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CARDIAC DISEASE IN PREGNANCY

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ABSTRACT

Cardiac surgery remains rarely necessary in pregnancy, particularly in the developed world and due to the high risks should be used only when other alternatives are not valid. However, should cardiac surgery in pregnancy become necessary, then it is imperative that a team of clinicians with the appropriate expertise plans and carries out the surgery and that there is access to high-level neonatal care.

KEYWORDS: Cardiac disease, pregnancy.

INTRODUCTION

Cardiac disease complicates approximately 1-2% of pregnancies, but it accounts for up to 15% of maternal deaths, with the overall number of deaths not showing any decline even in the developed world.[1] Nevertheless, the number of women who require cardiac interventions during pregnancy remains small; a Swedish review of 720,000 pregnant women demonstrated that only 40 women (0.006%) underwent cardiopulmonary interventions during pregnancy.[2]

In the developing world, the need for cardiac intervention during pregnancy appears more common. In a review of 1000 women with known heart disease, who were followed up during pregnancy, a total of 47 (5%) underwent an intervention during pregnancy (over half were for percutaneous mitral valvuloplasties for underlying rheumatic heart disease).[3] These procedures are not without risk particularly to the fetus and so both surgical and percutaneous interventions in pregnancy are usually only undertaken when other therapies have failed or are inappropriate. Furthermore, because they are so rare, surgical interventions during pregnancy should be undertaken by specialists practicing as part of a multidisciplinary team of cardiac surgeons, cardiac anesthetists, obstetricians, hematologists, neonatologists, and cardiologists. Indications for percutaneous and surgical interventions.[4]

Cardiac disease of pregnancy encompasses a broad arena of pathologies. Many cardiac diseases during pregnancy are under investigation, and many others which are still not understood require further inquiry. Some of these diseases may be exacerbations of pre-existing conditions that the pregnant woman may already have, or they may develop a new disease process that presents because of the complex hormonal changes and physiology of pregnancy. Pre-existing conditions which can predispose the pregnant woman to cardiovascular disease include hypertension, diabetes mellitus, and congenital heart disease.[5]

Regardless, a cardiac disease of pregnancy is a significant cause of or morbidity and mortality and has been cited to be present between 1-4% of all pregnancies.[6]

Although there is a significant risk involved with such pregnancies, one can successfully treat the majority of these incidents if early detection and careful follow-up are a part of routine care.

Etiology

The etiology of cardiovascular diseases of pregnancy is variable and dependent on the pathology involved. The following summarizes some common cardiovascular diseases of pregnancy and their hypothesized etiologies:

- Cardiomyopathy: There are several hypotheses regarding the etiology of this disease process. Some of the most common theories are viral myocarditis, autoimmune causes, hemodynamic instability, microchimerism, as well as others[7] It is important to note that the risk factors which exist towards causing cardiomyopathy in non-pregnant individuals continue to exist during pregnancy and the weeks following pregnancy, and the heart may even be at a higher susceptibility to these exposures. These causes include alcohol abuse, doxorubicin use, and abuse of drugs such as cocaine and methamphetamines[8]
- Coronary artery disease: The etiology of ischemic heart disease in pregnant women is similar to that of non-pregnant women. Risk factors which expose these individuals to ischemic heart disease include hypertension, hyperlipidemia and hypertriglyceridemia, diabetes mellitus, obesity, smoking, and immobility.[9]
- Pregnancy-associated myocardial infarction: The same risk factors which exist for coronary artery disease also exist for pregnancy-associated MI. It has been hypothesized that certain conditions of pregnancy such as pre-eclampsia and eclampsia could contribute to myocardial infarction.[10]

- Valvular disease: Although the hemodynamics of pregnancy can exacerbate certain valvular diseases, it is inconclusive whether pregnancy has a specific role in the etiology of newly diagnosed valvular disorders of pregnancy.

Epidemiology

The frequency of cardiac disease in women has not been clearly established. It is also unknown if there is an increased frequency of individuals in developed vs. under-developed countries. Based on the best data, estimates are that at least 0.2% of pregnancies have complications with cardiac disease.[11] This frequency has been reported to be as high as 4%.[12] If one includes a hypertensive disease in this value, this number would be even higher, given that hypertensive disorders have been approximated to occur in up to 8% of pregnancies.[13]

Pathophysiology

The underlying physiology of pregnancy and the changes that occur are often a core aspect in promoting some of these disease processes of the heart. Speculations are that women may undergo these physiological changes as early as 5 weeks into their pregnancy.[14]

It is essential to understand these changes and adaptation can vary among individuals. The belief is that many of these changes are the result of attachment of the placenta to uterine walls, which induces the release of hormones and subsequent changes to maternal physiology. These changes are often hemodynamic, and are counter-regulatory and still maintain the basic vascular principles of maintaining the new mean arterial pressure of pregnancy.[15]

Cardiac output: Estimates for increases in a cardiac output range from 20 to 50%. These findings are seen within the first 5 weeks of gestation and increase until the late gestational age; this is usually accounted for by an increased stroke volume of about 25% in the first trimester. This considerable increase in the cardiac output is one reason why pregnant women with pre-existing heart conditions can experience such dramatic effects, especially later on in pregnancy. Those with diseases such as cardiomyopathy may not adequately compensate for this stress and may develop complications such as pulmonary edema or fluid overloaded states.[16]

Heart rate: Along with an increase in stroke volume, there is an increase in heart rate of approximately 15 to 30% in the first trimester of pregnancy, which also contributes to an increase in cardiac output.

- Systemic vascular resistance: Systemic vascular resistance decreases during pregnancy. Estimates are that this change may be as much as 30%. Some hormonal changes include decreased responsiveness of maternal vasculature to angiotensin II and norepinephrine.[17] There is also an increased rate of release of vasodilators in the maternal female such as prostaglandins and nitric oxide.[18]
- Blood pressure: Blood pressure slightly decreases early in pregnancy. Overall, more commonly diastolic blood pressure decreases predominate over-systolic blood pressure early in pregnancy. Usually, this value normalizes, or even increases by the end of pregnancy.

A combination of the above physiological and hormonal changes are hypothesized as contributing to certain decompensated states of pregnancy such as cardiomyopathy, congenital heart diseases, and valvular disease.

It is, however, without doubt, that specific structural changes occur to the maternal heart, and such changes can cause dysfunction in some of these pre-existing diseases. Because of the increase in the volume of pregnancy, a common effect is an enlargement of both atria and both ventricles by the end of pregnancy.[19]

Left ventricular mass increases by up to 50% by the third trimester and eccentric hypertrophy is also noted with increases in septal thickness.[20] Some degree of cardiac remodeling exists to the maternal heart, as many of the changes that occur to the maternal heart are often seen to be reversed 6 to 8 months postpartum.[21] For disease processes such as peripartum cardiomyopathy, it is easy to see why such dramatic changes would contribute to exacerbation of disease processes. However, no specific studies have concluded the exact reason these females are much more vulnerable to this disease process than others. Therefore, theories such as concurrent myocarditis, an autoimmune phenomenon, or familial linkage are potential explanations towards resultant peripartum cardiomyopathy.[22] In mouse models, misregulation of VEGF and angiogenesis have been theorized to have a vital role in this disease process.[23]

Regarding pre-existing valvular disorders such as mitral stenosis, mitral regurgitation, aortic stenosis, and others, the chamber and valvular enlargement along with a potential volume overloaded state can contribute to morbidity and mortality. All of these conditions can contribute to the fluid overloaded state, and place patients at risk for respiratory compromise, and poorly perfused states.

History & Physical

An accurate history is essential towards diagnosing the various conditions of heart conditions of pregnancy. Certain features which would lead to a consideration of cardiac disease would include:

- Fatigue
- Shortness of breath
- Dyspnea on exertion
- Paroxysmal nocturnal dyspnea
- Orthopnea
- Increasing edema
- Chest pain or angina
- Lightheadedness
- Syncope
- Personal or familial history of heart disease especially in pregnancy

Physical exam findings would include:

- Tachypnea
- Tachycardia
- Hypotension
- Cyanosis
- Clubbing
- Jugular venous distension
- Rales
- Ascites
- Hepatomegaly
- Peripheral edema
- S3
- S4

- Hepato-jugular Reflex
- Prominent a and v waves
- Shifted apical impulse laterally to the midclavicular line
- Gallop.[24]

Many of these findings can also be present in normal pregnancy; thus, it is a challenge for the clinician to identify which of these processes are physiologic and which are pathologic. Combination of history and physical elements is critical to further delineate between these two.

Evaluation

Evaluation of cardiac disease in pregnant females will often require advanced workup. Initial basic workup with labs such as CBC, CMP, and urinalysis can give necessary clues to underlying processes that may be occurring. Elevated white blood cell count can help test for inflammatory conditions of the heart such as myocarditis or myocardial infarction. Routine serum creatinine measurement can help the provider test if the patient has had periods of hypo-perfusion in recent history. Liver enzymes could help identify congestive hepatopathy as they would in non-pregnant individuals. Urinalysis could reveal protein to help identify a state of pre-eclampsia. Labs such as brain natriuretic peptide (BNP) may have utility as some note to double during pregnancy.[25]

Still, those who have overt peripartum cardiomyopathy have been found to have higher levels of BNP than those who do not.

An electrocardiogram may be done and reveal various findings as well as similar to those who have cardiovascular disease outside of pregnancy. Normal heart changes in pregnancy will cause rotation of heart to the left and a resultant mild left axis deviation. As previously mentioned, dilation of all chambers of the heart occur in pregnancy, and thus this predisposes these individuals to develop dysrhythmias. Some of the most common dysrhythmias seen in pregnancy include atrial premature beats, supraventricular tachycardias, and ventricular premature beats.[26]

Ventricular tachyarrhythmias may also form but are much rarer.[27] If an individual is undergoing ischemic changes, one would expect to find ECG changes consistent with an ischemic burden, including ST-elevations or depressions, T-wave inversion, or formation of

Q-waves. Non-specific changes to ST segment or T-waves present in up to 14% of pregnancies.[28]

An echocardiogram is essential towards evaluating those undergoing cardiac insults of pregnancy. Physiologic findings may reveal chamber enlargement, physiologic aortic, mitral, and tricuspid regurgitation, and valvular dilatation.[29]

Clinical manifestations of these processes along with the degree of echocardiographic findings will require evaluation by a clinician to evaluate their significance. No strict cutoff for each of these has been deemed "normal" or "abnormal" in pregnancy. Findings of cardiomyopathy may reveal exaggerated septal thickening, end-diastolic posterior wall thickening, and resultant eccentric hypertrophy.[30]

Echocardiography can diagnose peripartum cardiomyopathy if ejection fraction reveals to be less than 45% and/or M-mode shortening below 30%, and end-diastolic dimension is greater than 2.7cm/m2.[31] Localized wall motion abnormalities may present in myocardial ischemia or infarction. Pericardial effusion may also be evident in pregnancy, and in small amounts can be physiologic, however, if the patient is exhibiting signs of hypotension, JVD, or pulses paradoxes, then evaluation of tamponade should be undertaken with echocardiography.

Treatment

There are no recommended empiric regimens towards preventing cardiac disease in pregnancy. Those who have a prior history of cardiac disease should merit increased vigilance, and these individuals should continue their prior regimen. If such regimens contain teratogenic drugs, a qualified provider should substitute these medications. Treatment modalities for the cardiac disease of pregnancy vary based upon the disease process occurring and required an individualized approach. The following discusses some common cardiac disorders and their appropriate recommended treatment regimens:[32]

- Ventricular dysfunction of pregnancy: Many females enter pregnancy with previous heart failure. These individuals may be aware or unaware of these before pregnancy based upon the level of function. The physiologic changes of pregnancy can prove challenging for these patients to compensate. By the time these physiologic changes of pregnancy (increased heart rate, increased circulating volume) are in full effect in the second trimester, these pregnant patients may experience a severe exacerbation of their underlying disease. Besides angiotensin-converting enzyme inhibitors and angiotensin

receptor blockers, other medications used to treat heart failure can be resumed. ACE's and ARB's which are often a mainstay of treatment in heart failure with reduced ejection fraction, are known to be teratogenic with reported effects of renal dysplasia, renal failure, oligohydramnios, and intrauterine growth retardation.[33] A combination of hydralazine and nitrates can be used instead to elicit a similar effect. Beta-blockers may be continued, with a preference for cardio-selective beta-blockers such as metoprolol. If diuretics are required, they may be continued.[34]

- Peripartum cardiomyopathy is a dilated cardiomyopathy which presents in the last 4 weeks of pregnancy or up to 5 months postpartum will require similar treatment regimen to those with ventricular dysfunction of pregnancy.[35] An exception is with a diagnosis of peripartum cardiomyopathy, ACE inhibitors or ARB therapy may resume after delivery.
- Mitral stenosis: The obstructive nature of mitral stenosis results in high morbidity and mortality in the pregnant patient.v There are no medications shown to reverse this disease in these individuals; however, beta-blockers remain the medication of choice. Beta-blockers are thought to decrease trans-mitral gradient. Diuretics are also useful for heart failure symptoms.
- Aortic stenosis: Although aortic stenosis in pregnancy is less common, it is often more challenging to treat. Just as in aortic stenosis in non-pregnant individuals, there are no medications which reverse disease or are mainstays of treatment. Beta-blockers are not as effective as they are mitral stenosis in reducing trans-valvular gradient. Ace inhibitors are contraindicated in pregnant patients. Diuretic therapy necessitates caution because of the potential of reduced diastolic filling and further diminished cardiac output.
- Tachyarrhythmias: Tachyarrhythmias require treatment on an individualized basis. However, drugs which appear to be safe to use in pregnant women with tachyarrhythmias include adenosine, verapamil, digoxin, flecainide, and beta blockers. Amiodarone should be avoided given its proclivity to cause fetal hypothyroidism.[36]
- Acute coronary syndrome: ACS and MI are uncommon in pregnant women, however, given the increasing average age of that women are becoming pregnant, is becoming more common. Advanced age allows the risk factors towards developing ACS to develop. These risk factors include diabetes mellitus, hyperlipidemia, and hypertension. Exposure to fluoroscopy for a pregnant mother is not ideal however given the high mortality with acute coronary syndromes, PCI should be attempted with a lead covering the mother. Thrombolysis is also an option, however, must be administered under close monitoring,

given the documented reports of maternal hemorrhage, spontaneous abortion, subchorionic hematomas, and uterine bleeding.[37]

- Drug-eluting stents should be avoided if possible, because of the prolonged need for dual antiplatelet therapy. Given the increasing incidence of cesarian sections deliveries, dual antiplatelet therapy might be problematic.[38] A list of commonly used drugs and their pregnancy category class are listed below.[39] Morphine (Risk Category C)
- Beta-blockers (Category B: metoprolol; Category C: atenolol)
- Calcium channel blockers: (Category C)
- Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) (Category C)
- Statins (Risk Category X)
- Unfractionated heparin (Category C)
- Low-molecular-weight heparin (Category B)
- Aspirin (Category C)
- Glycoprotein IIb/IIIa inhibitors (Category B: eptifibatide, tirofiban; Category C: abciximab).[40]

Cardiac diseases of pregnancy need evaluation as new processes or exacerbations of previous disease processes. With any cardiac disease process detected in pregnancy, the pre-existing pathology must be ruled out. Such include prior dilated cardiomyopathy, restrictive cardiomyopathy, hypertensive obstructive cardiomyopathy, ischemic heart disease, or previous valvular disorders.[41]

RESULTS AND DISCUSSION

Although heart disease in pregnancy is a high-risk state, successful outcomes are possible, and even common, in patients that have regular follow up. Some conditions of pregnancy carry more morbidity and mortality than others, however.

- Peripartum cardiomyopathy: Peripartum cardiomyopathy occurs in approximately 1 in 2289 live births. About 75% of women with this disease process have full return of normal ventricular function.[42]
- Congenital heart defects: Regurgitant lesions have improved morbidity over stenotic lesions. Overall, however, mortality is negligible in patients with congenital heart disease, with one study identifying no maternal deaths in an analysis of 90 individuals.

- The same study did, however, report that 17% of these patients had pulmonary edema and 12% had cardiac events (mostly nonsustained tachyarrhythmia). A meta-analysis of over 2000 pregnancies revealed a spontaneous abortion rate of 15%. However, this study found an 8% incidence of congenital heart disease in the offspring.[43]
- Acute coronary syndrome: ACS and MI are rare in pregnancy with some estimates reporting 1 to 2 per 35000 deliveries. In a study looking at the prognosis of pregnancies with coronary artery disease or acute coronary syndromes, 16% of adverse obstetric events occurred, while it reported 30% adverse neonatal events. Reported maternal mortality is 7.3% with the highest risk of this for those who present with ACS in the third trimester.[44]

Complications related to cardiac disease in pregnancy include:

- Excess weight gain during pregnancy
- Preeclampsia
- Preterm birth
- Intrauterine growth restriction
- Hemorrhage
- Placental abruption
- Gestational diabetes
- Progressive heart failure
- Maternal or fetal death

Consultations should include:

- High-risk obstetrician
- Cardiology
- Perinatologist

CONCLUSIONS

Each pregnancy requires a team of professionals working together to provide coordinated and effective care. This level of cohesion is even more necessary in pregnant patients with cardiac disease. Physicians play an essential role in distinguishing normal versus abnormal pregnancy states; this can be difficult to decipher regarding cardiac disease because often, pregnant females might exhibit symptoms of cardiac disease in a healthy pregnancy. Nurses have a vital role in the healthcare setting for pregnant patients with cardiac disease. With the admission of these patients to the hospital, their nurses must be cognizant of the complex

dynamics of pregnancy and especially when interventions may be necessary. Early recognition of disease states is essential to prevent worse outcomes for these patients. Pharmacists also have a unique role in the care of pregnant females with cardiac disease. A vast number of drugs and medications routinely used at other times may be detrimental to pregnant women and/or their unborn children. Pharmacists have the unique role of being aware of these medications and interactions and recommending adjustments when they may be needed. Lynch et al. highlighted the critical role of communication between physicians and pharmacists for the best outcomes of pregnancy.[41] The interdisciplinary team is an essential part of the healthcare system, and the need for balanced coordination of care only expands in managing the pregnant patient through a safe pregnancy for the mother and child.

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