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Peripartum Cardiomyopathy: It is Possible to Make a Prenatal Diagnosis

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About the Study

Earlier diagnosis of peripartum cardiomyopathy (PPCM) can identify systolic dysfunction in a less severe stage. I urge all providers of medical care to peripartum subjects and all peripartum subjects to become aware of the potential for pregnancy-associated heart failure to develop as well as the possibility of making an earlier diagnosis. Steps in this direction include adding blood tests available to assist with earlier diagnosis of PPCM [serum NT-ProBNP and potentially serum fms-like tyrosine kinase (sFLT-1) or soluble vascular endothelial growth factor receptor-1 to placental growth factor (PlGF) ratio]. In addition, the simple, no cost "Self-Test" for recognizing pregnancy-associated heart failure can be included in routine obstetrical care. Together, they have the potential to help victims of PPCM experience earlier diagnosis with better preserved heart function; and then to reach full recovery using effective evidence-based available treatment, saving many lives of mothers and their unborn or newborn children.

Peripartum cardiomyopathy (PPCM) or pregnancy-associated cardiomyopathy (PAC) is one of the leading causes of maternal mortality occurring with variable incidence all over the world and this is an appeal to obstetricians, midwives, birthing center workers, medical care providers and indeed to all women themselves experiencing pregnancy. Your help is urgently needed [1-7].

My experience in researching PPCM over the past quarter-century and my privilege to be a part of the North American Investigations of Pregnancy-Associated Cardiomyopathy (IPAC) convince me that one of the greatest needs is to make the diagnosis of PPCM at earlier stages because to recognize the process early can identify the developing heart failure even before there is severe deterioration of left ventricular ejection fraction (LVEF) [1]. With that early diagnosis the current "evidence based" treatment will bring full recovery to all or almost all.

We learned a great deal about how to detect pregnancy-associated heart failure earlier by monitoring post-PPCM pregnancies. Evidence from those subjects who had already experienced PPCM led to increased monitoring to help detect relapse earlier. Now, we know this increased monitoring can help to make a prenatal diagnosis of PPCM a reality [7,8].

Recovery rates at 12 months postpartum are significantly higher when a diagnosis of PPCM is made with LVEF above 35% compared to those with a diagnosis with LVEF below that level [1]. In fact, an earlier diagnosis of PPCM is possible—many times even before delivery. The cardiomyopathy process starts much earlier in pregnancy; but so often the diagnosis is not made until time of delivery or postpartum. Here are some suggested steps that can be taken in the direction of earlier detection:

It is now possible to do blood testing during pregnancy to help identify developing PPCM earlier. An established blood test that merits consideration is serum B-type Natriuretic Peptide (BNP), which frequently rises before any deterioration of LVEF [8]. I also hypothesize that soluble FLT-1 will rise significantly, as well as the ratio sFLT-1 to Placental Growth Factor (PlGF) [Figure 1].

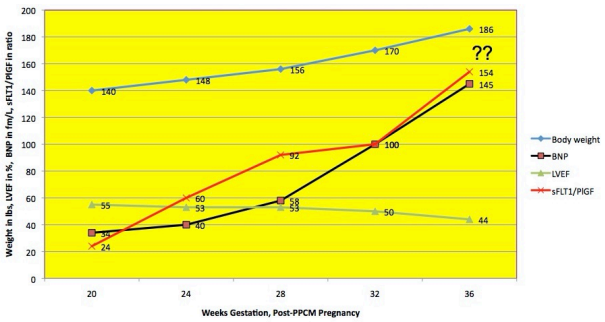
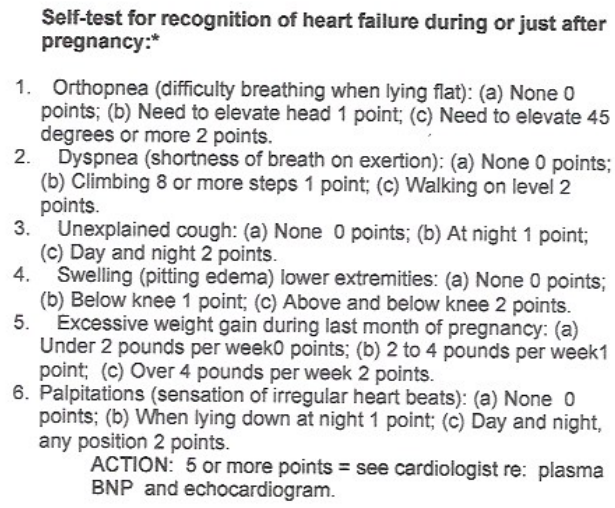


Figure 1: Ratio of sFLT-1 to Placental Growth Factor.

Proposal: Monitoring serum B-type Natriuretic Peptide (BNP), soluble FLT-1 (sFLT-1) and ratio of serum sFLT-1 to Placental Growth Factor (PlGF) during pregnancy; and especially post-PPCM pregnancies. (Hypothesis: In PPCM, just as demonstrated in preeclampsia, the ratio of sFLT-1 to PlGF will be higher and rise significantly as pregnancy progresses) :

These tests show the pathway to a prenatal diagnosis of PPCM, something at one time considered impossible to do.

The "Self-Test" as a screening tool has been documented as valid in helping to identify heart failure [9,10] [Figure 2].



Self-test for recognition of heart failure during or just after pregnancy:*

1. Orthopnea (difficulty breathing when lying flat): (a) None 0 points; (b) Need to elevate head 1 point; (c) Need to elevate 45 degrees or more 2 points.
2. Dyspnea (shortness of breath on exertion): (a) None 0 points; (b) Climbing 8 or more steps 1 point; (c) Walking on level 2 points.
3. Unexplained cough: (a) None 0 points; (b) At night 1 point; (c) Day and night 2 points.
4. Swelling (pitting edema) lower extremities: (a) None 0 points; (b) Below knee 1 point; (c) Above and below knee 2 points.
5. Excessive weight gain during last month of pregnancy: (a) Under 2 pounds per week0 points; (b) 2 to 4 pounds per week1 point; (c) Over 4 pounds per week 2 points.
6. Palpitations (sensation of irregular heart beats): (a) None 0 points; (b) When lying down at night 1 point; (c) Day and night, any position 2 points.

ACTION: 5 or more points = see cardiologist re: plasma BNP and echocardiogram.

Figure 2: Self-test for Recognision of heart failure during or Just after pregnancy.Its use in each trimester of pregnancy is educational for medical providers and all subjects in pregnancy.

It helps women in pregnancy to become aware of signs and symptoms of heart failure that are often difficult to distinguish from normal signs and symptoms of pregnancy because it provides a quantitative measure of intensity. Furthermore any additional costs are negligible or non-existent. We have documented that anyone with a score greater than "5" has always had an abnormal echocardiogram [8-10]. Continuing use of this test in scores of PPCM subjects has confirmed its utility.

Important proteins coming from the placenta are sFLT1 (soluble FLT-1);also called fms-like tyrosine kinase and soluble vascular endothelial growth factor receptor-1, and PlGF (Placental Growth Factor). It appears that they subsequently also come from vascular endothelium. They are part of the " angiogenic imbalance " that results when their amounts become pathologically altered. PlGF is pro-angiogenic, anti-inflammatory and cardio-protective while sFLT-1 is anti-angiogenic, pro-inflammatory and cardio-toxic [11,12]. Many factors enter into the onset of this pathological imbalance, including maternal/paternal genetics, placental hypoperfusion, maternal endovascular dysfunction, micronutrients, viral infections, pregnancy-altered hormones and immune system function. It is uncertain if the initial deviation from normal is over-production of sFLT-1 or the under-production of PlGF; but there is always too much sFLT-1 and a rising ratio of serum sFLT-1 to PlGF [3].

Once PPCM is diagnosed, the treatment (to be prescribed and monitored by experienced cardiologist/PPCM clinician) that will bring the best potential for full recovery is well understood, with "evidence-based" guidelines. Again, one of the keys to reaching that full recovery is to make the diagnosis before LVEF drops below 35% [13].

Making an earlier diagnosis has an even more important impact in "Third World" poverty conditions relating to newborn survival and the lack of substitute for maternal breast milk nutrition. IPAC Study has demonstrated that there appears to be no adverse impact from breastfeeding upon PPCM recovery rates. Safirstein et al, reported improved survival among breastfeeding PPCM mothers. Those mothers who chose to continue breastfeeding while receiving treatment for their PPCM experienced comparable recovery rates as those PPCM mothers who chose not to breastfeed.

When alternative infant nutrition options are readily available and affordable there is not a problem for infant growth and health. However, in many areas of the world, lack of maternal breast milk can have devastating negative impact on newborn health.

As an example, in Haiti, although healthy at delivery, almost two-thirds of newborns (14/22 or 63.6%), born to mothers who died of PPCM were known to be dead at one-year follow-up. The cause of infant death in all cases was malnutrition and its associated medical complications related to lack of maternal breast milk [14,15].

UNICEF studies have shown that "Optimal breastfeeding of infants under two years of age has the greatest potential impact on child survival of all preventive interventions, with the potential to prevent over 800,000 deaths (13 per cent of all deaths) in children under five in the developing world." This becomes a very important issue faced with the controversial use in treatment of PPCM with bromocriptine, a prolactin inhibitor, leading to cessation of flow of breast milk. Prenatal diagnosis when LVEF is still >35 % would make it unnecessary to stop lactation by the use of bromocriptine, since the evidence-based treatment with BB + ACEI/ARB is so effective in promoting full recovery.

Current available evidence shows that the dilated cardiomyopathy heart failure of PPCM can develop in those mothers who have a genetic link as well as in those mothers who do not have a genetic link. Also, there is evidence that a genetic link can come from the father [16,17]. It appears from IPAC studies that when there is both a genetic link and the angiogenic imbalance of sFLT-1 and PlGF from the placenta, then, despite similar severity at diagnosis, that combination makes it harder to reach full recovery even with the same evidence-based effective treatment [6].

Closer surveillance of those at highest risk during pregnancy could change this risk because with earlier diagnosis the treatment is even more effective. Earlier diagnosis appears to make treatment even more likely to restore full recovery, no matter what, if any, genetic component [8].

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