**Introduction:**
Peripartum cardiomyopathy (PPCM) is an idiopathic form of cardiomyopathy where heart failure (HF) occurs due to impairment of left ventricular (LV) systolic function toward the end of the pregnancy or during the post-partum period in the absence of preexisting heart disease. The European Society of Cardiology (ESC) Working Group on PPCM has set the diagnostic criteria.\(^1\) In presence of heart failure, LV ejection fraction should be less than 45% but LV may not be overtly dilated.\(^2\) Though right ventricular dysfunction is not included in the diagnostic criteria but its presence denotes poor prognosis.\(^3\) It is a cause of significant mortality & morbidity among young woman throughout the world.

**Epidemiology:**
The exact incidence & prevalence of PPCM is unknown. It varies widely across different part of the world with highest incidence in north-south gradient, ranging from about one per 300 in Haiti, one per 1000 live births in South Africa and up to one per 3000 live births in the US and Western Europe.\(^4,5\) Genetic and environmental factors, lack of uniformity in diagnostic criteria, cultural and puerperal practices may be responsible for these heterogeneity and its incidence is increasing over time reflecting growing awareness about this fatal entity.\(^1,4,5\)

There is no data regarding the incidence of PPCM in Bangladesh.

**Pathogenesis and contributing factors**
The pathophysiology of PPCM is yet to be clarified. Though there are some attractive hypotheses but none is proven as single etiology. The identifiable contributing factors are black ethnicity, advanced maternal age, obesity, multifetal pregnancy, prolonged use of tocolytics and history of hypertensive disorders of pregnancy.\(^6\) Oxidative stress–prolactin axis hypotheses, angiogenic imbalance, viral myocarditis, abnormal response to hemodynamic stress of pregnancy, immune mediated injury, genetic predisposition, micronutrient deficiency are some probable pathophysiologic mechanism.\(^7-13\)

Oxidative stress–prolactin axis hypothesis suggests oxidative stress activates lysosomal enzyme, cathepsin D that in turn cleaves serum prolactin into its antiangiogenic and proapoptotic 16-kDa prolactin sub fragment.\(^10\) This subunit may cause microvascular dysfunction and cardiac injury.

**Diagnosis**

**Clinical presentation**
It’s a diagnosis of exclusion & high index of clinical suspicion is required. Symptoms of PPCM (dyspnea, orthopnea, oedema, palpitations) mimick symptoms of normal pregnancy so late presentation with complications like ventricular arrhythmias, venous or arterial emboli are not infrequent.\(^14\) Approximately 75%
of cases are diagnosed within the first month after delivery, and 45% occur in the first week. Physical examination may reveal signs of heart failure, including tachycardia, hypotension, elevated jugular venous pulsation, peripheral edema, and pulmonary crackles. Signs of LV dilatation like displaced apical impulse, third heart sound may be found but not invariably present.

ECG
Usually show sinus tachycardia with nonspecific changes. Bundle branch block, T-wave changes (59%), P-wave abnormality (29%), QRS-axis deviation (25%) were found in a case series.

Echocardiography
It is the single most important tool to diagnose PPCM, exclude the differentials, and find out the complications like embolism and pericardial effusion. It usually demonstrates global hypokinesia of LV with impairment of systolic function(LVEF<45%). LV dilatation is not obligatory. Diastolic dysfunction of LV may also predominate sometimes. Right ventricle is frequently affected though its not included in the diagnostic criteria. Functional regurgitation involving mitral and tricuspid valve may be found along with pulmonary hypertension. New echocardiographic modalities like speckle tracking is yet to be validated in PPCM.

Chest X ray
Features of vascular redistribution, cardiomegaly and pleural effusion are usually found.

Biomarkers
B type natriuretic peptide are increased in acute stage which reflects increased end diastolic pressure

Novel biomarkers
Few potential novel biomarkers that need to be validated in near future are combination of cathepsin D, miR-146a, ratio VEGF/sFlt1 and serum asymmetric dimethylarginine (ADMA), a marker of endothelial dysfunction.

Cardiac magnetic resonance imaging (MRI)
CMRI can exclude other form of cardiomyopathy and detect LV volumes and function more precisely but can not predict LV function recovery. Whether PPCM is characterized by a specific late gadolinium enhancement (LGE) pattern predictive of recovery is still debated.

Endomyocardial biopsy
Endomyocardial biopsy is not currently recommended in diagnosis and prognosis assessment of PPCM.

Differential Diagnoses
As it is a diagnosis of exclusion so more common cause of heart failure like rheumatic heart disease, myocarditis, dilated cardiomyopathy from other cause, coronary artery disease must be excluded prior to making diagnosis.

Management
Acute phase
Treatment is focused on controlling volume status, counteracting maladaptive neurohormonal response and preventing complications like thromboembolism and arrhythmias. In case of congested patients salt and fluid should be restricted. Judicious use of diuretics should be ensured during pregnancy as there is risk of placental hypoperfusion. If systolic blood pressure allows then intravenous vasodilators like hydralazine and nitroglycerine can be considered. Angiotensin converting enzyme inhibitors and angiotensin receptors blockers should be avoided during pregnancy due to fetotoxicity. Enalapril, captopril and benazepril are preferred during breastfeeding. Beta blockers preferably metoprolol can be used throughout the entire period after stabilization of acute heart failure. In our center, digoxin is being used along with standard treatment with reasonably good outcome.

In case of low cardiac output syndrome, inotropes like drotamine and levosimendan can be used. If the patient does not response to the medical management then mechanical circulatory support in the form of intra-aortic balloon counterpulsation (IABP) is instituted. In case of multiorgan dysfunction syndrome and non responder to IABP is managed with ECMO as a bridge to recovery, to LV assist device (LVAD) implantation or to heart transplantation.

Patient should be anticoagulated and continued for at least two months postpartum, if LVEF<35% or other indications for anticoagulations are present. Vitamin K antagonists (VKAs) are contraindicated in first trimester if the dose exceeds 5mg per day. Heparin and unfractionated heparin are safe in all trimester , and the former is preferred near term because of its shorter half-life.

Targeted therapy
Bromocriptine, an ergot alkaloid and dopamine D2-receptor antagonist has emerged as a potential useful treatment for PPCM. Due to lack of consistent results in the trials and risk of thromboembolic complications
like cerebral ischaemia and myocardial infarction its routine use is currently limited.\textsuperscript{23}

Immunomodulation by pentoxifylline and intravenous immunoglobulin have failed to offer any benefit.\textsuperscript{24,16}

**Long term management**
As clinical course is variable and LVEF recovery may take up to six months in the majority of patients invasive therapies (cardiac resynchronization therapy and/or intracardiac defibrillator (ICD) implantation) may be wisely postponed for up to six months.\textsuperscript{1} However, in case of increased risk of sudden cardiac death, subcutaneous ICD or wearable external defibrillator may be considered immediately.\textsuperscript{25}

In advanced and refractory HF or in whom LVAD weaning fails, heart transplantation is the only therapeutic option though the prognosis is variable.\textsuperscript{1}

**Treatment duration**
There is no general agreement, for how long the treatment should be continued. ESC working group on PPCM has advocated to continue ACE inhibitors and beta blockers for at least one year but decision should be individualized based on clinical and echocardiographic recovery.\textsuperscript{1}

**Obstetric management**

**Delivery**
There is no data available to support optimum timing and mode of delivery and decision should be taken by a team consisting of cardiologists and obstetricians. Strategy and timing depend upon hemodynamic status of mother, fetal maturity and obstetrical factors.\textsuperscript{26} In case of hemodynamic instability, urgent delivery should be targeted preferably by C section, irrespective of gestational age.\textsuperscript{26} Vaginal delivery is preferred in stable cases as it is associated with less blood loss, less thromboembolic and infectious complications.\textsuperscript{1}

Pain control
Epidural analgesia is preferred.\textsuperscript{1}

**Breast Feeding**
Though breast feeding avoidance may be theoretically beneficial according to oxidative stress-prolactin axis hypothesis but it is not evidence based. Rather recovery rate is higher in lactating mother challenging this hypothesis.\textsuperscript{27}

**Subsequent pregnancies**
Recurrence risk of PPCM depends upon extent of LV recovery. Patients with full recovery (LVEF>55%) have 17% chance of recurrent failure whereas who recover incompletely (LVEF<55%) have 46.2% risk of heart failure in subsequent pregnancies.\textsuperscript{28} So, family planning counselling is of paramount importance. Dobutamine stress echocardiography can be used to risk stratify women with subnormal LVEF.\textsuperscript{29}

**Predictors of recovery and prognosis**
Improvement of LVEF>50% at six months is defined as recovery from PPCM.\textsuperscript{1} In BSMMU, 72% patients improved clinically, 15% developed persistent cardiomyopathy, 14% had thromboembolic events and 13% died.\textsuperscript{30}

LVEF and LV dimensions are the best predictors of recovery.\textsuperscript{16} Lower level of plasma troponin and brain natriuretic peptide, diagnosis made after delivery, breast feeding, non-African ethnicity favorably affect the outcome.\textsuperscript{16,27}

**Conclusion:**
High index of clinical suspicion is required to diagnose this potentially dangerous syndrome. Significant progresses have been made regarding the pathogenesis over the last few years but this attractive hypotheses should be translated into treatment benefit. Further studies are required regarding safety and efficacy of bromocriptine prior to its routine use. Though the chance of recovery is high but chance of relapse is also not less in subsequent pregnancies.

**References:**