

Cardiovascular Diseases Associated with Pregnancy : An Overview

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ABSTRACT

Valvular heart disease is the most common cardiac problem complicating pregnancy, and pregnancy in most women with heart disease has a favourable maternal and fetal outcome. With the exception of patients with Eisenmenger syndrome, pulmonary vascular obstructive disease, and Marfan syndrome with aortopathy, maternal death during pregnancy in women with heart disease is rare. However, pregnant women with heart disease do remain at risk for other complications including heart failure, arrhythmia, and stroke. Women with congenital heart disease now comprise the majority of pregnant women with heart disease seen at referral centres. The next largest group includes women with rheumatic heart disease. Peripartum cardiomyopathy, though infrequent, will be discussed in view of its unique relation to pregnancy. Two groups of conditions not discussed further are coronary artery disease which is infrequently encountered, and isolated mitral valve prolapse, which generally has an excellent outcome. Hormonally mediated increases in blood volume, red cell mass, and heart rate result in a major increase in cardiac output during pregnancy; cardiac output peaks during the second trimester, and remains constant until term. Gestational hormones, circulating prostaglandins, and the low resistance vascular bed in the placenta result in concomitant decreases in peripheral vascular resistance and blood pressure. During labour and delivery, pain and uterine contractions result in additional increases in cardiac output and blood pressure. Immediately following delivery, relief of caval compression and autotransfusion from the emptied and contracted uterus produce a further increase in cardiac output. Most haemodynamic changes of pregnancy resolve by two weeks postpartum.

Keywords: cardiovascular diseases; pregnancy; valvular heart disease; cardiac problem

INTRODUCTION

Pregnancy is a physiologic condition of having a developing embryo or fetus in the womb after union of oocyte and spermatozoon... It is marked by cessation of menses, nausea on arising in the morning (morning sickness), enlargement of the breasts, pigmentation of the nipples and progressive enlargement of the abdomen.¹ The absolute signs of pregnancy are fetal movements, sounds of the fetal heart and demonstration of the fetus on ultrasound. Heart disorders account for about 10% of maternal obstetric deaths, and despite dramatic improvements in survival and quality of life for patients with severe congenital heart

defects and other heart disorders, pregnancy remains inadvisable for women with certain high-risk disorders such as: Pulmonary hypertension (pulmonary artery systolic pressure >25 mm Hg), Coarctation of the aorta if uncorrected or if accompanied by an aneurysm, Marfan syndrome with aortic root diameter of >4.5 cm, Severe symptomatic aortic stenosis or severe mitral stenosis, A single ventricle and impaired systolic function (whether treated with the Fontan procedure or not), Cardiomyopathy with ejection fraction <30% or New York Heart Association (NYHA) class III or IV heart failure.²

CARDIOVASCULAR DISEASES

HYPERTENSION

In pregnancy, cardiac output increases by 40%, with most of the increase due to an increase in stroke volume. Heart rate increases by 10 beats/min during the third trimester.³ In the second trimester, systemic vascular resistance decreases, and this decline is associated with a fall in blood pressure. During pregnancy, a blood pressure of 140/90 mmHg is considered to be abnormally elevated and is associated with an increase in perinatal morbidity and mortality.¹ In all pregnant women, the measurement of blood pressure should be performed in the sitting position, because the lateral recumbent position may result in a lower blood pressure. The diagnosis of hypertension requires the measurement of two elevated blood pressures at least 4hrs apart. Hypertension during pregnancy is usually caused by preeclampsia, chronic hypertension, gestational hypertension, or renal disease.³

i. Preeclampsia is a disorder of widespread vascular endothelial malfunction and vasospasm that occurs after 20 weeks gestation and can present as late as 4-6 weeks post-partum. It is clinically defined by hypertension and proteinuria, with or without pathologic edema.²

ii. Chronic hypertension is blood pressure exceeding 140/90mmHg before pregnancy or before 20 weeks of gestation. When hypertension is first identified during a woman's pregnancy and she is at less than 20 weeks gestation, blood pressure elevations usually represent chronic hypertension.³ Pregnancy complicated by chronic essential hypertension is associated with intrauterine growth restriction and increased perinatal mortality. Pregnant women with chronic hypertension are at increased risk for superimposed preeclampsia and abruptio placentae. Women with chronic hypertension should have a thorough prepregnancy evaluation, both to identify remediable causes of hypertension and to ensure that the prescribed antihypertensive agents (e.g., angiotensin-converting enzyme [ACE] inhibitors, angiotensin-receptor blockers) are not associated with an adverse outcome of pregnancy. Labetalol and nifedipine are the most commonly used medications for the treatment of chronic hypertension in pregnancy. The target blood pressure is in the range of 130-150 mmHg systolic and 80-100 mmHg diastolic.³

iii. Gestational hypertension is a new hypertension presenting after 20 weeks of pregnancy without significant proteinuria and resolves 6 weeks postpartum.¹

iv. Renal hypertension is a hypertension due to or associated with renal disease with a factor of parenchymal ischemia. Normal pregnancy is characterized by an increase in glomerular filtration rate and creatinine clearance.³ This increase occurs secondary to a rise in renal plasma flow and increased glomerular filtration pressures. Patients with underlying renal disease and hypertension may expect a worsening of hypertension during pregnancy. If superimposed preeclampsia develops, the additional endothelial injury results in a capillary leak syndrome that may make management challenging. In general, patients with underlying renal disease and hypertension benefit from aggressive management of blood pressure.¹ Preconception counseling is also essential for these patients so that accurate risk assessment and medication changes can occur prior to pregnancy. In general, a prepregnancy serum creatinine level <133 $\mu\text{mol/L}$ (<1.5 mg/dL) is associated with a favorable prognosis. When renal disease worsens during pregnancy, close collaboration between the internist and the maternal-fetal medicine specialist is essential so that decisions regarding delivery can be weighed to balance the sequelae of prematurity for the neonate versus

long-term sequelae for the mother with respect to future renal function.³

MITRAL STENOSIS

This is the valvular disease most likely to cause death during pregnancy. The pregnancy-induced increase in blood volume, cardiac output, and tachycardia can increase the transmitral pressure gradient and cause pulmonary edema in women with mitral stenosis. Women with moderate to severe mitral stenosis (mitral valve area $\leq 1.5 \text{ cm}^2$) who are planning pregnancy and have either symptomatic disease or pulmonary hypertension should undergo valvuloplasty prior to conception, preferably with percutaneous balloon valvotomy (PBV).³ Pregnancy associated with long-standing mitral stenosis may result in pulmonary hypertension. Sudden death has been reported when hypovolemia occurs. Careful control of heart rate, especially during labor and delivery, minimizes the impact of tachycardia and reduced ventricular filling times on cardiac function. Pregnant women with mitral stenosis are at increased risk for the development of atrial fibrillation and other tachyarrhythmias. The immediate postpartum period is a time of particular concern secondary to rapid volume shifts. Careful monitoring of cardiac and fluid status should be observed.³

MITRAL REGURGITATION AND AORTIC REGURGITATION AND STENOSIS

The pregnancy-induced decrease in systemic vascular resistance reduces the risk of cardiac failure with these conditions, especially in women with chronic lesions.¹ Acute onset of mitral or aortic regurgitation may not be well tolerated during pregnancy. For women with severe aortic stenosis, treatment before pregnancy should be considered for a peak-to-peak valve gradient >50 mmHg. In women with aortic stenosis and a mean valve gradient <25 mmHg, pregnancy is likely to be well tolerated. For women with mitral or aortic regurgitation and left ventricular dysfunction (LVEF <30%) pregnancy should be avoided.³

CONGENITAL HEART DISEASE

Advances in medical and surgical treatments have led to more than 90% of children with congenital heart disease (CHD) surviving into adulthood.⁴ As a consequence, many affected women reach childbearing age and request guidance regarding pregnancy options.⁵ Patients with repaired congenital heart disease now form the largest proportion of women becoming pregnant with significant cardiac issues.⁶ Preconception counseling is an important aspect of cardiac care for women with CHD and should begin early, ideally in adolescence, by cardiologists and maternal-fetal medicine specialists with experience in pregnancy and CHD. A multidisciplinary approach to managing pregnancy in these women is essential.⁷ Despite surgical repair, many women with CHD will have residual, sequelae and late complications those could have important implications for pregnancy. Women who have not regular cardiac care prior to pregnancy should be re-assessed by a cardiologist in early pregnancy.⁸

Outcomes Associated with Specific Cardiac Lesions: Congenital heart lesions

i. Left to right shunts

Left to right shunts occur in atrial septal defect (ASD), or the left ventricle in ventricular septal defect (VSD) and patent ductus arteriosus. In the absence of pulmonary hypertension, pregnancy, labour and delivery are well tolerated.⁹ However arrhythmias, ventricular dysfunction, and progression of pulmonary hypertension may occur, especially when the shunt is large or when there is pre-existing elevation of pulmonary artery pressure.¹⁰

ii. Left ventricular outflow tract obstruction

Obstruction to left ventricular outflow is seen in aortic stenosis and it is recommended that these patients have a surgical correction before pregnancy, especially if severe.¹¹ This is because pregnancy increases the preload and the metabolic demands of the patient and if this CHD is not corrected, it can lead to heart failure or ischemia.

iii. Coarctation of the aorta

The management of hypertension in uncorrected coarctation is particularly problematic in pregnancy because satisfactory control of upper body hypertension may lead to excessive hypotension below the coarctation site, compromising the fetus.¹¹ Intrauterine growth restriction and premature labour and delivery are more common. Following coarctation repair, the risk of dissection and rupture is likely reduced but not eliminated.

iv. Pulmonary stenosis

Those with severe pulmonary stenosis are at risk of developing right sided heart failure. Mild pulmonic stenosis, or pulmonic stenosis that has been alleviated by valvuloplasty or surgery, is well tolerated during pregnancy and fetal outcome is favourable. However, balloon valvuloplasty may be feasible if symptoms of pulmonary stenosis progress.¹²

v. Cyanotic heart disease: unrepaired and repaired

In uncorrected or palliated pregnant patients with cyanotic congenital heart disease such as tetralogy of Fallot, single ventricle, etc, the usual pregnancy associated fall in systemic vascular resistance and rise in cardiac output exacerbate right to left shunting leading to increased maternal hypoxaemia and cyanosis. Corrected cyanotic heart disease reduces the risk associated with pregnancy.¹²

SUPRAVENTRICULAR TACHYCARDIA

This is a tachyarrhythmia characterized by a heart rate above 120 beats per minute. Patients with SVT exhibit the following symptoms: palpitations, dyspnea, chest pain, hemodynamic instability, or possibly asymptomatic.¹³ The increase in cardiac output and the increase in resting heart rate during pregnancy predispose pregnant women to SVT. The management of SVT in pregnancy, although remarkably similar, varies slightly based on the trimester of pregnancy. Atenolol and verapamil are effective methods of treating SVT, which can be used during the second and third trimesters. Both medications are contraindicated in the first trimester.¹³ At the same time, intravenous adenosine can be used in all three trimesters, including labor. Electrical cardioversion is an effective treatment method for hemodynamically unstable or drug-refractory patients, which has proven to be safe in all three trimesters, including labor but can result in pre-term labor in the third trimester. Non-fluoroscopic ablation proved to be the only treatment method that definitively resolved SVT without recurrence.¹⁴

PERIPARTUM CARDIOMYOPATHY

This is a cardiac enlargement and congestive heart failure of an undermined origin, beginning in the last month of gestation or the first few months after delivery.¹⁵ It is an uncommon disorder of pregnancy and its etiology remains unknown. Approximately 10% of women with peripartum cardiomyopathy carry a truncating mutation in the gene encoding the titin sarcomere protein. Treatment is directed toward symptomatic relief and improvement of cardiac function. Many patients recover completely; others are left with progressive dilated cardiomyopathy.¹⁶ Recurrence in a subsequent pregnancy has been reported, and women who do not have normal baseline left-ventricular function after an episode of peripartum cardiomyopathy should be counseled to avoid pregnancy.¹⁷

MARFAN SYNDROME

This autosomal dominant disease is associated with an increased risk of aortic dissection and rupture.¹⁸ An aortic root diameter <40mm is associated with a favorable outcome of pregnancy; conversely, an aortic root diameter >40mm is associated with an increased risk of aortic dissection.¹⁹ Prophylactic therapy with beta blockers has been advocated to reduce aortic dilation and the risk of dissection. A cardiac delivery with reduced pushing and early intervention with operative delivery is often recommended to reduce increases in aortic wall stress caused by the Valsalva maneuver.¹⁹

EHLERS-DANLOS SYNDROME

Is a group of inherited disorders of the connective tissue with hyperextensible skin and joints, easy bruisability, friability of tissues with bleeding and poor wound healing, calcified subcutaneous spheroids and pseudotumors as its major manifestations.²⁰ It may be associated with premature labor, and in type IV EDS there is increased risk of organ or vascular rupture that may cause death. For women with vascular EDS, pregnancy is relatively contraindicated because of the high risk of vascular and uterine rupture.²¹

PULMONARY HYPERTENSION

Maternal mortality in the setting of severe pulmonary hypertension is high, and primary pulmonary hypertension is a contraindication to pregnancy.²² Termination of pregnancy may be advisable in these circumstances to preserve the life of the mother. In the Eisenmenger syndrome, i.e., the combination of pulmonary hypertension with right-to-left shunting due to congenital abnormalities, maternal and fetal deaths occur frequently.²³ Systemic hypotension may occur after blood loss, prolonged Valsalva maneuver, or regional anesthesia; sudden death secondary to hypotension is a dreaded complication. Management of these patients is challenging, and invasive hemodynamic monitoring during labor and delivery is recommended in severe cases. In patients with pulmonary hypertension, vaginal delivery is less stressful hemodynamically than cesarean section, which should be reserved for accepted obstetric indications.²⁴

SUMMARY

With improved diagnostic and therapeutic modalities as well as advances in the treatment of infertility, more patients with serious cardiovascular complications will be seeking to become pregnant and will require complex obstetric care. Improved outcomes of pregnancy in these women will be best attained by a team of internists, maternal-fetal medicine (high-risk obstetrics) specialists, pediatricians and anesthesiologists assembled to counsel these patients about the risks of pregnancy and to plan their treatment prior to, and following, conception. The importance of preconception counseling cannot be overstated. It is the responsibility of all physicians caring for women in the reproductive age group to assess their patients' reproductive plans as part of their overall health evaluation.

REFERENCES

- [1] European Society of Gynecology (ESG); Association for European Paediatric Cardiology (AEPC); German Society for Gender Medicine (DGesGM): ESC Guidelines on the management of cardiovascular diseases during pregnancy: The Task Force on the Management of Cardiovascular Diseases During Pregnancy of the European Society of Cardiology (ESC). *Eur Heart J* 32 (24):3147–3197, 2011. doi: 10.1093/eurheartj/ehr218.

- [2] NICE (June 2019). Hypertension in pregnancy - the management of hypertensive disorders during pregnancy.
- [3] MOADDAB A et al: Health care disparities and state-specific pregnancy-related mortality in the United States, 2005-2014. *Obstet Gynecol* 126:869, 2016.
- [4] B.M. Weiss et al. Outcome of cardiovascular surgery and pregnancy: a systematic review of the period 1984-1996. *Am Obstet Gynecol.* 1998; 179: 1643-1653.
- [5] Siu SC, Colman JM, Sorensen S, et al. Adverse neonatal and cardiac outcomes are more common in pregnant women with cardiac disease. *Circulation* 2002; 105:2179-84.
- [6] E. Goldszmidt et al. Anesthetic management of a consecutive cohort of women with heart disease for labor and delivery. *Int J Obstet Anesth.* 2010.
- [7] Shaline R. and Jonathan N.G. Adult congenital heart disease and pregnancy. *Seminars in Perinatology.* 2014;38 (5):260-272.
- [8] Koichiro Niwa. Adult Congenital Heart Disease with Pregnancy. *Korean Circ J.* 2018 Apr;48(4):251-276 <https://doi.org/10.4070/kcj.2018.0070>.
- [9] Shime J, Mocarski E, Hastings D, et al. Congenital heart disease in pregnancy: short- and long-term implications. *Am J Obstet Gynecol.* 1987; 156:313-322.
- [10] Siu SC, Sermer M, Harrison DA, et al. Risk and predictors for pregnancy-related complications in women with heart disease. *Circulation.* 1997; 96:2789-2794.
- [11] Bonow RO, Carabello B, de Leon AC Jr., et al. Guidelines for the management of patients with valvular heart disease: executive summary. A report of the American College of Cardiology/American Heart Association task force on practice guidelines. 1998; 98:1949-1984.
- [12] Siu SC, Colman JM. Heart disease and pregnancy. *Heart* 2001; 85:710-715.
- [13] Ibetoh, Crystal N, et al. Supraventricular Tachycardia in Pregnancy: Gestational and Labor Differences in Treatment. *Cureus*, 4 Oct. 2021, 10.7759/cureus.18479. Ramlakhan, Karishma P., et al.
- [14] Supraventricular tachycardia during pregnancy. Lehtoranta L, Valta M, Aantaa R, Perheentupa A. <https://pubmed.ncbi.nlm.nih.gov/26939491/> *Duodecim.* 2016; 132:173-175.
- [15] Michael C Honigberg, Michael M Givertz: peripartum cardiomyopathy. *BMJ* 2019;364: k5287.
- [16] Sliwa K, Hilfiker-Kleiner D, Petrie MC, et al., Heart Failure Association of the European Society of Cardiology Working Group on Peripartum Cardiomyopathy. 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; 12:767-78. doi:10.1093/eurjhf/hfq120 pmid:20675664.
- [17] [Guideline] Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, et al, for the ESC Scientific Document Group. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. *Eur Heart J.* 2018 Sep 7. 39(34):3165-241.
- [18] Lachandani S, Wingfield M. Pregnancy in women with Marfan syndrome. *Eur J Obstet Gynecol.* 2003; 110:125-130.
- [19] J.E. Ferguson et al. Marfan Syndrome: acute aortic dissection during labour resulting in fetal distress and caesarean section followed by successful surgical repair *Am. J. Obstet. Gynecol.* (1983).
- [20] Akilandeswari; Karthikeyan and Narayanaswamy Venkat Raman. Hypermobility Ehlers-Danlos syndrome and pregnancy. *Obstet med;* Sept 2018. 11(3): 104-109, published online 20 Mar 2018.
- [21] Joan Carvalho PhD. Women with EDS have higher risk of pregnancy, delivery complications, study finds. 18th September 2020.
- [22] Weiss BM, Zempl L, Seifert B, Hess OM. Outcome of pulmonary vascular disease in pregnancy: a systematic overview from 1978 through 1996. *Am Coll Cardiol.* 1998;31(7):1650-1657.
- [23] Kiely DG, Condliffe R, Webster V, et al. Improved survival in pregnancy and pulmonary hypertension using a multi-professional approach. *BJOG.* 2010;117(5):565-574.
- [24] Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, et al. 2018, ESC Guidelines for the management of cardiovascular diseases during pregnancy. *Eur Heart J.* 2018;39(34):3165-3241.