postpartum	3	12
6.	Socioecconomic status		
	Lower	20	80
	Lower middle	5	20

Table 2: Maternal characterstics

S.NO.	Parameters	Number	Percentage(%)
1.	Type of disease		
	• PPCM	19	76
	• DCMP	6	24
	• HOCM	0	0
2.	Associated disease		
	• RHD	1	4
	• Hypertension	9	36
	• Pulmonary edema	3	12
	• Multiple pregnancy	2	8
	• GDM/hypothyroid	0/1	0/4
	• Anemia	6	24
3.	Diagnostic criteria		
	• EF(≤45%) • <25 • 25-35 • 35-45 • Mean±SD=31.33±8.11	25 2 14 9	100 8 56 36
	• With Heart failure	9	36

4.	NYHA		
	• I	0	0
	• II	8	32
	• III	8	32
	• IV	9	36
5.	Gestational Age in weeks		
	• Preterm	5	20
	• Term	20	80
6.	Mode of delivery		
	• NVD	14	56
	• Instrumental delivery	2	8
	• Elective LSCS	5	20
	• Emergency LSCS	4	16
7.	Postpartum complication		
	• Sudden breathlessness	6	24
	• Heart failure	1	4
8.	Number of patient had		
	ICU Stay(days) Mean±SD=1.8±1.3	6	24
9.	HDU Stay • <1 week • 1-4week • >4week	25 13 9 3	100 52 36 12
10.	Maternal death	2	8
11.	Postnatal day on discharge • <7days • 7-14 days • >14days	 3 18 4	 12 72 16
12.	no. of cardiac drugs used • 2 • 3 • 4	 9 9 7	 36 36 28

Table 3: Perinatal Outcome of all 25 cases with cardiomyopathy complicating pregnancy.

S.NO	Fetal/neonatal Parameter	Number	Percentage
1.	Maturity		
	• Preterm	9	36
	• Term	16	64
	• Postdated	0	0
2.	Fetal growth		
	• SGA	0	0
	• AGA	20	80
	• IUGR	5	20
3.	Apgar-9/10		
	• 0	23	92
	• 5 min	23	92
4.	Complication		
	• Birth asphyxia	2	8
	• Specific	1	4
	• Mortality/IUD	2	8

DISCUSSION

PPCM develops during the last trimester or within the first 6 month postpartum. The frequencies being 1:2000 and 1:15000 deliveries.[1] From the literature the incidence of PPCM is reported as 1 in 1374 live births from a tertiary referral hospital from South India, 1 in 837 in a study from Pakistan and 34 per 1,00,000 live births in a hospital from Malaysia,1:2000-4000 live births in USA, i:1000 live births in Africa and 1:300 in Haiti.[8,9,10,11] In the present study the frequency of

cardiomyopathy complicating pregnancy is very high 1.2:1000 deliveries/1:800 deliveries and PPCM frequency being 0.09/1000 deliveries or 1:900 deliveries. This is due to availability of Cardiologist service in the associated GB Pant Hospital and the antenatal cases being referred here. The risk factors associated with PPCM are increased maternal age, increased parity, twin pregnancy, malnutrition, use of tocolytic therapy for premature labour and preeclampsia and eclampsia of pregnancy.[1] In the present study the most common association was hypertension or anaemia with cardiomyopathy.

Heart failure early after delivery was previously common in Nigeria due to their customs of salt ingestion and immobilisation of new mothers. On myocardial biopsy of PPCM patients are found to have lymphocytic myocarditis. This inflammation could be due to increased succeptibility to viral myocarditis or an autoimmune myocarditis due to cross reactivity of anti-uterine antibodies against cardiac muscle. Another proposed mechanism invokes an abnormal prolactin cleavage fragment, which is induced by oxidative stress and may trigger myocardial apoptosis; this observation has lead to investigation of Bromocriptin as possible therapy. Recent investigation shows PPCM has been found to be associated with antiangiogenic signalling as seen triggered in cases of preeclampsia. In animal model of this disease proangiogenic therapies has proven curative. It is crucial to the diagnosis of PPCM that there be no evidence of pre-existing cardiac disorder as the increased circulatory demand of pregnancy can aggravate other cardiac disease that was clinically unrecognised. Heart failure presenting earlier in pregnancy has been termed pregnancy associated cardiomyopathy (PACM). Both PACM and PPCM have been found in some families with other presentations of dilated cardiomyopathy, in some cases with known sarcomeric protein mutation. Pregnancy may represent environmental trigger for accelerated phenotypic expression of genetic cardiomyopathy.[1]

Demakis et al published the 1st case series of patients with PPCM. They described 27 cases presented in late pregnancy or early puerperium with heart failure.[7] Nowadays more and more researches being conducted but a little is known about the pathophysiology, epidemiology, diagnosis and clinical outcome of disease.

Clinical features of PPCM are palpitations, fatigue, shortness of breath, cough and paroxysmal nocturnal dyspnoea or orthopnoea, less common are- precordial pain and postural hypotension in third trimester or early puerperium.[11,12] In a prospective follow up study Mishra et al found 62.5% of the patients presented in postpartum period but in another follow up study in Turkey found 72.7% of the patients in postpartum period.[13] In the present study 12% of the cases were diagnosed in the postpartum period. Clinical signs of PPCM include pedal edema, pulmonary rales, raised jugular venous pressure, hepatomegaly, regurgitant murmurs and gallop rhythm etc depending on severity of disease. Diagnosis is always by exclusion of other causes of heart failure. Rare features may be peripheral or pulmonary embolic episodes or cardiac arrest. On Echocardiography findings include a dilated left ventricle, increase in left ventricular diameter and an ejection fraction less than 45%. An ejection fraction of less than 27% in Echocardiography predict poor long term prognosis in these patients.[14] Cardiac MRI may provide more accurate measurement of cardiac dimensions and functions and can be used to take guided myocardial biopsy.[15]

Treatment of cardiomyopathy during pregnancy is mainly standard heart failure treatment until the EF recovers. Most commonly used drugs are Angiotensin converting enzyme inhibitors (contraindicated during pregnancy), beta blockers and diuretics. Salt restricted diet and avoidance of nonsteroidal anti-inflammatory should be advised to the patients. Some patients may require cardiac resynchronisation therapy, internal defibrillators, or cardiac transplantation. Once the systolic function normalises drugs can be discontinued.[16] As these patients are at risk of thromboembolic event heparin during antepartm period and warfarin during postpartum period, anticoagulation may be required for prevention of morbidity and mortality from thromboembolism.[17] Progressive systolic dysfunction or sudden cardiac death or fatal thromboembolic events may lead to mortality.[17] Patients with persistent LV dysfunction are advised to avoid further pregnancy due to high recurrence rates.[18]

Patient with heart failure will require ICCU management, with monitoring of arterial blood pressure (ABP), central venous pressure (CVP). Coordinated management with cardiologist should be done. Digoxin (inotropic and rate reducing effect), loop diuretic (reduce preload) and drugs that affect after load such as hydralazine and nitrate are the drugs commonly used. These drugs are relatively safe in pregnancy and lactation but caution should be taken regarding volume depletion which may result into dehydration causing uterine hypoperfusion and fetal distress. During postpartum period the treatment of PPCM is also same as that for nonpregnant women with dilated cardiomyopathy. Diuretics given for symptomatic relief, spironolactone or digoxin is used in patients who have NYHA class III or IV symptoms. The dose of spironolactone is 25mg/day after dosing of other drugs is maximised. Digoxin therapy should be lowest to obtain a detectable serum digoxin level, which should be kept at less than 1.0ng/ml. Betablockers like carvedilol (25mg twice a day) and metoprolol (100mg once a day)are used as they improve symptoms, ejection fraction and survival. Ventricular arrhythmia associated with cardiomyopathy can be treated with quinidine and procainamide or betablockers may be considered. For atrial arrhythmia digoxin is considered.[19] For ventricular tachycardia Amiodarone 200-400mg 6hrly

used if patient is hemodynamically stable and unstable patients may require defibrillators. Pentoxyfyline & bromocriptin, intravenous immunoglobulin and plasmapheresis found to improves left ventricular function in patients with idiopathic dilated cardiomyopathy. Other drugs can be used are calcium antagonist, statins, monoclonal antibodies and interferon beta.[20-23] Severe Heart failure not responding to any treatment may require cardiac transplantation.[24] Compensated patients may undergo vaginal delivery with appropriate monitoring. Patients with significant hemodynamic compromise, elective caesarean with invasive hemodynamic monitoring of the mother should be considered. Controlled epidural anaesthesia is preffered.[25]

CONCLUSION

Cardiomyopathy associated with pregnancy is a rare but challenging situation because of the risk of morbidity and mortality. In this study it appears to be high incidence of cardiomyopathy and PPCM due to the hospital being tertiary referral centre and presence of associated super speciality hospital with cardiology department. The outcome of the patients was fairly good with 8% maternal mortality.

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REFERENCES

1. Lakadwala NK, Stevention LW, Loscalzo J, cardiomyopathy and myocarditis in Harrison's Principle of Internal Medicine. 19th edn.Editors-Kasper DL, Fauci AS, Hauser SL, Longo DL, Jameson JL, Loscalzo J. McGraw Hill. New york, 2015; 287: 1562.
2. Sliwa K, Hilfiker-Kleiner D, Petrie MC, Mebazaa A, Pieske B, Buchmann E, *et al*. Current state of knowledge on aetiology, diagnosis, management, and therapy of peripartum cardiomyopathy: A position statement from the Heart Failure Association of the European Society of Cardiology Working Group on peripartum cardiomyopathy. Eur J Heart Fail, 2010; 12: 767-8.
3. Hibbard JU, Lindheimer M, Lang RM. A modified definition for peripartum cardiomyopathy and prognosis based on echocardiography. Obstet Gynecol. 1999; 4(2): 311–5.
4. Tidswell M. Peripartum cardiomyopathy. Crit Care Clin. 2004; 20: 777–8.
5. Pearson G, Veille J, Rahimtoola S, Hsia J, Oakley CM, Hosenpud JD et al. Peripartum cardiomyopathy: National Heart, Lung and Blood Institute and Office of Rare Diseases (National Institutes of Health) workshop recommendations and review. JAMA. 2000; 283(9): 1183–8.
6. Elkayam U, Tummala PP, Rao K, et al. Maternal and fetal out-comes of subsequent pregnancies in women with peripartum cardiomyopathy. N Engl J Med. 2001; 344(21): 1567–71.
7. Demakis JG, Rahimtoola SH, Sutton GC, Meadows WR, Szanto PB, Tobin JR et al. Natural course of peripartum cardiomyopathy. Circulation. 1971; 44: 1053-61.
8. Pandit V, Shetty S, Kumar A, Sagir A. Incidence and outcome of peripartum cardiomyopathy from a tertiary hospital in South India. Trop Doct, 2009; 39: 168-9.
9. Hasan JA, Qureshi A, Ramejo BB, Kamran A. Peripartum Cardiomyopathy characteristic and outcome in a tertiary care hospital. J Pak Med Assoc, 2010; 60: 377-80.
10. Chee KH, Azman W. Prevalence and outcome of peripartum cardiomyopathy in Malaysia. Int J Clin Pract, 2009; 63: 722-5.
11. Pyatt JR, Dubey G. Peripartum cardiomyopathy. Current understanding, comprehensive management review and new developments. Postgrad Med J, 2011; 87: 34-9.
12. Mishra TK, Ewain S, Routray SN. Peripartum cardiomyopathy Int J Gynecol Obstet, 2006; 95: 104-9.
13. Duran N, Gunes H, Duran I, Biteker M, Ozkan M. Predictors of prognosis in patients with peripartum cardiomyopathy. Int J Gynecol Obstet, 2008; 101: 137-40.
14. Ibebuogu UN, Thornton JW, Reed GL. An unusual case of peripartum cardiomyopathy manifesting with multiple thromboembolic phenomena. Thromb J, 2007; 5: 18.
15. Mouquet F, Lions C, De Groote P, Bouabdallaoui N, Willoteaux S, Dagorn J, et al. Characterisation of Peripartum Cardiomyopathy by cardiac Magnetic Resonance Imaging. Eur Radiol, 2008; 18: 2765-9.
16. Amos AM, Jaber WA, Russel SD. Improved outcomes in peripartum cardiomyopathy with contemporary. American Heart Journal, 2006; 152(3): 509-13.
17. Elkayam U, Akhter M W, Singh H et al. Pregnancy-associated cardiomyopathy: clinical characteristics and a comparison between early and late presentation. Circulation, 2005; 111(16): 2050-55.
18. Silwa K, Forster O, Zhanje F, Candy G, Kachope J, Essop R. Outcome of subsequent pregnancy in patients with documented cardiomyopathy. American Journal of Cardiology. 2004; 93(11): 1441-3.
19. Ray P, Murphy GJ, Shutt LE; Recognition and management of maternal cardiac disease in pregnancy. Br J Anesth, 2004; 93: 428-39.
20. Silwa K, Skudicky D, Candy G et al; The addition of pentoxyfiline to conventional therapy improves outcome in patients with peripartum cardiomyopathy. Eur J Heart Fail, 2002; 4: 305-9.
21. Jahns BG, Stein W, Hilfuker-Kleiner D et al, Peripartum cardiomyopathy a new treatment option

by inhibition of prolactin secretion. Am J Obstet Gynecol, 2008; 199: 5-6.
22. de Jong JS, Reitveld K, van Lochem LT et al; Rapid left ventricular recovery after cabergoline treatment in a patient with peripartum cardiomyopathy. Eur J Heart Fail, 2009; 11: 220-2.
23. Bozkurt B, Villaneuva FS, Halubkoy R et al; Intravenous immunoglobulin in the therapy of peripartum cardiomyopathy J Am Coll Cardiol, 1999; 34: 177-80.
24. Peter R, Rickenbacher MD; long term outcome after heart transplantation for peripartum cardiomyopathy. Am Heart J, 1994; 127: 1318-23.
25. Witlin AG, Mabie WC, Sibai BM. Peripartum cardiomyopathy; an ominous diagnosis. Am J Obstet Gynecol, 1997; 176: 182-8.