REVIEW ARTICLE

Mitral valve disease in pregnancy: outcomes and management

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Summary: Young women may have asymptomatic mitral valve disease which becomes unmasked during the haemodynamic stress of pregnancy. Rheumatic mitral stenosis is the most common cardiac disease found in women during pregnancy. The typical increased volume and heart rate of pregnancy are not well tolerated in patients with more than mild stenosis. Maternal complications of atrial fibrillation and congestive heart failure can occur, and are increased in patients with poor functional class and severe pulmonary artery hypertension. Patients can be diagnosed by echocardiography and symptoms treated with beta-1 antagonists and cautious diuresis. Patients with heart failure unresponsive to treatment can undergo percutaneous balloon mitral valvuloplasty. Labour and delivery goals include reducing tachycardia by adequate pain control and minimized volume shifts. Mitral valve regurgitation, even when severe, is usually very well tolerated in pregnancy as the increase in volume is offset by a decrease in vascular resistance. On the other hand, patients with left ventricular dysfunction, moderate pulmonary hypertension or NYHA functional class III-IV are at increased risk for heart failure and arrhythmias. They may need cautious diuresis and limitations on physical activity during pregnancy, as well as invasive haemodynamic monitoring for labour and delivery. Vaginal delivery is preferred and caesarean section reserved for obstetric indications.

Keywords: pregnancy, mitral valve stenosis, mitral regurgitation, heart disease, labour and delivery

INTRODUCTION

The presence of valvular disease in pregnant women increases the risk of adverse maternal and fetal outcomes and poses a challenge to physicians. Mitral valve disease, specifically mitral stenosis, is the most common valvular disease seen in pregnancy. The overall prevalence of rheumatic mitral stenosis in developed countries is estimated at 1–2%,[1] but in developing countries it is much more prevalent and accounts for 40–50% of the cardiac disease seen in pregnancy. In areas with large immigrant populations, internists and obstetricians will likely continue to see pregnant women with rheumatic mitral stenosis.

The normal cardiovascular changes that occur during pregnancy are well described and include increased intravascular volume, resting heart rate and cardiac output. The changes in volume begin early in the first trimester and plateau by the third trimester. Cardiac output increases by 30–60%; these changes are determined by a 30–40% increase in preload early in pregnancy and maintained by a 10–20% increase in heart rate later in pregnancy.[2] There is also decreased systemic vascular resistance with a mild decrease in systolic blood pressure. Predictably, these changes are poorly tolerated in patients with mitral stenosis due to restricted left ventricular inflow and resultant increases in left atrial and pulmonary pressures. Conversely, in patients with mitral regurgitation, the increase in intravascular volume (preload) is offset by the decrease in systemic vascular resistance (afterload) and hence is generally well tolerated. The care of pregnant women with mitral valve disease requires an experienced, multidisciplinary team comprising obstetricians, cardiologists and anaesthesiologists. Ideally, care should begin with preconception counselling, assessment and optimization of haemodynamic status, and should continue through gestation, labour and delivery. This article will address maternal and fetal outcomes in women with mitral valve disease and the optimal management of these patients.

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MITRAL STENOSIS

Maternal outcomes

The adverse maternal events in women with mitral stenosis include pulmonary oedema, arrhythmia and thromboembolism; the complication rate is related to the severity of mitral stenosis and the patient's functional class. A 2001 case-control study that looked at the effect of valvular heart disease on maternal and fetal outcome in 46 pregnancies in 44 patients with mitral stenosis found a high incidence of maternal

morbidity but no mortality. Heart failure requiring hospitalization occurred in 61% of women with moderate stenosis (mitral valve area [MVA] 1–1.5 cm^2) and 78% of women with severe stenosis. Of those with moderate or severe stenosis, deterioration in functional status was noted in 82% of class I and 61% of class II patients. Outcomes in patients with mild mitral stenosis were not statistically different from controls.[3]

A Canadian cohort study that looked at 80 pregnancies in 74 women provides further evidence that severity of stenosis is an important predictor of cardiac events. The overall adverse cardiac event rate was 35%, but varied based on the severity of the valvular disease; in patients with mild (MVA $>1.5\ cm^2$), moderate (MVA 1.1–1.5 cm^2) and severe (MVA $\leq 1\ cm^2$) stenosis, the adverse cardiac event rates were 26%, 38% and 67%, respectively. Twenty-five pregnancies (31%) were complicated by pulmonary oedema and nine pregnancies (11%) were complicated by arrhythmias (atrial fibrillation and SVT), but there were no incidences of stroke, need for invasive intervention, cardiac arrest or death. Independent predictors of cardiac complications were moderate or severe stenosis (odds ratio 3.4, 95% CI 1.2–10) and a history of arrhythmia, pulmonary oedema, transient ischemic attack (TIA) or stroke prior to pregnancy (odds ratio 6.8, 95% CI 1.8–25.9).[4]

A prospective multicentre study of 599 pregnancies in women with heart disease, including 48 with mitral stenosis, identified four predictors of primary cardiac events that they defined as pulmonary oedema, sustained arrhythmia, stroke, cardiac arrest or death. The predictors were: (1) any prior cardiac event (heart failure, TIA, stroke or arrhythmia); (2) baseline NYHA class >II; (3) left heart obstruction defined by MVA $<2.0\ cm^2$ or peak left ventricular outflow gradient >30 mmHg by echocardiography; and (4) ejection fraction (EF) <40%. They found that the estimated risk of a primary cardiac event for women with 0, 1 and ≥ 2 predictors was 5%, 27% and 75% respectively. They qualify this risk index with the statement that in women with severe mitral stenosis, the model had a lower discriminative accuracy. However, this risk index may be helpful when counselling women with mitral stenosis who are considering pregnancy.[5] A summary of maternal outcomes in women with mitral stenosis is outlined in Table 1.

Fetal outcomes

Adverse fetal outcomes associated with mitral stenosis include preterm delivery, intrauterine growth retardation, low birth weight and fetal or neonatal death. The most likely explanation for these adverse events is uteroplacental insufficiency secondary to left heart obstruction. The large 2001 multicentre study by Siu *et al.* identified five predictors of neonatal events including: NYHA class >II; maternal left heart obstruction; smoking during pregnancy; multiple gestations; and use of anticoagulants during pregnancy. This places women with mitral stenosis and poor functional status among the most likely to experience adverse neonatal outcomes.[5]

In a subsequent substudy, Siu *et al.* looked at 302 pregnancies in women with heart disease compared with 572 normal pregnancies and found that neonatal events were more frequent in women with all types of heart disease (18% versus 7% in controls), but specifically left heart obstruction, cyanosis and poor functional class. Adverse outcomes were further increased in the presence of obstetric risk factors, specifically anticoagulant use, multiple gestations, maternal age and tobacco, emphasizing the importance of smoking cessation and optimization of obstetric status prior to conception. Lesion-specific risk was not addressed in this study.[6]

There is limited data regarding the risk of adverse neonatal outcome specifically in women with mitral stenosis. The case-control study by Hameed (46 pregnancies in 44 women with mitral stenosis) found that haemodynamically significant mitral stenosis increased the rate of IUGR and resulted in lower birth weights (Table 2).[3] The rate of preterm birth and stillbirth among women with mitral stenosis was higher compared with controls, but was not statistically significant.

Management

Preconception

Patients with mild-moderate mitral stenosis may first become symptomatic and be diagnosed during pregnancy when increased plasma volume and resting heart rate stress a previously compensated system. Ideally, however, women should be evaluated by a multidisciplinary team of physicians prior to a planned

Table 1 **Maternal outcomes**

Degree of stenosis	Pulmonary oedema	Arrhythmias	Need for cardiac medications	Hospitalizations	Stroke	Cardiac arrest or death
Mild (>1.5 cm^2)	19.7% (12/61)	8.2% (5/61)	5.3% (1/19)	10.5% (2/19)	0% (0/42)	0% (0/61)
Moderate (1.0–1.5 cm^2)	44.7% (21/47)	14.9% (7/47)	72.2% (13/18)	61.1% (11/18)	0% (0/29)	0% (0/47)
Severe (<1.0 cm^2)	66.7% (12/18)	33.3% (6/18)	100% (9/9)	77.8% (7/9)	0% (0/9)	0% (0/18)

Combined data from Silversides and Hameed

Table 2 **Fetal outcome in patients with valvular heart disease versus controls**

	IUGR			Birth weight (g)		
Degree of stenosis	PTS	CTRL	*P*	PTS	CTRL	*P*
Mild *n*=19	16%	0%	0.6	3.135 ± 419	3.288 ± 531	0.3
Moderate *n*=18	27%	0%	0.1	2.706 ± 1.039	3.427 ± 426	0.02
Severe *n*=9	33%	0%	0.5	2.558 ± 947	3.332 ± 403	0.05
All *n*=46	24%	0%	<0.001	2.845 ± 818	3.372 ± 486	0.02

*Adapted from Hameed *et al.*[3]
IUGR = intrauterine growth restriction; PTS = patients; CTRL = controls

pregnancy. They should be informed of the maternal and fetal morbidity and mortality associated with their condition. Assessment should include a thorough cardiac, obstetric and family history, physical exam, CBC, EKG and echocardiogram. Ideally, an echocardiogram should be obtained within six to 12 months prior to pregnancy. During pregnancy, echocardiographic gradients across the mitral valve will be falsely elevated secondary to increased cardiac output, and thus will overestimate the severity of mitral stenosis (the gradient increases by the square root of the CO). Hence, MVA should be based on independent echocardiographic measurements and calculations.[7]

Women with moderate to severe mitral stenosis (MVA $\leq$1.5 cm^2 or mean gradient $\geq$5 mmHg) who are symptomatic (NYHA functional class II) should be evaluated for percutaneous balloon mitral valvuloplasty (PBMV) prior to conception.[3,4,8] This is a class I indication for all patients from the 2006 The American College of Cardiology/American Heart Association (ACC/AHA) guidelines. Furthermore, women with at least moderate mitral stenosis have an increased risk of pulmonary oedema and arrhythmias, and an increased fetal morbidity and mortality.

Medical management

Medical therapy should be targeted towards decreasing heart rate, which will increase left ventricular filling time and thereby decrease left atrial pressure. Many women with moderate to severe stenosis will do well with a limitation of physical activity, avoiding the increase in heart rate and blood pressure associated with exercise. However, in the case-control study by Hameed *et al.*, 50% of patients with mitral stenosis required cardiac medications during their pregnancy. These included beta-blockers, calcium channel blockers, digoxin, heparin, hydralazine and aspirin.[3] Although ACE inhibitors are effective afterload-reducing agents in the non-pregnant population, they are contraindicated in pregnancy secondary to their teratogenic effects. Beta-blockers are the cornerstone of medical therapy in patients with haemodynamically significant mitral stenosis. The resultant decrease in heart rate allows left ventricular filling at lower left atrial and hence pulmonary pressures. Beta-1 selective agents are recommended to minimize the beta-2-mediated effects of uterine relaxation. At least two studies have demonstrated an increase in IUGR in women treated with atenolol during pregnancy, so metroprolol is the drug of choice.[9,10] In a study of 25 pregnant women with symptomatic, moderate to severe mitral stenosis (MVA = 1.1 cm^2), treatment with beta-blockers resulted in improvement in or stabilization of NYHA functional class to $\leq$II in 92%.[11]

Chronic diuretics should be used with caution to avoid hypoperfusion of the placenta, but they have been used successfully in women with acute pulmonary oedema due to peripartum cardiomyopathy and mitral stenosis without adverse risk to the fetus.[12] Sodium restriction and modest fluid restriction should be recommended in symptomatic women. In women who develop atrial fibrillation, digoxin has been shown to improve rate control and has a long safety record in pregnancy.[13] Atrial fibrillation confers an increased risk of thromboembolism; therefore, subcutaneous unfractionated heparin in doses of 10–20,000 units twice-daily adjusted to target a partial thromboplastin time (PTT) 1.5 times normal should be initiated.[14] Conversely therapeutic, adjusted-dose low-molecular-weight heparin has been used with careful monitoring of antifactor Xa levels as most pregnant patients will require an upward dose adjustment to maintain therapeutic levels.[15] Patients with a dilated left atrium are at increased risk for developing both atrial fibrillation and thrombus. However, because the majority of fibrillation episodes will be symptomatic in this population, routine anticoagulation based on left atrial dimensions alone is not currently recommended.[16]

Endocarditis prophylaxis at the time of labour and delivery is a controversial topic in pregnant women with rheumatic mitral stenosis. The ACC/AHA guidelines do not recommend prophylactic antibiotics in women with valvular disease undergoing uncomplicated vaginal delivery or caesarian section. Antibiotics are optional in women who have a prior history of endocarditis.[17] A study from Ireland in 1980 demonstrated that the rate of bacteraemia following spontaneous vaginal delivery in the absence of a known infection was 2.15%. This compares with a peripheral blood bacterial isolation rate after dental extraction of 60–90%.[18] More recent studies, however, have demonstrated a higher rate of bacteremia following labour and delivery, ranging from 5–19%.[12] Given this data, the use of antibiotics is probably prudent for women who experience prolonged rupture of the membranes prior to delivery. The American Heart Association recommends ampicillin plus gentamicin at the initiation of labour or within 30 minutes of caesarean section, with a second dose of ampicillin or amoxicillin six hours later. Vancomycin may be substituted for ampicillin if allergies preclude its administration.

Percutaneous balloon mitral valvuloplasty

Percutaneous balloon mitral valvuloplasty (PBMV) is the treatment of choice for isolated, non-calcified mitral stenosis and should ideally be performed preconception in symptomatic patients. The indications are congestive heart failure (CHF), NYHA Class >II and MVA <1.5–1.7 cm^2 and contraindications include left atrial thrombi, >2+ mitral regurgitation (MR), and subvalvular stenosis. Complications of the procedure are rare, the most common being mitral regurgitation, which occurs in 12% of patients.[19] A randomized trial of 60 patients with severe mitral stenosis found PBMV to be comparable to open surgical commissurotomy both initially and at three years follow-up.[20]

PBMV has been well established in several case series as a treatment option for pregnant women with class III and IV heart failure who are refractory to medical management. The immediate short-term success rate approaches 100% with few adverse maternal or fetal events. Esteves *et al.* recently reported on a cohort of 71 women who underwent PBMV in Brazil. All of the women were in class III or IV heart failure despite maximal medical therapy and had echocardiographic findings of severe mitral stenosis. PBMV resulted in significant decreases in mean left atrial (LA) pressure (25.3 $\pm$ 8.1 to 12 $\pm$6.1 mm Hg, P <0.001), mean diastolic mitral gradient (18.0 $\pm$ 7.0 to 3.9 $\pm$ 3.1 mmHg, $P < 0.01$) and mean pulmonary artery pressure (38 $\pm$ 15 to 24 $\pm$ 11 mmHg, $P < 0.05$). The mean MVA increased from 0.9 to 2.0 cm^2. Thromboembolic events occurred in two of the 71 patients, but with no permanent vascular or neurological sequelae. At the conclusion of the pregnancy, 98% of women were in NYHA functional class I or II.[21]

Mitral valve surgery

If PBMV is not available, open mitral valve commissurotomy can be safely and quickly performed, but does require general anaesthesia with the attendant risks. Several case series and

reviews have suggested that pregnancy does not confer an increased risk of maternal morbidity and mortality. However, a review of the period from 1984 to 1996 including 58 patients with native valve disease found a maternal mortality rate of 9%, approximately two- to four-fold higher than the non-pregnant population. Fetal or neonatal mortality was significant at 29%.[22] In an older, non-randomized study comparing PBMV with open commissurotomy, de Souza *et al.*[23] found that PBMV resulted in significantly less fetal morbidity and mortality (neonatal mortality rate 1/21 in the PBMV group and 8/24 in the surgical group, $P = 0.025$). If surgery is required prior to delivery, cardiopulmonary bypass should be done at normal temperature and high flow and pressure for as brief a time period as possible. In patients with mixed stenosis and regurgitation, mitral valve replacement is the only treatment of choice but, given then higher maternal and fetal morbidity and mortality, should be reserved for symptomatic patients who have failed aggressive, in-house medical therapy.

Labour and delivery

Cardiovascular loading conditions are dramatically altered during labour and delivery and are predominately driven by pain and anxiety. The first stage of labour results in a 20–30% increase in cardiac output; uterine contractions cause an additional 20% increase of cardiac output and blood pressure. Following delivery, relief of vena caval compression and autotransfusion from the emptied and contracted uterus cause additional rises in cardiac output. An older study in healthy women found that epidural anaesthesia resulted in a significant blunting of the heart rate and cardiac output.[24] Furthermore, continuation into the postpartum period may provide increased venous capacitance to accommodate the extra blood volume, thereby reducing the risk of pulmonary oedema.

In patients with mitral stenosis, the primary treatment goal during labour is the avoidance of tachycardia and excess preload. Therefore, carefully titrated epidural analgesia with narcotics should be recommended for pain relief and prompt treatment of the anticipated hypotension by the judicious use of crystalloids and pure vasoconstrictors such as phenylephrine. In patients with severe mitral stenosis, Swan–Ganz catheterization for haemodynamic monitoring can allow optimization of filling pressures and should be continued for 12–24 hours postpartum. For these patients, the second stage of labour and Valsalva efforts should be reduced and shortened by instrumental delivery.[12] In this way, vaginal delivery can be safely accomplished in women with mitral stenosis, with caesarean section reserved for obstetric indications. This was the primary mode of delivery in the series by Hameed *et al.*[3] (92%) and Silversides *et al.*[4] (74%).

MITRAL REGURGITATION

In women of childbearing years, mitral regurgitation is most commonly due to mitral valve prolapse or acquired rheumatic heart disease and rarely due to acute endocarditis. Chronic mitral regurgitation, even if severe, is well tolerated in pregnancy if the patient has good left ventricular systolic function and is asymptomatic. The decreased systemic vascular resistance and systolic blood pressure are haemodynamically favourable for patients with mitral regurgitation. Mitral valve repair or replacement prior to pregnancy should only be done if there are clinical indications based on the ACC/AHA guidelines, particularly since pregnancy after mechanical mitral valve replacement is complicated by the concomitant use of anticoagulation. Angiotension-converting enzyme inhibitors are contraindicated in pregnancy and should be avoided. If vasodilatory agents are required for symptomatic relief, hydralazine and nitrates can be used. As mentioned above, the risks of cardiovascular surgery during pregnancy are significant, and surgery should be reserved for patients failing maximal medical therapy. In the patient with severe regurgitation and reduced ventricular ejection fraction or Class III and IV functional status, labour and delivery should take place with carefully titrated epidural anaesthesia and invasive haemodynamic monitoring.

CONCLUSIONS

Mitral stenosis is the most common cardiac condition affecting women during pregnancy and is poorly tolerated due to the increased intravascular volume, cardiac output and resting heart rate that predictably occur during pregnancy. Patients at high risk for complications include those with class II–IV symptoms with mitral stenosis, III and IV symptoms with mitral regurgitation, severe pulmonary hypertension defined as 75% of systemic pressures or left ventricular dysfunction defined as EF $<40\%$.[16] Moreover, the severity of the stenosis is an important predictor of adverse maternal outcomes, including congestive heart failure and atrial arrhythmias. Patients with mild mitral stenosis appear to do as well as controls. Close follow-up and medical management with beta-1 selective antagonists and cautious use of diuretics is recommended for symptomatic relief in patients with mitral stenosis and heart failure symptoms. PBMV has been performed successfully in women who fail medical therapy and is recommended over open commissurotomy. The goal of labour and delivery is to minimize tachycardia by controlling pain with the use of epidural anaesthesia. Vaginal delivery can be safely performed, with caesarian section reserved for patients with obstetric indications. In contrast to the negative impact of the haemodynamic changes of pregnancy on mitral stenosis, the decreased systemic vascular resistance is haemodynamically favourable for patients with mitral regurgitation. Mitral regurgitation with a normal ejection fraction is well tolerated during pregnancy. Patients with mitral valve disease should be evaluated preconception when possible and should be followed closely by a team of specialists, including obstetricians, cardiologists and anaesthesiologists, throughout the pregnancy and early postpartum period.

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(Accepted 14 May 2008)