Cardiac Diseases in Pregnancy-A Review.

K. Pushpalatha

Department of Obstetrics and Gynaecology, All India Institute of Medical Sciences, New Delhi, India

***Abstract**: Cardiac diseases complicate 1% to 4% of pregnancies in women without preexisting cardiac abnormalities. Major hemodynamic alterations occur during pregnancy, labor, and delivery and the postpartum period. The American Heart Association no longer recommends antibiotic prophylaxis for the prevention of bacterial endocarditis during genitourinary procedures, such as vaginal delivery and cesarean section, including high-risk patients. Preeclampsia and eclampsia have been linked to the future development of cardiovascular disease. Emerging risk factors for future cardiovascular disease in women include maternal obesity and gestational diabetes. Familiarity with the treatment of commonly encountered cardiac diseases during pregnancy is becoming increasingly important for internists and cardiologists as they join the team of obstetricians and anesthesiologists in the care of these complicated patients.This review is an effort to appraise about the various types of cardiac diseases in pregnancy, their implications on the maternal and fetal outcome, long-term effects on the woman.*

INTRODUCTION

Cardiac diseases complicate 1% to 4% of pregnancies in women without preexisting cardiac abnormalities. A working knowledge of the normal physiology of pregnancy is often helpful in the management of patients with heart disease. Patients with preexisting cardiac lesions should be counseled in advance about the risk of pregnancy. Familiarity with the treatment of commonly encountered cardiac diseases during pregnancy is becoming increasingly important for internists and cardiologists as they join the team of obstetricians and anesthesiologists in the care of these complicated patients.

NORMAL PHYSIOLOGIC CHANGES DURING PREGNANCY

Major hemodynamic alterations occur during pregnancy, labor, and delivery and the postpartum period (Table 1). These changes begin to take place during the first 5 to 8 weeks of pregnancy and reach their peak late in the second trimester. In patients with preexisting cardiac disease, cardiac decompensation often coincides with this peak.

***Table 1:** Normal Hemodynamic Changes During Pregnancy*

Hemodynamic Parameter	Change During Normal Pregnancy	Change During Labor and Delivery	Change During Postpartum
Blood volume	↑ 40%-50%	↑	↓ (auto diuresis)
Heart rate	↑ 10-15 beats/min	↑	↓
Cardiac output	↑ 30%-50% above baseline	↑ Additional 50%	↓
Blood pressure	↓ 10mmHg	↑	↓
Stroke volume	↑ First and second trimesters; ↓ third trimester	↑ (300-500mL/contraction)	↓
Systemic vascular resistance	↓	↑	↓

Blood volume increases 40% to 50% during normal pregnancy. The increase in blood volume is greater than the increase in red blood cell mass, contributing to the fall in hemoglobin concentration (i.e., the "anemia of pregnancy"). Similarly, cardiac output rises 30% to 50% above baseline, peaking by the end of the second trimester and reaching a plateau until delivery. The increase in cardiac output is achieved by three factors: (1) an increase in preload because of greater blood volume; reduced afterload because of a decrease in systemic vascular resistance; and (3) a rise in the maternal heart rate by 10 to 15 beats/min. Stroke volume increases during the first and second trimesters, but declines in the third trimester because of in-ferior vena caval compression by the uterus. Blood pressure typically falls about 10 mm Hg below baseline by the end of the second trimester because of reduction in systemic vascular resistance and the addition of new blood vessels in the uterus and placenta.

During labor and delivery, hemodynamic fluctuations can be profound. Each uterine contraction displaces 300 to 500 mL of blood into the general circulation. Stroke volume increases, with a resultant rise in cardiac output by an additional 50% with each contraction. Thus, it is possible for the cardiac output during labor and delivery to be 75% above baseline. Mean arterial pressure also rises, in part because of maternal pain and anxiety. Blood loss during delivery (300 to 400 mL for a vaginal delivery and 500 to 800 mL for a cesarean section) can contribute to hemodynamic stress.

Hemodynamic changes during the postpartum state are equally dramatic. Relief of inferior vena caval compression results in an increase in venous return, which augments cardiac output and causes a brisk diuresis. The hemodynamic changes return to the prepregnant baseline within 2 to 4 weeks following vaginal delivery and within 4 to 6 weeks after cesarean section.

These marked hemodynamic changes during pregnancy account for the development of several signs and symptoms during normal pregnancy that can mimic the signs and symptoms of heart disease. Normal pregnancy is typically associated with fatigue, dyspnea, and decreased exercise capacity. Pregnant women usually have mild peripheral edema and jugular venous distention. Most pregnant women have audible physiologic systolic murmurs, created by augmented blood flow. A physiologic third heart sound (S_3), reflecting the increased blood volume, can sometimes be auscultated.

Noninvasive testing of the heart may include an electrocardiogram (ECG), chest radiograph, and echocardiogram. The ECG may reveal a leftward shift of the electrical axis, especially during the third trimester, when the diaphragm is pushed upward by the uterus. Routine chest radiography should be avoided, especially in the first trimester. Echocardiography is an invaluable tool for the diagnosis and evaluation of suspected cardiac disease in the pregnant patient. Normal changes attributable to pregnancy include increased left ventricular mass and dimensions.

ASSESSMENT OF RISK IN PATIENTS WITH PREEXISTING CARDIAC DISEASE

Maternal and Fetal Outcomes

Ideally, women with preexisting cardiac lesions should discuss the impact of their heart condition on pregnancy well in advance of

***Correspondence: Dr. K. Pushpalatha,** Senior Research Associate, Department of Obstetrics and Gynaecology, All India Institute of Medical Sciences, New Delhi-110029, India **Tel.:** 9958009705 **E-mail:** pushpak_73@yahoo.com*

becoming pregnant. They should discuss contraception, maternal and fetal risks of pregnancy, and potential long-term maternal morbidity and mortality with their physician. Combined input from maternal fetal medicine specialists, the patient's obstetrician, and a cardiologist may be a great asset in managing the pregnancy. Certain preexisting cardiac conditions carry an extremely high maternal risk. Pregnancy in these patients is not advised; it is important for women with these conditions to understand the implications of pregnancy on their health. For example, women with a NYHA functional Class III or IV heart condition face a mortality rate of 7% or higher and a morbidity rate higher than 30% during pregnancy.

A validated cardiac risk score has been shown to predict a woman's chance of having adverse cardiac complications during pregnancy (Table 2)[1,2]. Each risk factor was given a value of 1 point. The maternal cardiac event rates for 0, 1, and higher than 1 points are 5%, 27%, and 75%, respectively.

Table 2: *Predictors of Maternal Risk for Cardiac Complications*

Criteria	*Example*	*Points* *
Prior cardiac events	Heart failure, transient ischemic attack, stroke before current pregnancy	*1*
Prior arrhythmia	Symptomatic sustained tachyarrhythmia or bradyarrhythmia requiring treatment	1
NYHA III or IV or cyanosis		1
Valvular and outflow tract obstruction	Aortic valve area < 1.5 cm^2, mitral valve area < 2 cm^2, or left ventricular outflow tract peak gradient > 30 mm Hg	1
Myocardial dysfunction	LVEF < 40%, restrictive cardiomyopathy, or hypertrophic cardiomyopathy	1

**Maternal cardiac event rates for 0, 1, and >1 points are 5%, 27%, and 75%, respectively. LVEF, left ventricular ejection fraction; NYHA, New York Heart Association. Adapted from Siu SC, Sermer M, Colman JM, et al: Prospective multicenter study of pregnancy outcomes in women with heart disease. Circulation 2001;104:515-521.*

SPECIFIC CONGENITAL OR ACQUIRED CARDIAC LESIONS

Specific congenital or acquired cardiac lesions can be classified as low, intermediate, or high risk during pregnancy (Box 1).

Box 1: *Maternal Cardiac Lesions and Risk of Cardiac Complications During Pregnancy*

Low Risk

•Atrial septal defect •Ventricular septal defect •Patent ductus arteriosus •Asymptomatic AS with low mean gradient (<50 mm Hg) and normal LV function (EF > 50%) •AR with normal LV function and NYHA Class I or II •MVP (isolated or with mild or moderate MR and normal LV function) •MR with normal LV function and NYHA Class I or II •Mild or moderate MS (MVA > 1.5 cm^2, mean gradient < 5 mm Hg) without severe pulmonary hypertension •Mild or moderate PS •Repaired acyanotic congenital heart disease without residual cardiac dysfunction.

Intermediate Risk

•Large left to right shunt •Coarctation of the aorta •Marfan syndrome with a normal aortic root •Moderate or severe MS •Mild or moderate AS •Severe PS.

High Risk

• Eisenmenger's syndrome • Severe pulmonary hypertension • Complex cyanotic heart disease (TOF, Ebstein's anomaly, TA, TGA, tricuspid atresia) •Marfan syndrome with aortic root or valve involvement •Severe AS with or without symptoms•Aortic or mitral valve disease, or both (stenosis or regurgitation), with moderate or severe LV dysfunction (EF < 40%) •NYHA Class III or IV symptoms associated with any valvular disease or with cardiomyopathy of any cause •History of prior peripartum cardiomyopathy.

AR, aortic regurgitation; AS, aortic stenosis; EF, ejection fraction; LV, left ventricular; MVP, mitral valve prolapse; MS, mitral stenosis; MVA, mitral valve area; NYHA, New York Heart Association; PS, pulmonary stenosis; TOF, tetralogy of Falot; TA, truncus arteriosus; TGA, transposition of the great arteries.

Low-Risk Lesions

Young women with uncomplicated secundum-type atrial septal defect (ASD) or isolated ventricular septal defect (VSD) usually tolerate pregnancy well. Patent ductus arteriosus (PDA) is not associated with an additional maternal risk for cardiac complications if the shunt is small to moderate and if pulmonary artery pressures are normal. Once these shunts are repaired, the risk during pregnancy is minimal. It is unusual for women with such left to right shunts to develop pulmonary hypertension during the childbearing years; however, the presence of pulmonary hypertension with a left to right shunt substantially increases the risk of complications during pregnancy.

MITRAL REGURGITATION

Chronic mitral regurgitation most commonly is the result of myxomatous degeneration or rheumatic heart disease and usually is well tolerated during pregnancy. However, new-onset atrial fibrillation or severe hypertension can precipitate hemodynamic deterioration. Acute mitral regurgitation (e.g., from rupture of chordae tendineae) may produce flash pulmonary edema and life-threatening cardiac decompensation. Women with severe mitral regurgitation and signs of cardiac decompensation before pregnancy are advised to undergo operative repair before conception. Mitral valve prolapse in isolation rarely causes any difficulties during pregnancy.

AORTIC REGURGITATION

Aortic regurgitation may be encountered in women with rheumatic heart disease, a congenitally bicuspid or deformed aortic valve, infective endocarditis, or connective tissue disease. Aortic regurgitation generally is well tolerated during pregnancy. Ideally, women with severe aortic regurgitation and signs of cardiac decompensation should undergo operative repair before conception. Women with bicuspid aortic valves, with or without aortic regurgitation, are at increased risk for aortic dissection and should be followed carefully for signs and symptoms of this complication. Congestive heart failure from mitral or aortic regurgitation can be treated with digoxin, diuretics, and vasodilators, such as hydralazine. Angiotensin-converting enzyme (ACE) inhibitors are teratogenic and therefore contraindicated. Beta blockers are generally safe during pregnancy, although fetal bradycardia and growth retardation have been reported.

MODERATE-RISK LESIONS

Mitral Stenosis.

Mitral stenosis in women of childbearing age is most often rheumatic in origin. Patients with moderate to severe mitral stenosis often experience hemodynamic deterioration during the third trimester or

during labor and delivery. The physiologic increase in blood volume and rise in heart rate lead to an elevation of left atrial pressure, resulting in pulmonary edema formation. Additional displacement of blood volume into the systemic circulation during contractions makes labor particularly hazardous.

The development of atrial fibrillation in the pregnant patient with mitral stenosis may result in rapid decompensation. Digoxin and beta blockers can be used to reduce heart rate, and diuretics can be used to reduce the blood volume and left atrial pressure gently. With atrial fibrillation and hemodynamic deterioration, electrocardioversion can be performed safely. The development of atrial fibrillation increases the risk of stroke, necessitating the initiation of anticoagulation (see later, "Medication Guidelines During Pregnancy").

Mild mitral stenosis can often be managed with careful medical therapy during pregnancy. In contrast, patients with moderate to severe mitral stenosis should be referred to a cardiologist. Severe mitral stenosis is associated with a high likelihood of maternal complications (including pulmonary edema and arrhythmias) or fetal complications (including premature birth, low birth weight, respiratory distress, and fetal or neonatal death), approaching 80% of pregnancies[3]. These women may require correction via operative repair or replacement or percutaneous mitral balloon valvotomy before conception or during pregnancy. During pregnancy, percutaneous valvotomy is usually deferred to the second or third trimesters to avoid fetal radiation exposure during the first trimester.

Most patients with mitral stenosis can undergo vaginal delivery. However, patients with symptoms of congestive heart failure or moderate to severe mitral stenosis may need close hemodynamic monitoring during labor, delivery, and for several hours into the postpartum period. In these patients, epidural anesthesia is usually better tolerated hemodynamically than general anesthesia during labor and delivery.

Aortic Stenosis.

The most common cause of aortic stenosis in women of childbearing age is a congenitally bicuspid valve. Mild to moderate aortic stenosis with preserved left ventricular function usually is well tolerated during pregnancy. Severe aortic stenosis (aortic valve area less than 1.0 cm^2, mean gradient more than 50 mm Hg), in contrast, is associated with a 10% risk of maternal morbidity, although maternal mortality is rare. Symptoms such as dyspnea, angina pectoris, or syncope usually become apparent late in the second trimester or early in the third trimester. Cardiac surgery is needed in approximately 40% of patients with severe aortic stenosis within 2.5 years of pregnancy[4].

Women with known severe aortic stenosis should be referred to a cardiologist. Ideally, they should undergo correction of the valvular abnormality before conception. Treatment options include surgical repair, surgical valve replacement, and percutaneous balloon valvotomy. The choice of an appropriate treatment for severe aortic stenosis before pregnancy is complicated and will likely require a number of discussions. When severe symptomatic aortic stenosis is diagnosed during pregnancy, maximal medical therapy is preferred over any intervention. However, if a patient has refractory symptoms and hemodynamic deterioration, despite maximal medical therapy, percutaneous balloon valvotomy may be performed .Spinal and epidural anesthesia are discouraged during labor and delivery because of their vasodilatory effects. As with mitral stenosis, hemodynamic monitoring is recommended during labor and delivery.

High-Risk Lesions

The high-risk conditions listed in Box 1 are associated with increased maternal and fetal mortality. Pregnancy is not advised. If pregnancy should occur, the risks of maternal mortality and morbidity must be assessed on an individual case basis. If these risks are extremely high, consideration of medical termination of the pregnancy is advised to safeguard maternal health. If the pregnancy is continued, these patients are best managed with the assistance of a cardiologist and maternal-fetal medicine specialist at a center with high-risk obstetric facilities and a level 3 neonatal unit.

PREPREGNANCY CARDIOVASCULAR RISK FACTORS

Over the past decade, birth rates for older women (age 25 to 44 years) have increased. Older women have a higher prevalence of traditional cardiovascular risk factors, such as diabetes and chronic hypertension, and of preexistent cardiovascular disease than younger women. The impact of preexisting cardiovascular risk factors on the mother and fetus are profound. Traditional risk factors, such as smoking, diabetes, hypertension, hyperlipidemia, and thrombophilia, are associated with increased risks of spontaneous abortion, maternal placental syndromes (see next section), preterm labor or premature rupture of membranes, and acute arterial or venous thromboses during pregnancy. Furthermore, the presence of such risk factors also predicts the future development of coronary artery disease, chronic hypertension, stroke, and peripheral arterial disease in the mother.

Emerging risk factors for future cardiovascular disease in women include maternal obesity and gestational diabetes. Maternal obesity and morbid obesity are associated with increased risks for gestational hypertension, preeclampsia, gestational diabetes, and fetal birth weight of more than 4000 g [5]. Gestational diabetes can progress to the development of type 2 diabetes. Although the reported incidence of type 2 diabetes in women with gestational diabetes varies widely, the cumulative incidence of type 2 diabetes appears to increase markedly in the first 5 years after pregnancy[6].

ACQUIRED CARDIOVASCULAR DISORDERS DURING PREGNANCY

Maternal Placental Syndromes

A group of disorders, known collectively as maternal placental syndromes, have been associated with an increased maternal risk of premature cardiovascular disease. In the CHAMPS study, a maternal placental syndrome (MPS) was defined as the presence of preeclampsia, gestational hypertension, placental abruption, or placental infarction during pregnancy. MPS occurred in 7% of the 1.03 million women who were free from cardiovascular disease before pregnancy. Interestingly, traditional cardiovascular risk factors were more prevalent in women with MPS than in women without MPS. Women with MPS were twice as likely to experience a hospital admission or revascularization procedure for coronary, cerebrovascular, or peripheral vascular disease compared with women without MPS[7]. The growing body of evidence linking cardiovascular risk factors, MPS, and future cardiovascular disease may indicate an underlying abnormal vascular health that predates pregnancy and can manifest as MPS during pregnancy or as chronic cardiovascular disease later in life.

Hypertension in Pregnancy

Hypertension during pregnancy is defined as a systolic pressure of 140 mm Hg or higher, a diastolic pressure of 90 mm Hg or higher, or both. Hypertension during pregnancy can be classified into three main categories-chronic hypertension, gestational hypertension, and preeclampsia, with or without preexisting hypertension. In general, hypertensive disorders can complicate 12% to 22% of pregnancies and are a major cause of maternal morbidity and mortality.

Chronic hypertension is defined as blood pressure of 140/90 mm Hg or higher that was present before pregnancy, before the 20th week of gestation, or persisting beyond the 42nd postpartum day. Frequently, women with chronic hypertension must change their medical regimens when they anticipate pregnancy to maximize the safety of the growing fetus. Women of childbearing age who take chronic antihypertensive medications should be counseled about the safety of theses medications in the event of pregnancy well in advance of a potential pregnancy. Options for drug therapy are shown in table 4.

Box 2: *Drug Therapy of Hypertension in Pregnancy*

First line

1.Alpha methyldopa (PO).2. Labetolol (PO).

Second Line

1.Hydralazine (PO).2.Nifedipine (PO).3. Beta blockers (PO).

Contraindicated

1. Angiotensin-converting enzyme inhibitors (PO).2. Angiotensin receptor blockers (PO).3. Aldosterone antagonists (PO).

Avoid

1. Thiazide diuretics.

Severe Hypertensive Urgency or Emergency First Line

1. Labetolol (IV).2. Hydralazine (IV).3. Beta blockers (IV).4. Nifedipine (PO)

PO = oral administration; IV = intravenous administration.

Gestational hypertension is defined as hypertension that (1) develops in the latter part of pregnancy, (2) is not associated with proteinuria or other features of preeclampsia, and (3) resolves by 12 weeks postpartum. This condition is also known as pregnancy-induced hypertension. Although it resolves postpartum, women with this condition may be at risk for the development of hypertension or cardiovascular disease, or both, in the future. They should undergo an annual physical examination and screening for traditional risk factors for cardiovascular disease after their pregnancy.

Preeclampsia, also known as toxemia, occurs in 3% to 8% of pregnancies in the United States. The classic clinical triad involves accelerating hypertension, proteinuria (higher than 300 mg/24 hours), and edema. Symptoms usually begin in the third trimester. Although definitive treatment includes delivery of the baby, most women with preeclampsia will require treatment with antihypertensive medications before delivery and for some time postpartum. Hypertensive urgency caused by preeclampsia can be treated with intravenous labetolol or hydralazine. The cause of preeclampsia is still unclear. Eclampsia is the development of grand mal seizures in a woman with preeclampsia. Preeclampsia and eclampsia have been linked to the future development of cardiovascular disease. As with pregnancy-induced hypertension, women with preeclampsia or eclampsia should undergo an annual physical examination and screening for traditional risk factors for cardiovascular disease after their pregnancy.

PERIPARTUM CARDIOMYOPATHY

Peripartum cardiomyopathy (PPCM) is defined as the development of idiopathic left ventricular systolic dysfunction (demonstrated by echocardiography) in the interval between the last month of pregnancy up to the first 5 postpartum months in women without preexisting cardiac dysfunction. The incidence of PPCM in the United States is estimated to be 1 in 3000 to 4000 live births. The exact cause of PPCM is unknown, although viral myocarditis, autoimmune phenomena, and specific genetic mutations that ultimately affect the formation of prolactin have been proposed as possible causes[8].

Although it was believed that women who develop PPCM rarely have symptoms before 36 weeks' gestation, Elkayam and colleagues [8] have recently described an earlier presentation, with symptoms occurring as early as the 17th week of gestation[9]. The clinical presentation and outcome of women who developed the early presentation pregnancy-associated cardiomyopathy were similar to those of women with traditional PPCM. Women with preexisting cardiac dysfunction usually experience cardiac deterioration during the end of the second trimester. Typical signs and symptoms include fatigue, dyspnea on exertion, orthopnea, nonspecific chest pain, peripheral edema, and abdominal discomfort and distention.

Medical therapy for PPCM may be initiated during pregnancy and continue postpartum. Attention to the safety profiles of drug therapies during pregnancy, the postpartum period, and breast-feeding is important. Digoxin, diuretics, and hydralazine may be used safely during pregnancy and while breast-feeding. Beta blockers may improve left ventricular function in patients with cardiomyopathy. Beta blockers are considered safe during pregnancy, although there have been case reports of fetal bradycardia and growth retardation. ACE inhibitors, angiotensin receptor blockers, and aldosterone antagonists are contraindicated during pregnancy. Most ACE inhibitors can be initiated during the postpartum period, even in women who breast-feed. Anticoagulation can be considered for select patients with severe left ventricular dilation and dysfunction. As with other causes of dilated cardiomyopathy, when conventional medical therapy is unsuccessful, women with PPCM may require intensive intravenous therapy, mechanical assist devices, or even cardiac transplantation. Cardiac transplantation is required for about 4% of women with PPCM.

More than half of women with PPCM completely recover normal heart size and function, usually within 6 months of delivery. Complete recovery is more likely in women with a left ventricular ejection fraction of more than 30% at diagnosis[8]. The remainder experience persistent stable left ventricular dysfunction or continue to experience clinical deterioration. Maternal mortality is approximately 9%. Women with PPCM and persistent left ventricular dysfunction who attempt subsequent pregnancy face a high risk of maternal morbidity and mortality[10]. These women should be counseled *against* subsequent pregnancies.

CORONARY ARTERY DISEASE

Acute myocardial infarction (AMI) during pregnancy is rare, occurring in 1 in 35,000 pregnancies. Independent predictors of AMI during pregnancy include chronic hypertension, maternal age, diabetes, and preeclampsia. Most myocardial infarctions occur during the third trimester in women older than 33 years who have had multiple prior pregnancies. Coronary spasm, in situ coronary thrombosis, and coronary dissection occur more frequently than classic obstructive atherosclerosis. Maternal mortality is highest in the antepartum and intrapartum periods. Recent studies have found a 5% to 7% case-fatality rate in women with pregnancy-associated AMI, which may reflect improvements in diagnosis and therapy over the past decade [11].

Medical therapy for acute myocardial infarction must be modified in the pregnant patient. Although thrombolytic agents increase the risk of maternal hemorrhage substantially (8%), their use is permitted for situations in which cardiac catheterization facilities are not available. Low-dose aspirin and nitrates are considered safe. Beta blockers are generally safe. Short-term heparin administration has not been associated with increased maternal or fetal adverse effects. ACE inhibitors and statins are contraindicated during pregnancy. Hydralazine and nitrates may be used as substitutes for ACE inhibitors. Clopidogrel and glycoprotein IIb/IIIa receptor inhibitors

have been used safely in individual pregnant patients. Percutaneous coronary intervention using both balloon angioplasty and stenting has been successfully performed in pregnant patients with AMI, with the use of lead shielding to protect the fetus[12].

ARRHYTHMIAS IN PREGNANCY

Premature atrial or ventricular complexes, or both, are the most common arrhythmias during pregnancy. They are not associated with adverse maternal or fetal outcomes and do not require antiarrhythmic therapy. Supraventricular tachyarrhythmia (SVT) is also common. Patients with SVT should be instructed about the performance of vagal maneuvers. In addition, the use of beta blockers or digoxin, or both, can be useful for controlling the ventricular rate. Adenosine and direct current cardioversion are both safe during pregnancy and can be used to treat SVT. De novo atrial fibrillation and atrial flutter are rare during pregnancy. However, women with a history of prepregnancy tachyarrhythmias have a high likelihood of recurrence during pregnancy. Furthermore, recurrent tachyarrhythmias during pregnancy are associated with an increased risk of adverse fetal complications, including premature birth, low birth weight, respiratory distress syndrome, and death[13]. Rate control of atrial fibrillation and flutter is similar to that for the treatment of SVT. Direct current cardioversion can be performed safely during any stage of pregnancy. Other arrhythmias should be managed with the assistance of a cardiologist.

MEDICATION GUIDELINES DURING PREGNANCY

Cardiovascular Drugs

Commonly used cardiovascular drug classes and their potential adverse effects during pregnancy are shown in Table 3 . For drugs used to treat hypertension, see Box 2.

Table 3: *Cardiovascular Drugs Used During Pregnancy*

Drug	Use	Potential Side Effects	Safe During Pregnancy	Safe During Breast-Feeding
Adenosine	Arrhythmia	None reported	Yes	No data
Beta blockers	Hypertension arrhythmias, MI, ischemia, HCM, hyperthyroidism, mitral stenosis, Marfan syndrome, cardiomyopathy	Fetal bradycardia, low birth weight, hypoglycemia, respiratory depression, prolonged labor	Yes	Yes
Digoxin	Arrhythmia, CHF	Low birth weight, prematurity	Yes	Yes
Diuretics	Hypertension, CHF	Reduced uteroplacental perfusion	Unclear	Yes
Lidocaine	Arrhythmia, anesthesia	Neonatal CNS depression	Yes	Yes
Low-molecular-weight heparin	Mechanical valve, hypercoagulable state, DVT, AF, Eisenmenger's syndrome	Hemorrhage, unclear effects on maternal bone mineral density	Limited data	Limited data
Nitrates	Hypertension	Fetal distress with maternal hypotension	Yes	No data
Procainamide	Arrhythmia	None reported	Yes	Yes
Unfractionated heparin	Mechanical valve, hypercoagulable state, DVT, AF, Eisenmenger's syndrome	Maternal osteoporosis, hemorrhage, thrombocytopenia, thrombosis,	Yes	Yes
Warfarin	Mechanical valve, hypercoagulable state, DVT, AF, Eisenmenger's syndrome	Warfarin embryopathy, fetal CNS abnormalities, hemorrhage	Yes, after week 12 of gestation	Yes

AF, atrial fibrillation; CHF, congestive heart failure; CNS, central nervous system; DVT, deep vein thrombosis; HCM, hypertrophic cardiomyopathy; MI, myocardial infarction. Adapted from Elkayam U: Pregnancy and cardiovascular disease. In Zipes DP, Libby P, Bonow RO, Braunwald E (eds): Braunwald's Heart Disease. A Textbook of Cardiovascular Medicine, 7th ed. Philadelphia, Elsevier Saunders, 2005, p 1965.

ANTIBIOTIC PROPHYLAXIS

The American Heart Association no longer recommends antibiotic prophylaxis for the prevention of bacterial endocarditis during genitourinary procedures, such as vaginal delivery and cesarean section, including high-risk patients.

ANTICOAGULANTS

Several conditions require the initiation or maintenance of anticoagulation during pregnancy, including mechanical valves, certain prothrombotic conditions, prior episode of venous thromboembolism, acute deep vein thrombosis or thromboembolism during pregnancy, antiphospholipid antibody syndrome, and atrial fibrillation. The three most common agents considered for use during pregnancy are unfractionated heparin (UFH), low-molecular-weight heparin (LMWH), and warfarin. The Seventh American College of Chest Physicians (ACCP) Consensus Conference on Antithrombotic Therapy has recommended three potential strategies for

anticoagulation during pregnancy[14]. In women with venous thromboembolism, LMWH has become the anticoagulant of choice. In women with mechanical heart valves, data are more limited and there has been some concern regarding the efficacy of heparins with respect to the prevention of valve thrombosis. In these patients, the maternal and fetal risks and benefits must be carefully explained before choosing one of the aforementioned three strategies. When an UFH or LMWH strategy is selected, careful dose monitoring and adjustment are recommended.

Warfarin freely crosses the placental barrier and can harm the fetus, but it is safe during breast-feeding. The incidence of warfarin embryopathy (abnormalities of fetal bone and cartilage formation) has been estimated at 4% to 10%; the risk is highest when warfarin is administered during weeks 6 through 12 of gestation. When administered during the second and third trimesters, warfarin has been associated with fetal central nervous system abnormalities. The risk of warfarin embryopathy may be low in patients who take 5 mg or less of warfarin per day.

UFH does not cross the placenta and is considered safer for the fetus. Its use, however, has been associated with maternal osteoporosis, hemorrhage, thrombocytopenia or thrombosis (HITT syndrome), and a high incidence of thromboembolic events with older generation mechanical valves. UFH may be administered parenterally or subcutaneously throughout pregnancy; when used subcutaneously for the anticoagulation of mechanical heart valves, the recommended starting dose is 17,500 to 20,000 U twice daily. The appropriate dose adjustment of UFH is based on an activated partial thromboplastin time (aPTT) of 2.0 to 3.0 times the control level. High doses of UFH are often required to achieve the goal aPTT because of the hypercoagulable state associated with pregnancy. Lower doses of UFH may be appropriate for anticoagulation in certain cases, such as the prevention of venous thromboembolism during pregnancy. Parenteral infusions should be stopped 4 hours before cesarean sections. UFH can be reversed with protamine sulfate.

Low-molecular-weight heparin (LMWH) produces a more predictable anticoagulant response than UFH and is less likely to cause HITT. Its effect on maternal bone mineral density appears to be minimal. LMWH can be administered subcutaneously and dosed to achieve an anti–factor Xa level of 1.0 to 1.2 U/mL 4 to 6 hours after injection. Although there are data to support the use of LMWH in pregnant women with deep vein thrombosis, data on the safety and efficacy of LMWH in pregnant patients with mechanical valve prostheses are limited. Experience with these agents is accruing.

In summary, anticoagulation in the pregnant patient can be difficult because of the risk profile associated with each drug regimen. In planned pregnancies, a careful discussion about the risks and benefits of warfarin, UFH, and LMWH will help the patient and physician involved to choose an anticoagulation strategy. Unplanned pregnancies are often diagnosed partway through the first trimester. It is advisable to stop warfarin when the pregnancy is discovered and to use UFH or LMWH, at least until after the 12th week. Dosing regimens for warfarin, UFH, and LMWH may vary by diagnosis; detailed dosing guidelines have been published[14].

SUMMARY

- Heart disease during pregnancy encompasses a wide spec-trum of disorders. Basic concepts to bear in mind include the following:
- Blood volume and cardiac output rise during normal pregnancy, reaching a peak during the late second trimester.
- Preexisting cardiac lesions should be evaluated with respect to the risk they impart during the stress of pregnancy.
- Contraindications to pregnancy include severe pulmonary hypertension or Eisenmenger's syndrome, cardiomyopathy with NYHA Class III or IV symptoms, history of peripartum cardiomyopathy, severe uncorrected valvular stenosis, unrepaired cyanotic congenital heart disease, and Marfan syndrome with an abnormal aorta.
- Awareness of major cardiac drug classes that are contraindicated during pregnancy is important for the treatment of hypertension and heart failure during pregnancy.
- Anticoagulation during pregnancy presents unique challenges because of the maternal and fetal side effects of warfarin, unfractionated heparin, and LMWH.

REFERENCES

1. ***Samuel C. Siu SM, Mathew Sermer, David A. Harrison, Elizabeth Grigoriadis, Grace Liu, Sheryll Sorensen, Jeffrey F. Smallhorn BS, Dan Farine, Kofi S. Amankwah, John C. Spears, Jack M. Colman.*** *Risk and predictors for pregnancy-related complications in women with heart disease. Circulation. 1997;96:2789-2794.*
2. ***Samuel C. Siu, Mathew Sermer, Jack M. Colman, A. Nanette Alvarez, Lise-Andree Mercier, Brian C. Morton, Catherine M. Kells, M. Lynn Bergin, Marla C. Kiess, Francois Marcotte, Dylan A. Taylor, Elaine P. Gordon, John C. Spears, James W. Tam, Kofi S. Amankwah, Jeffrey F. Smallhorn, Dan Farine, Sheryll Sorensen, RN .*** *Prospective multicenter study of pregnancy outcomes in women with heart disease. Circulation. 2001;104:515-521.*
3. ***Silversides CK, Colman JM, Sermer M, et al.*** *Cardiac risk in pregnant women with rheumatic mitral stenosis. Am J Cardiol. 2003;91:1382-1385.*
4. ***Silversides CK, Colman JM, Sermer M, Farine D, Siu SC.*** *Early and intermediate-term outcomes of pregnancy with congenital aortic stenosis. Am J Cardiol.2003;91:1386-1389.*
5. ***Hugh E. Mighty and Jenifer O. Fahey.*** *Obesity, obstetric complications and cesarean delivery rate—a population-based screening study. Am J Obstet Gynecol. 2004;190:1091-1097.*
6. *Gestational diabetes and the incidence of type 2 diabetes: A systematic review. Diabetes Care. 2002;25:1862-1868.*
7. ***Ray JG et al.*** *Cardiovascular health after maternal placental syndromes (CHAMPS): A population-based retrospective cohort study. Lancet. 2005;366:1797-1803.*
8. ***A cathepsin-D cleaved 16-kD*** *form of prolactin mediates postpartum cardiomyopathy. Cell. 2007;128:589-600.*
9. ***Radhakrishnan Ramaraj et al.*** *Pregnancy-associated cardiomyopathy: Clinical characteristics and a comparison between early and late presentation. Circulation. 111: 2005; 2050-2055.*
10. ***Uri Elkayam, Padmini P. Tummala, Kalpana Rao, Mohammed W. Akhter, Ilyas S. Karaalp, Omar R. Wani, Afshan Hameed, Israel Gviazda, B.S., and Avraham Shotan.*** *Maternal and fetal outcomes of subsequent pregnancies in women with peripartum cardiomyopathy. N Engl J Med. 2001;344:1567-1571.*
11. ***AH James, MG Jamison, MS Biswas.*** *Acute myocardial infarction in pregnancy: A United States population-based study. Circulation. 2006;113:1564-1571.*
12. ***Dwyer BK, Taylor L, Fuller A, et al.*** *Percutaneous transluminal angioplasty and stent placement during pregnancy. Obstet Gynecol. 2005;106:1162-1164.*
13. ***Silversides CK, Harris L, Haberer K, Sermer M, Colman JM, Siu SC.*** *Recurrence rates of arrhythmias during pregnancy in women with previous tachyarrhythmia and impact on fetal and neonatal outcomes. Am J Cardiol. 2006;97:1206-1212.*
14. ***Bates SM, Greer IA, Hirsh J, Ginsberg JS.*** *Use of antithrombotic agents during pregnancy. Chest. 2004;126:627S-644S.*