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Pregnancy with congenital heart disease

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Abstract

Pregnancy is complicated by maternal cardiovascular disease in 1%-4% of cases. With advances in management of congenital heart diseases (CHDs), the survival to adulthood and childbearing age is increasing all over the world. The physiological adaptation during pregnancy adds to the hemodynamic burden of CHD, and, hence, many women are diagnosed with CHD for the first time during pregnancy, more so in developing countries. The type of underlying CHD and pre-pregnancy hemodynamics determine the risk of developing complications during pregnancy. Hence, pre-pregnancy risk stratification and counseling are a crucial part of management plan. Some of the serious CHDs are best treated in the preconception stage. The maximum chance of developing complications is between 28 and 32 weeks of gestation, during labor, and up to two weeks after delivery. Common complications in women with CHD during pregnancy and labor include heart failure, arrhythmias, bleeding/thrombosis, infective endocarditis, and rarely maternal death. Fetal complications include abortion, stillbirth, prematurity, low birth weight, and CHD. Comprehensive knowledge of these complications and their management is very important as an experienced multidisciplinary team is critical for improving outcome of these patients. Special care is required for pregnant women who have pulmonary hypertension, due to either Eisenmenger syndrome or other causes, severe valve stenosis, aortopathy associated with bicuspid aortic valve/coarctation, or severe cyanotic CHDs. Most women with CHD are at low risk, and successful pregnancy is feasible in the majority with optimal management.

Keywords: Adult congenital heart disease, maternal cardiac disease, maternal mortality, maternal morbidity, risk stratification, pregnancy complications

INTRODUCTION

Maternal cardiac diseases complicate 1%-4% of all pregnancies and are the leading cause of maternal mortality in high-income countries (HIC), constituting about 15% of all causes[1,2]. Among the cardiac diseases, congenital heart diseases (CHDs) are now the most common form seen in four-fifths of all maternal cardiac diseases[1,3]. The advancements in medical and surgical treatment of CHDs have led to improved survival of these patients to adulthood[4]. This increased survival coupled with significant decline in incidence of rheumatic heart disease (RHD) has resulted in CHD becoming the most common cardiovascular problem during pregnancy in HIC. Despite a relative increase in pregnancy related cardiac deaths over the last two decades, the proportion of CHD-related deaths has remained relatively low[5]. On the other hand, in low- and middle-income countries (LMIC), RHD continues to be the most common cardiovascular disease during pregnancy[6-8]. Though the data regarding maternal cardiac diseases in LMIC are scarce, global progress reports have emphasized the increasing importance of indirect maternal deaths due to preexisting heart diseases[9]. Therefore, as the incidence of RHD declines and standards of medical care improve in these countries, maternal CHD is likely to gain more importance[7,8].

Unlike HIC where patients with CHD have excellent access to robust surgical centers, most patients with CHD in LMIC have no access to surgery[10,11]. Therefore, most patients have uncorrected CHD in LMIC. Moreover, many patients are diagnosed to have CHD for the first time during pregnancy[7,8]. This is the cause of high morbidity and worse outcomes in pregnant females with CHD in LMIC[6,7,12]. A recent study reported that the risk of maternal mortality was seven times higher in women with uncorrected CHD than corrected CHD ($P = 0.01$)[12].

CHDs comprise of a broad spectrum of anatomic abnormalities but have a limited spectrum of pathophysiologic states. As pregnancy has a marked impact on the cardiovascular system, women with CHD are at high risk of developing cardiovascular complications, which affect the maternal and fetal outcomes. In one of the largest studies on pregnant women with CHD, Schlichting *et al.*[13] reported that the odds of occurrence of an adverse maternal cardiac event during delivery were 2.4-27.6 times higher for women with CHD compared with women without CHD. Ramage *et al.*[14] studied 2114 women with CHD and reported the risk of serious maternal morbidity during pregnancy to be 4.0% in comparison to 1.1% in women without CHD.

Optimum care for these patients requires a coordinated effort by a cardio-obstetric team as they need careful antenatal and postnatal surveillance and an individualized plan for labor and delivery. A recent large multicenter study of pregnant patients with maternal cardiac disease found that almost half of serious complications in patients are preventable and are due to failure on the part of healthcare provider to identify the high-risk patients and institute timely appropriate management[15]. Therefore, these women require appropriate preconception assessment, risk stratification, and counseling. There exists a wide gap in quality of care between HIC and LMIC which needs to be bridged[2,3,6,7].

SCOPE OF THE ARTICLE

We highlight the current understanding of the issues related to pregnancy in women with congenital heart disease and describe the management of the issues as per existing literature.

HEMODYNAMIC CHANGES DURING PREGNANCY, DELIVERY AND POSTPARTUM PERIOD

Pregnancy and childbirth require significant adaptation of the cardiovascular system in the mother to cope with the increased metabolic demands of the mother and fetus. The various hemodynamic changes that occur during pregnancy in normal women are highlighted in Figure 1A. The usual pattern of hemodynamic adaptation to pregnancy is attenuated in women with CHD[16]. Moreover, these hemodynamic alterations can sometimes have deleterious effects on the mother with CHD as well as on the developing fetus.

Plasma volume and cardiac output reach a maximum of 40%-50% above baseline at 32 weeks of gestation, while 75% of this increase occurs by the end of first trimester. These are then maintained at the same level throughout the pregnancy. The increase in cardiac output is initially achieved by an increase in stroke volume in the first half of pregnancy and a gradual increase in heart rate after this period[17,18]. The heart size increases while ventricular function is preserved. In women with CHD, ventricular adaptation to pregnancy may be suboptimal and can result in impaired uteroplacental flow and suboptimal fetal outcome[19].

There is generally a minor change in systolic blood pressure (BP), but there is a fall in diastolic BP due to hormone-induced vasodilation. Diastolic BP reaches a minimum of 10 mmHg below baseline in the second trimester of pregnancy and returns to pre-pregnancy levels by term[17,18]. In the third trimester, BP can decrease due to the compression of the inferior vena cava by the enlarged uterus, especially in the right decubitus position or while lying supine. Since the fall in BP is primarily due to the fall in systemic vascular resistance, it is likely to aggravate the right-to-left shunt in cyanotic CHD.

Patients with CHD are at higher risk of arrhythmias due to intrinsic conduction abnormalities, residual hemodynamic problems, and operative scars, and they are further burdened by the tachycardia and volume overload due to pregnancy[20]. The occurrence of tachyarrhythmias or failure to adequately increase heart rate can cause decompensation and adverse outcomes[21]. The incidence of arrhythmias was ~2% in one of the largest registries of pregnant CHD patients[22]. The fragility of the arterial wall increases during pregnancy due to increased serum levels of estrogen and relaxin. This is an adaptive response during pregnancy but can result in formation of ascending aortic aneurysms or even dissection of aorta in predisposed women, e.g., women with bicuspid aortic valve, coarctation of aorta, and Marfan syndrome[23,24].

The red blood cell counts increase by 20%-30%, and the increased plasma volume causes relative anemia. There is a hypercoagulable state in late pregnancy due to an increase in vitamin K-dependent clotting factor and a reduction in free protein S. This is of particular concern in pregnant women with prosthetic heart valves, atrial fibrillation, preexisting ventricular dysfunction, or uncorrected CHD. In contrast to the 0.1% risk of thromboembolism risk in normal pregnancy[25], the rate of thromboembolism was found to be 1.2% in those with CHD as per a recent multicentric registry[22]. Other obstetric issues such as hypertensive disorders of pregnancy, preeclampsia, or multiple pregnancies further increase the risk of maladaptation to hemodynamic needs and thus the risk of cardiovascular complications in susceptible patients[3,5].

Further changes in hemodynamics occur at the time of labor and delivery. Cardiac output and other hemodynamic parameters fluctuate markedly with each uterine contraction[17]. The changes during normal labor are shown in Figure 1B. The BP and cardiac output increase during labor and post-partum. Volume shifts at the time of delivery is poorly tolerated by women with some CHD where cardiac output is highly dependent on preload[20]. After delivery, the cardiac output and heart rate start decreasing as early as 24 h after delivery.

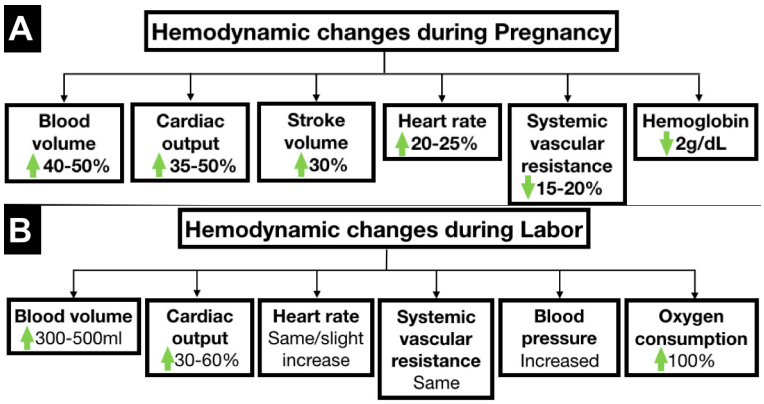

Figure 1. Hemodynamic changes during (A) pregnancy and (B) labor.

Most cardiovascular parameters return to preconception values within two weeks. The stroke volume, cardiac output, and heart size take a longer time and reach preconception levels by 3-6 months. In patients with CHD, cardiovascular maladaptation can persist even six months after delivery[16]. The critical periods for a pregnant woman with CHD are gestation between 28 and 32 weeks, during labor, and up to two weeks after delivery.

PRE-PREGNANCY RISK ASSESSMENT AND COUNSELING IN MOTHERS WITH CONGENITAL HEART DISEASE

It is recommended that all women with CHD should undergo careful pre-pregnancy assessment and detailed counseling before conceiving. The counseling should include maternal cardiac and obstetric risks as well as the fetal risks. This requires a multidisciplinary team approach comprising of an obstetrician, cardiologist, neonatologist, and other specialists in some cases.

Maternal risk

Maternal risk stratification of women with CHD is based on the type of underlying CHD, whether the CHD has been repaired or not, the presence of residual lesions with the resulting hemodynamics, and assessment of patient specific cardiac and obstetric risk factors[1,4,5]. The assessment includes patient's history, electrocardiogram, detailed echocardiography, oxygen saturation, and additional testing, such as exercise testing, catheterization, and advanced imaging in some cases. Maternal functional status is an important determinant of pregnancy outcome. Cardiopulmonary exercise testing performed before conception can predict maternal and neonatal outcomes in pregnant women with CHD[26]. Lui *et al.*[27] found that the peak heart rate, percentage of maximum age predicted heart rate, and chronotropic index were associated with the risk of maternal cardiac and neonatal adverse events. B-type natriuretic peptide or N-terminal pro B-type natriuretic peptide may also be helpful[28].

The aim of risk stratification is not only to stratify but also identify modifiable risk factors and decide whether a pre-pregnancy intervention may reduce the risk. Pre-pregnancy assessment should also include careful review of medication for teratogenic potential. Commonly used cardiac medications such as spironolactone, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, endothelin receptor antagonists, and amiodarone are contraindicated during pregnancy. Oral anticoagulant use during pregnancy is associated with increased risk of bleeding and thrombotic events as well as fetal loss and teratogenicity (warfarin). These medications may have to be stopped before conception, if considered safe for the mother[1,4].

Risk-stratification scores have been developed based on various studies to predict adverse outcomes in women with CHD. The commonly used scoring systems include the Cardiac Disease in Pregnancy (CARPREG) score, the modified World Health Organization (WHO) classification scores, and the ZAHARA score[1,29,30]. The modified WHO classification system is currently recommended by both American and European guidelines for care of women with CHD in pregnancy, although it is probably more appropriate for developed rather than developing countries.

The modified WHO classification is primarily based on underlying congenital cardiac condition, and it also includes lists of CHD that contraindicate pregnancy. The general principle of classification is given in Table 1. Women in mWHO Class IV should be advised against pregnancy. Patients with a high-risk CHD which is a contraindication for pregnancy must be counseled at a young age explaining the harmful effects of pregnancy on their hemodynamics. It is equally important to assure women with milder forms of CHD that they can go through pregnancy with a low risk. High-risk patients must be managed at centers with expertise. In general, risk of pregnancy increases with increased complexity of CHD. All women with CHD must be assessed at least once before pregnancy and then during pregnancy.

Fetal risk

The fetal risks mainly include the risk of prematurity, low birth weight/small for gestational age, fetal/neonatal death, and the risk of recurrence of CHD. Maternal and neonatal events are highly correlated. The risk of adverse fetal/neonatal outcome is closely correlated with the severity of impairment of maternal hemodynamics due to the direct effect on uteroplacental blood flow. Fetal/neonatal mortality is more frequent in women with CHD (4%) than in the general population[31]. The risk of adverse outcomes for fetus in maternal CHD is quite high in women with severe forms, such as univentricular physiology, Eisenmenger physiology, and unrepaired cyanotic defects. In women with cyanotic CHD, cyanosis poses a significant risk to the fetus, and a live birth is highly unlikely (< 12%) if oxygen saturation is below 85%, while more than 90% of fetuses survive to birth if maternal arterial saturation is more than 90%. Some important risk predictors of neonatal events include mothers with left heart obstruction, mechanical heart valve prosthesis, use of oral anticoagulants, and, most importantly, maternal New York Heart Association (NYHA) Class III/IV at baseline.

Risk of transmission of CHD in presence of a positive family history (up to third degree relatives) is variable depending on maternal CHD type, presence of a syndrome, and other factors but is in the range of 3%-7% and slightly higher when the affected member is the mother [Table 2][32,33]. The recurrence risk is also higher with heterotaxy, conotruncal anomalies, atrioventricular septal defect, and obstructive lesions of the left ventricular outflow tract. Therefore, the chance of recurrence of CHD in offspring should be discussed with all women with CHD. It is important to record a detailed family history and examine for syndromic features as these can help in identifying subtle syndromes and inheritance patterns.

The etiology of CHD is multifactorial, with only 20%-30% of CHD cases having an identifiable genetic or environmental cause[34]. In addition, most genetic mutations in patients with CHD are sporadic. Nevertheless, genetic testing using cord blood samples can be offered to all women with CHD with discussion of the advantages and limitations of genetic testing. An important advantage of genetic testing is that it can help in recognition or prediction of extracardiac comorbid conditions which can affect long-term outcome and thus allow more accurate prognostication in some cases[34]. Newer genetic tests such as chromosomal microarray and next generation sequencing are now in widespread use and have increased the chances of identifying genetic etiology of CHD but have the limitation of identifying variants of unknown significance.

Table 1. Modified World Health Organization classification of maternal cardiovascular risk[1]

A

mWHO Class	Diagnosis (if otherwise well and uncomplicated)
mWHO I	Small or mild pulmonary stenosis, patent ductus arteriosus, mitral valve prolapse Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage) Atrial or ventricular ectopic beats, isolated
mWHO II	Unoperated atrial or ventricular septal defect Repaired Tetralogy of Fallot Most arrhythmias (supraventricular arrhythmias) Turner syndrome without aortic dilatation
mWHO II-III	Mild left ventricular impairment (EF > 45%) Hypertrophic cardiomyopathy Native or tissue valve disease not considered WHO I or IV (mild mitral stenosis, moderate aortic stenosis) Marfan without aortic dilatation Aorta < 45 mm in bicuspid aortic valve pathology Repaired coarctation Atrioventricular septal defect
mWHO III	Moderate left ventricular impairment (EF = 30%-45%) Previous peripartum cardiomyopathy without any residual left ventricular impairment Mechanical valve Systemic right ventricle with good or mildly decreased ventricular function Fontan circulation (if the patient is otherwise well and the cardiac condition uncomplicated) Unrepaired cyanotic heart disease Other complex heart disease Moderate mitral stenosis Severe asymptomatic aortic stenosis Moderate aortic dilatation (40-45 mm in Marfan syndrome, 45-50 mm in bicuspid aortic valve, Turner syndrome ASI 20-25 mm/m^2, Tetralogy of Fallot < 50 mm) Ventricular Tachycardia
mWHO IV	Pulmonary arterial hypertension Severe systemic ventricular dysfunction (EF < 30% or NYHA Class III-IV) Previous peripartum cardiomyopathy with any residual left ventricular impairment Severe mitral stenosis Severe symptomatic aortic stenosis Systemic right ventricle with moderate or severely decreased ventricular function Severe aortic dilatation (> 45 mm in Marfan syndrome, > 50 mm in bicuspid aortic valve, Turner syndrome ASI > 25 mm/m^2, Tetralogy of Fallot > 50 mm) Vascular Ehlers-Danlos Severe (re)coarctation Fontan with any complication

B

WHO Class	mWHO I	mWHO II	mWHO II-III	mWHO III	mWHO IV
Risk	No detectable increased risk of maternal mortality and no/mild increased risk in morbidity	Small increased risk of maternal mortality or moderate increase in morbidity	Intermediate increased risk of maternal mortality or moderate to severe increase in morbidity	Significantly increased risk of maternal mortality or severe morbidity	Extremely high risk of maternal mortality or severe morbidity
Maternal cardiac	2.5%-5%	5.7%-10.5%	10%-19%	19%-27%	40%-100%

event rate					
Counseling	Yes	Yes	Yes	Yes, expert counseling required	Yes, pregnancy contraindicated: if pregnancy occurs, termination should be discussed
Care during pregnancy	Local hospital	Local hospital	Referral hospital	Expert center for pregnancy and cardiac disease	Expert center for pregnancy and cardiac disease
Minimal follow-up visits during pregnancy	Once or twice	Once per trimester	Bimonthly	Monthly or bimonthly	Monthly
Location of delivery	Local hospital	Local hospital	Referral hospital	Expert center for pregnancy and cardiac disease	Expert center for pregnancy and cardiac disease

ASI: Aortic size index; EF: ejection fraction; mWHO: modified World Health Organization classification; NYHA: New York Heart Association; WHO: World Health Organization.

Assessment for other risk factors (parental obesity, diabetes, hypertension, infections, alcohol, smoking, and teratogenic medications) that can compromise fetal well-being and increase the risk of fetal birth defects should also be routinely done.

Preconception counseling

A multidisciplinary management plan should be devised and discussed with the patient and her family. It is extremely important in setting appropriate expectations and minimizing complications. In addition to the general recommendations, specific topics of discussion during counseling include education on maternal and fetal risks, pre-pregnancy optimization plan, modification of medications, planned schedule of cardiac evaluation and testing during pregnancy and in the peripartum time period, mode of delivery, and possible persistence of cardiovascular abnormalities after pregnancy when applicable.

DIAGNOSIS OF CHD DURING PREGNANCY

The physiological adaptations occurring during pregnancy make the clinical diagnosis of CHD challenging. It is usual to have some exertional dyspnea and fatigue during pregnancy. Edema of feet can be seen in 80% of healthy pregnant women. However, many disorders can be identified by a thorough history and physical examination. Unexplained dyspnea, pathological murmurs, presence of cyanosis, *etc*. must not be ignored as they are indicators of underlying CHD, and an echocardiography is indicated in these cases[1].

Echocardiography is a widely available imaging tool which gives diagnosis of CHD with great accuracy. Mild dilatation of cardiac chambers could be a normal finding during pregnancy. An exercise test, although best performed prior to planning pregnancy, can also be performed in asymptomatic pregnant patients with underlying CHD. It is recommended to perform a submaximal exercise to attain 80% of the predicted maximal heart rate[1]. The developing fetus is vulnerable (highest during first trimester) to develop neurological abnormalities, growth restriction, and malignancies on ionizing radiation exposure, and, hence, chest radiograph and computed tomography must be avoided if possible[1,35].

Table 2. Risk of CHD recurrence in the fetus

Type of CHD in mother	Risk of recurrence
Tetralogy of Fallot	2.0-4.5
Patent ductus arteriosus	4.1
Coarctation of aorta	4.1-6.3
Atrial septal defect	4.6-11
Pulmonary stenosis	5.3-6.5
Ventricular septal defect	6.0-15.6
Atrioventricular septal defect	7.9-13.9
Aortic stenosis	8.0-13.9
Marfan syndrome	50
22q11 deletion syndrome	50

CHD: Congenital heart disease.

In LMIC, women often present for the first time with clinical features of heart disease when already pregnant. When these patients present with symptoms in the emergency room for the first time, the treating physician should formulate a diagnostic impression based on the cursory history and focused examination, supplemented by electrocardiogram for planning immediate management to stabilize the patient. Chest radiography should be avoided if possible. The physician should identify the subgroup in which the patient falls, i.e., cyanotic or acyanotic (shunt/obstructive) disease with increased or decreased pulmonary blood flow, followed by identification of precipitating cause (anemia, polycythemia, infective endocarditis, arrhythmia, physiological changes of pregnancy, ventricular dysfunction, thromboembolism, *etc*.) for presenting symptoms. Once stabilized, patients should undergo detailed echocardiography followed by other imaging, as deemed necessary.

These patients need complete assessment by a multidisciplinary team and risk stratification as is performed preconception. Periodic follow-ups should be planned as per the risk stratification [Table 1A and B]. If the assessment reveals a high-risk condition, termination of pregnancy should be recommended early in pregnancy. However, termination of pregnancy also carries risks in women with high-risk lesions and should be performed at a center with the necessary expertise.

MANAGEMENT OF PREGNANCY IN WOMEN WITH CONGENITAL HEART DISEASE

For each case, a clear follow-up and delivery plan should be made and discussed with the patient. The frequency of follow-up visits depends on the risk assessment. The European Society of Cardiology has given recommendations for management of CHD during pregnancy [Table 1B][1]. High-risk pregnancies are best managed by an experienced multidisciplinary team in a tertiary care center, while those with low risk can be managed in state-level regional centers. The patient and her family should be educated about the anticipated symptoms and need for frequent assessment. In addition, fetal echocardiography should be offered to all mothers with CHD between 18 and 22 weeks of gestation. It may be performed earlier if there is suspicion of CHD on ultrasonography. The fetal echocardiography protocol should include complete sequential segmental analysis and should not be limited to screening views. It is important to highlight that the recurrence of CHD in the fetus may not be identical to the CHD type in the affected family member.

Timing and mode of delivery

The timing of delivery depends on maternal hemodynamic status and obstetric evaluation including cervical assessment, fetal well-being, and fetal lung maturity. Guidelines recommend elective induction of labor at 40 weeks of gestation under controlled conditions in all women with cardiac disease as it reduces the risk of

emergency caesarean delivery and the risk of stillbirth[1]. The obstetrician should be wary of the adverse effects of inducing drugs such as misoprostol (arrhythmias and coronary vasospasm), oxytocin (systemic hypotension), and prostaglandin F analogs (systemic hypotension and increase in pulmonary pressure), and their use needs to be individualized. Mechanical methods such as artificial rupture of membranes and cervical ripening balloon might be preferable for induction of labor in some of the patients.

Vaginal delivery, often with epidural analgesia, is the preferred mode of delivery for the majority of women with CHD[1,36]. Vaginal delivery is associated with lesser blood loss and lesser risk of infection and venous thromboembolism. The indications for caesarean delivery are few and listed in Table 3[1]. Epidural analgesia can be used to provide anesthesia for caesarean delivery as well, but it can cause systemic hypotension and therefore must be carefully titrated, especially in patients with left heart obstruction and diminished ventricular function[1].

Mobilization of patient may facilitate fetal head descent, and a lateral decubitus position during labor can decrease the hemodynamic impact of inferior vena cava compression. Early epidural catheter placement to reduce labor pain can help in reducing hemodynamic load of labor. Historically, patients with significant cardiac disease have been dissuaded from doing the Valsalva maneuver due to associated increase in oxygen consumption and decrease in venous return. However, some studies have shown that allowing passive head descent and assisting the second stage of labor (use of forceps/ventouse to reduce maternal effort and epidural analgesia which suppresses Valsalva reflex due to fetal pelvic descent) can prolong labor and may be associated with a higher risk of postpartum hemorrhage and high-degree vaginal or cervical laceration[37]. Therefore, it should be reserved for patients at highest risk.

Patients requiring hydration should receive intravenous crystalloids with closely monitored fluid balance. All patients with intracardiac right-to-left shunts must have filters in intravenous lines to prevent paradoxical air embolization. In patients with uncorrected or partially corrected complex CHD, it is vital to maintain balance of systemic and pulmonary blood flow. A decrease in systemic vascular resistance or an increase in pulmonary vascular resistance can lead to increased right-to-left shunting, thus increasing hypoxemia and increasing the risk of maternal and fetal death[37].

No antibiotic prophylaxis is recommended against infective endocarditis (IE) for vaginal delivery. Maternal BP, saturation, and heart rate should be monitored in all women with CHD and invasive cardiac monitoring is rarely required. Patients with history of arrhythmias and symptomatic ventricular dysfunction should have continuous ECG monitoring. Continuous fetal heart rate monitoring is recommended.

Peripartum care

Although the risk of serious cardiac events was higher in the antepartum period (66%), intrapartum and postpartum period accounted for one-third of all serious cardiac events in a recent study by Pfaller *et al.*[15] Therefore, patients with CHD should continue to receive good care in the peripartum period as well, as fatal events are well known to occur during this period. Significant hemodynamic changes and fluid shifts in the first 24-48 h after delivery can precipitate heart failure; hence, intensive hemodynamic monitoring should be continued for at least 24-48 h in at-risk patients[38]. Cardiac rhythm and saturation should be monitored in high-risk patients. Good hydration must be maintained especially in patients with cyanotic CHD and for this intravenous fluid administration may be necessary. Care must be taken to prevent air embolism. Meticulous leg care, elastic support stockings, and early ambulation are important to reduce the risk of thromboembolism. Hemoglobin values must be optimized, by blood transfusions if required. Symptoms

Table 3. Indications for caesarean delivery in women with congenital heart disease[1]

Indications for caesarean delivery
Significant aortopathy with ascending aorta dilation > 45 mm
Severe forms of pulmonary hypertension (including Eisenmenger's syndrome)
Severe left heart obstruction
Severe ventricular dysfunction with heart failure
Pre-term labor on oral anticoagulation

and signs of apparently minor problems must be taken seriously and managed promptly. Ergometrine is best avoided in the third stage of labor. Lactation should be encouraged whenever possible as it is associated with a low risk of bacteremia secondary to mastitis. In women with moderate to severe CHD, mixed feeding (artificial and breast feeding) is better than breastfeeding alone.

Interventions for CHD during pregnancy

The decision to perform intervention during pregnancy requires careful assessment by the cardio-obstetric team. The indication of intervention is usually severe cardiac failure with significant risk to both the mother and fetus. Procedures should be performed by experienced teams at tertiary care centers only.

Percutaneous therapy

Women with CHD having an absolute indication for percutaneous intervention (e.g., symptomatic severe aortic stenosis/severe pulmonary stenosis/coarctation of aorta, mitral stenosis, and refractory arrhythmias amenable to ablation) should preferably undergo the procedure in the second trimester. This is because organogenesis is complete by this time and the uterus is still small and away from the chest which is exposed to radiation. The principle of "as low as reasonably achievable" radiation dose must be followed. Some of the maneuvers for minimizing radiation exposure include use of alternative imaging such as echocardiography, using low-dose fluoroscopy, avoiding oblique and lateral projections, and minimizing the area exposed and fluoroscopy time[1,39]. Abdominal shielding also helps to lower the radiation dose to the fetus.

Cardiac surgery under cardiopulmonary bypass

Open heart surgery is recommended only if medical therapy and percutaneous intervention fail and the mother's life is threatened. Some of the indications for surgery during pregnancy include aortic aneurysm with impending rupture, worsening heart failure due to infective endocarditis, and severe symptomatic left heart obstruction. Optimal time for surgery is between 13 and 28 weeks of gestation. When gestational age is more than 28 weeks, delivery after fetal lung maturity induction should be considered before cardiac surgery. Surgery under cardiopulmonary bypass (CPB) carries about 20% risk of fetal loss, while the maternal mortality is not higher than usual[1]. To diminish the risk of fetal loss during CPB, it is recommended to minimize CPB time, maintain pump flow > 2.5 L/min/m^2 and perfusion pressure of > 70 mmHg, and use pulsatile flow and normothermic perfusion[1,40].

MANAGEMENT OF COMMON COMPLICATIONS SEEN IN WOMEN WITH CHD

Heart failure

The results from the European registry revealed the overall incidence of heart failure as 6.6% of all pregnant women with CHD, with a higher risk of 8.7% in those with uncorrected CHD[12,22]. The peak incidence of heart failure is towards the end of the second trimester and during or just after delivery[38]. It should be emphasized that the manifestation of heart failure may differ between different CHDs. Women with systemic right ventricle (RV), history of Fontan surgery, and dysfunctional RV after Tetralogy of Fallot

repair are more predisposed to develop heart failure. Reversible factors such as arrhythmia and anemia should be actively looked for. Management includes bed rest, supplemental oxygen, fluid balance, and careful diuretic use. Some of the drugs used in the treatment of heart failure, such as angiotensin converting enzyme inhibitors, angiotensin receptor blockers, and spironolactone, are contraindicated during pregnancy, although beta-blockers can be used if indicated. Hydralazine and nitrates can be used for afterload reduction, but angiotensin converting enzyme inhibitors are best started after delivery[1]. In the case of refractory heart failure in the mother, baby should be delivered irrespective of duration of gestation. Corticosteroid use for fetal lung maturity is avoided due to risk of fluid retention and worsening of heart failure[5].

Arrhythmias

Arrhythmias are one of the common complications in adults with CHD and complicate a substantial number of pregnancies[3,22,29]. The most common types of tachyarrhythmias are intra-atrial re-entrant tachycardia caused by atrial scars, and atrial fibrillation. The incidence of arrhythmia depends on time since surgery, underlying cardiac condition, and aging. Tachyarrhythmias can be associated with life threatening symptoms and increase the risk of thromboembolic complications and occurrence of heart failure. Therefore, in women with significant tachyarrhythmias, catheter ablation or implantable cardiac defibrillator implantation should be performed before conception, if clinically indicated[1]. If the indication emerges during pregnancy, then it is recommended to use echocardiographic guidance and 3D mapping to prevent radiation-induced fetal adverse effects.

Direct cardioversion is recommended in the case of hemodynamically unstable arrhythmias and is reported to be safe and effective during pregnancy[1]. Regarding antiarrhythmic therapy, beta-blockers are the first choice for most arrhythmias as most other anti-arrhythmic drugs come under United States Food and Drug Administration category C and therefore their use depends on the risk-benefit ratio[5,20].

Anticoagulation

Women with prosthetic heart valves, previous history of thromboembolic complications, or high-risk anatomy such as post-Fontan surgery may require anticoagulation during pregnancy. It is important to highlight that all anticoagulant regimes have an inherent risk of causing subplacental bleed leading to pregnancy loss[41]. Anticoagulation with warfarin provides the lowest risk for thrombosis but has a risk of causing warfarin embryopathy if used in the first trimester. Current guidelines recommend continuation of warfarin throughout pregnancy in women requiring low doses (< 5 mg) to maintain therapeutic international normalized ratio due to low risk of embryopathy[1,42]. These women should be mandatorily switched to unfractionated heparin after 36 weeks of gestation due to the risk of lethal intracranial hemorrhage in the fetus during vaginal delivery.

Infective endocarditis

IE is rare with an annual incidence of 1 per 1000 in patients with CHD[43]. Women with uncorrected cyanotic CHD or repaired CHD using artificial patch or prosthetic valve or previous history of endocarditis are eligible for IE prophylaxis, but the guidelines do not recommend antibiotic prophylaxis during delivery due to lack of convincing evidence[1]. The diagnosis and treatment of IE during pregnancy is the same as in the non-pregnant patient, but due consideration needs to be given to fetotoxic potential of antibiotics.

MANAGEMENT OF SPECIFIC CONGENITAL HEART DISEASES

Pulmonary hypertension and Eisenmenger syndrome

Pulmonary hypertension (PH) in the mother could be due to Eisenmenger syndrome, idiopathic pulmonary arterial hypertension and PH related to lungs, or left heart disease. Maternal mortality has classically been

reported to be very high in these patients (16%-30% for PH and 20%-50% for Eisenmenger syndrome), but the recent European registry results are optimistic with < 5% mortality in their cohort of 151 pregnant women with PH[44-47]. The greatest risk of mortality is during the first six weeks after delivery. The common causes of death include pulmonary hypertensive crisis, pulmonary thrombosis, or refractory right heart failure. Maternal death may occur even in patients with few symptoms before pregnancy[47]. Although there is no safe cut-off for elevated pulmonary arterial pressure, patients with mild PH may tolerate the pregnancy well. However, the recommendation to avoid pregnancy remains, and, if pregnancy occurs, termination is advisable. There is increased fetal and neonatal mortality (0-30%) with the severity of reduction in maternal cardiac output and degree of hypoxemia being the most important predictors[1].

If the patient chooses to continue pregnancy, extreme care during pregnancy, delivery, and in the postpartum period must be exercised. These patients are particularly at risk for thromboembolism, bleeding complications, and heart failure. Bed rest, meticulous fluid balance, and supplemental oxygen help. Phosphodiesterase inhibitors are often prescribed, with the addition of prostanoids in patients with persistent symptoms. Anticoagulation should be carefully considered as it may induce hemoptysis. Iron deficiency is common and should be treated with supplemental iron. Vaginal delivery or planned caesarean delivery are preferred over emergency caesarean delivery. Regional anesthesia is preferred over general anesthesia. Delivery should be performed in an experienced tertiary center.

Cyanotic Congenital heart disease with pulmonary stenosis

In women with repaired Tetralogy of Fallot, pulmonary regurgitation is the most common residual lesion and is generally tolerated well in pregnancy unless associated with RV dysfunction. Akagi *et al.*[48] reported data from 143 pregnancies in patients with repaired Tetralogy of Fallot. There were no maternal deaths, but a minority of patients had heart failure (11%), worsening of arrhythmia (8%), premature birth (10%), and miscarriage (5%). In general, patients eligible for pulmonary valve replacement or other interventions should undergo procedure before conceiving for best outcomes.

On the other hand, in patients with uncorrected CHD, the maternal outcome is determined by the underlying condition and ventricular function while the fetal outcome is predominantly determined by the saturation level regardless of the anatomical complexity[49]. Maternal complications (heart failure, thrombosis, arrhythmias, and endocarditis) can occur in almost one-third of women and pregnancy should be discouraged in such patients. However, in those who have already conceived, patients should be advised to restrict physical activity and use compression stockings to prevent venous stasis (to avoid paradoxical embolism). Thromboprophylaxis with low molecular weight heparin should be considered if there are no contraindications. Vaginal delivery is advisable unless there is an obstetric indication for caesarean delivery.

Left ventricular outflow tract obstruction

The morbidity and mortality in left ventricular outflow tract obstruction is related to the severity of obstruction and symptom status. The risk of obstetric complications is increased in patients with severe aortic stenosis. Preterm delivery, fetal growth retardation, and low birth weight occur in 20%-25% of offspring of mothers with moderate and severe AS, although miscarriages and fetal death rates are < 5%[50]. Severe symptomatic left ventricular outflow tract obstruction is an absolute contraindication for pregnancy[1]. Even asymptomatic patients with severe left ventricular outflow tract obstruction and impaired LV function or a pathological exercise test should be counseled against pregnancy. These patients should undergo intervention before conceiving. Asymptomatic patients with severe valvular aortic stenosis and normal left ventricular function may tolerate pregnancy well provided they remain asymptomatic. Guidelines recommend exercise testing in these asymptomatic patients before pregnancy to evaluate exercise tolerance, BP response, and arrhythmias[1]. Those with bicuspid aortic valve and associated dilated

aorta are at risk of aortic dissection and pregnancy is contraindicated if ascending aorta diameter is > 50 mm.

Activities should be restricted during pregnancy. Severely symptomatic patients not responding to medical therapy may have to undergo balloon valvuloplasty to relieve their symptoms. Elective caesarean delivery under general anesthesia is preferred in severe symptomatic aortic stenosis patients, while vaginal delivery is favored in asymptomatic severe and in non-severe cases.

Coarctation of aorta

Women with unrepaired coarctation of aorta (CoA), and those with residual lesions (persistent hypertension, re-coarctation, aortic aneurysms, aortopathy, and aortic valve disease) have an increased risk of dissection, rupture of aorta, and cerebral aneurysms during pregnancy and delivery. The most common complication even in women with well repaired CoA is hypertension and is seen in approximately 30%[51]. Therefore, these patients should be under close supervision throughout pregnancy for high BP.

In very severe cases with refractory hypertension and maternal or fetal compromise during pregnancy, balloon dilatation can be considered, but, due to high risk of aortic dissection, covered stent may be required.

Post-Fontan surgery

Women who have undergone Fontan surgery come under mWHO risk category III/IV due to unique hemodynamic abnormalities after this surgery. Even women with ideal Fontan circuit (mWHO III) are at increased risk of fertility issues, atrial arrhythmias, and worsening of functional class but may tolerate pregnancy. Occurrence of arrhythmias and thrombosis of Fontan circuit due to prothrombotic pregnancy state are major issues which can jeopardize fetal and maternal outcome. In mothers with a Fontan circulation, the offspring risk includes premature birth, small for gestational age, and fetal death in up to 50% of cases. Those with resting oxygen saturation < 85%, depressed ventricular function, moderate to severe atrio-ventricular valve regurgitation, arrhythmias, and protein losing enteropathy are at particularly high risk of maternal and fetal adverse outcomes and are best counseled against pregnancy[1].

Generally, vaginal delivery is possible and is preferred. Therapeutic anticoagulation should be considered since these patients are at significant risk of thromboembolism. Atrial arrhythmias need to be treated promptly and often need electrical cardioversion.

Repaired transposition of great arteries

The type of surgical correction and residual abnormalities are the major determinant of risks during pregnancy. Women with atrial switch operation (Mustard/Senning repair) often have systemic right ventricular dysfunction, tricuspid regurgitation (TR), and brady/tachyarrhythmias which often worsen during pregnancy[52]. Failure to increase cardiac output and heart rate adequately during pregnancy may occur due to chronological incompetence and rigid conduits, baffles. Generally, pregnancy is tolerated well in those with no residual defects, normal ventricular function, and in NYHA Class I, but patients with severe right ventricular dysfunction or severe tricuspid regurgitation are advised against pregnancy[1]. Vaginal delivery is recommended in asymptomatic patients with good ventricular function. The risk of pregnancy after arterial switch operation has not been adequately studied but is likely to be lower than after atrial switch operation.

Other congenital heart diseases

Pregnancy is well tolerated in most patients with an atrial septal defect (ASD) or a patent ductus arteriosus (PDA) as long as there is no PH. Thromboembolic complications and arrhythmias are slightly more common in patients with unrepaired ASD as compared to healthy women. The maternal and fetal outcomes are good, and no specific treatment is required. Prognosis is also good in women with corrected shunt lesions (ASD/ventricular septal defect/PDA) with no residual abnormalities.

Atrioventricular septal defects (ostium primum ASD) are best repaired before conception as arrhythmias and worsening of atrio-ventricular valve regurgitation are well described during pregnancy[53].

Mild to moderate pulmonary stenosis are well tolerated during pregnancy with good fetal and neonatal outcome. Severe pulmonary stenosis can result in right ventricular failure and arrhythmias and, in cases with severe symptoms, may necessitate percutaneous balloon dilatation.

Ebstein's anomaly without cyanosis and heart failure is tolerated well during pregnancy. The incidence of arrhythmias is higher during pregnancy and may worsen the outcome[54]. Women with right-to-left shunting through the defect in interatrial septum (patent foramen ovale/ASD present in 90% of cases) can develop progressive cyanosis during pregnancy and are at increased risk of paradoxical embolism. Women with Ebstein's anomaly having symptoms, cyanosis, or heart failure are best treated surgically before conception.

In women with congenitally corrected transposition of great arteries, the risk depends on functional status, systemic right ventricle function, and associated tricuspid regurgitation. They are at increased risk of developing arrhythmias and heart failure (WHO risk Class III). Women with NYHA Classes III or IV, severe ventricular dysfunction, or severe tricuspid regurgitation should be counseled against pregnancy[1].

CONCLUSION

CHD is the most common heart disease in pregnant patients in developed countries, and this cohort is gradually increasing even in developing countries. The risk of complications during pregnancy in women with CHD largely depends on the type of underlying CHD and pre-pregnancy cardiac state. This emphasizes the importance of risk assessment and counseling prior to pregnancy. High-risk patients are best treated by a multidisciplinary team in a specialized center. Lesion-specific considerations and risk stratification should determine management decisions during pregnancy, labor, delivery, and the postnatal period in these patients. Women with severe pulmonary hypertension, Eisenmenger syndrome, severe left ventricular dysfunction, bicuspid aortic valve with aortic dilatation > 50 mm, and severe symptomatic left ventricular outflow tract obstruction should be offered termination of pregnancy if detected in time. Improvement in existing practices of assessment and management of women with CHD will result in substantial improvement in outcomes for the mother and fetus.

DECLARATIONS

Authors' contributions

Did literature review and composed the first draft of the article: Saxena A
Reviewed data and worked on the subsequent revisions: Relan J
Conceptualized the study design, reviewed progress of the article at each step, and finalized the manuscript of the review article: Saxena A

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