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Cardiac Risk in Pregnant Women With Rheumatic Mitral Stenosis

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The primary objective of this report was to define the predictors for maternal cardiac complications in a contemporary cohort of pregnant Canadian women with rheumatic mitral stenosis (MS). We also examined changes in the echocardiographic assessment of lesion severity during and after pregnancy.

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This investigation examined consecutive women with rheumatic MS receiving obstetric care at the Toronto General or Mount Sinai Hospitals between 1986 and 2000. Baseline and pregnancy outcome data on all pregnancies in women with heart disease receiving care at the participating institutions were entered into the University of Toronto Pregnancy and Heart Disease Research Program computer database after validity checks.[1,2] Clinical data were obtained during the antepartum (baseline) period, peripartum period, and ≤6 weeks postpartum. The research ethics board of the participating institutions approved the study. Sixty-seven women in this study have also been included in previous non–lesion-specific studies examining women with a broad spectrum of cardiac lesions.[1,2] Women with prosthetic heart valves or severe rheumatic aortic stenosis (aortic valve area <1.0 cm^2) were excluded. Pregnancies that ended in termination (14 pregnancies) or miscarriage (fetal death <20 weeks gestation, 4 pregnancies) were also excluded.

MS was assessed echocardiographically in all patients. Transmitral mean gradient and mitral valve area were calculated using validated methods.[3] Classification of valve lesion severity was based on current guidelines (mild MS was defined as a valve area >1.5 cm^2, moderate MS between 1.1 and 1.5 cm^2, and severe MS ≤1 cm^2).[4] Mitral and aortic regurgitation was assessed by Doppler color flow criteria.[5,6] Right ventricular systolic pressure was estimated from the peak velocity of the tricuspid regurgitation jet.[7] Left ventricular systolic function was assessed visually.[8] In a subset of patients who underwent serial echocardiography at the Toronto General Hospital echocardiographic laboratory, comparisons were made between the echocardiographic measurement of the valve area, mean gradient, and right ventricular systolic pressure in the late antepartum period and within 4 to 12 months postpartum.

Data are presented as mean ± 1 SD. Characteristics of pregnancies in women who developed cardiac complications were compared with those who did not using chi-square or *t* tests as appropriate. Logistic regression was used to determine predictors of maternal cardiac complications. The Wilcoxon signed rank test was used to determine differences in serial echocardiographic measurements. A p value of 0.05 was considered statistically significant.

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TABLE 1 Baseline Characteristics

Variable	Pregnancies (n = 80)
No. of women	74
Mother's age (yrs) at time of entry into study (mean ± SD)	32 ± 5
Mean gestational age (mo) at time of entry into study	15 (range 5–39)
Parity	
0	28 (35%)
1	38 (47%)
2	10 (13%)
≥3	4 (5%)
NYHA functional class at entry	
I	71 (89%)
II	9 (11%)
Previous cardiac event*	14 (18%)
Cardiac medications before pregnancy†	10 (13%)
Anticoagulants before pregnancy‡	7 (9%)
Pulmonary hypertension§	11 (14%)
History of valvotomy/valvuloplasty	27 (34%)
Valvotomy	20 (25%)
Valvuloplasty	12 (15%)
Degree of MS: valve area (cm^2)	
>1.5	42 (53%)
1.1–1.5	29 (36%)
≤1.0	9 (11%)
Associated lesions	
Moderate mitral regurgitation	34 (43%)
Severe mitral regurgitation	4 (5%)
Moderate aortic regurgitation	12 (15%)
Severe aortic regurgitation	3 (4%)
Left ventricular ejection fraction <40%	1 (1%)

*Defined as arrhythmia, pulmonary edema, transient ischemic event, or stroke before to pregnancy (for those who underwent cardiac intervention, only events after intervention were considered).

†Medications included digoxin, diuretics, or β-adrenergic blockers.

‡Anticoagulants included warfarin, unfractionated heparin, and low molecular weight heparin (warfarin was not continued during pregnancy).

§Defined as a right ventricular systolic pressure >50 mm Hg by echocardiography in the absence of pulmonary stenosis.

NYHA = New York Heart Association.

Table 1 lists baseline characteristics of the cohort. Seventy-four women had 80 pregnancies; 77% of women were non-Caucasian. The baseline echocardiographic assessment was performed in the first, second, and third trimester in 39%, 44%, and 17% of pregnancies, respectively. Nineteen percent of pregnancies occurred in women with combined mitral and aortic valve disease. There were no significant baseline differences between the study group and those excluded (due to termination or miscarriage) with respect to maternal age, history of cardiac events, severity of MS, or systolic pulmonary artery pressure.

Thirty-five percent of pregnancies were associated with maternal cardiac complications (Table 2). Pulmonary edema occurred in 31% (25 of 80) and arrhythmias occurred in 11% (9 of 80) of pregnancies. Twenty percent of the pregnancies complicated by pulmonary edema occurred in the setting of atrial tachyarrhythmias. In 60% (15 of 25) of pregnancies complicated by pulmonary edema, the first episode of pulmonary edema occurred in the antepartum period (mean gestational age 30 ± 0.4 weeks). Of the 9 women who developed arrhythmias during pregnancy, 70% had atrial fibrillation and 30% had supraventricular tachycardia; there were no cases of ventricular tachycardia. There were no embolic events and no maternal cardiac deaths. Women with mild, moderate, and severe MS had cardiac complication rates of 26% (11 of 42), 38% (11 of 29), and 67% (6 of 9), respectively ($p < 0.001$; see Table 2, and Figure 1). Of the pregnancies in women with mild MS, there was no significant difference in the presence of severe mitral regurgitation (9% vs 6%, $p = 1.0$) or severe aortic regurgitation (0% vs 9%, $p = 0.56$) between those with and those without cardiac complications.

Eleven percent of women (9 of 80) were symptomatic before pregnancy and were in New York Heart Association functional class II (Table 3). There was no significant difference in cardiac complication rates between pregnancies in asymptomatic women and those who were symptomatic before pregnancy (35% vs 33%; $p = 0.29$). A higher fetal and/or neonatal complication rate was observed in women who were symptomatic before pregnancy compared with pregnancies in asymptomatic women (56% vs 26%, $p = 0.11$), but this difference did not reach statistical significance. Forty percent of pregnancies (32 of 80) were associated with worsening of New York Heart Association functional status by ≥2 classes when compared with prepregnancy status. Compared with 13% of women before pregnancy, 68% of women were receiving digoxin (25 of 80), β-adrenergic blockers (22 of 80), or diuretics (24 of 80) at the time of discharge from the hospital. All women who developed pulmonary edema during pregnancy responded to medical therapy; therefore, mitral valvuloplasty during pregnancy was not performed in this series.

Mean age of intervention was 7 ± 7 years before pregnancy in women who underwent a therapeutic intervention before pregnancy. There was no difference in the mean mitral valve area (1.6 ± 0.4 vs 1.7 ± 0.6 cm^2, $p = 0.18$) or the fetal and/or neonatal event rate (36% vs 26%; $p = 0.49$) between pregnancies in women who had undergone intervention and those who did not undergo valvotomy or valvuloplasty before pregnancy. There was a trend toward fewer cardiac events in women who underwent intervention before pregnancy (46% vs 29%; $p = 0.12$).

Adverse fetal or neonatal outcomes complicated 30% of all pregnancies (Table 2). The frequency of adverse fetal and/or neonatal events increased with the severity of MS ($p < 0.001$; Table 2). Respiratory distress syndrome occurred in conjunction with premature neonates or neonates small for gestational age in 6% of deliveries. One stillbirth (23 weeks gestation) occurred in a woman with mild MS and 1 neonatal death (7 days postpartum) occurred in a woman with severe MS.

Vaginal delivery with regional anesthesia was the mode of delivery in 74% of pregnancies (59 of 80; assisted delivery in the second stage of labor in 12).

TABLE 2 Maternal Cardiac and Fetal and/or Neonatal Outcomes (lesion severity)

Outcomes	All Pregnancies (n = 80)	Degree of MS		
		Mild (n = 42)	Moderate (n = 29)	Severe (n = 9)
Any maternal cardiac or fetal/neonatal event*	42 (53%)	17 (40%)	18 (62%)	7 (78%)
Maternal cardiac event*	28 (35%)	11 (26%)	11 (38%)	6 (67%)
Pulmonary edema	25	10	10	5
Arrhythmias	9	3	3	3
Stroke	0	0	0	0
Need for invasive intervention	0	0	0	0
Cardiac arrest or death	0	0	0	0
Fetal and/or neonatal event*	24 (30%)	9 (21%)	11 (38%)	4 (44%)
Premature birth	17	6	8	3
Small for gestational age	6	2	4	0
Respiratory distress	5	3	2	0
Intraventricular hemorrhage	0	0	0	0
Fetal and/or neonatal death	2	1	0	1
Maternal obstetric event	6 (8%)	4 (10%)	2 (7%)	0
Postpartum hemorrhage	5	3	2	0
Pregnancy-induced hypertension	1	1	0	0

*Events are not mutually exclusive.
n = number of pregnancies.

Cesarean delivery was performed in 26% of pregnancies (21 of 80); 1 cesarean delivery was performed for maternal cardiac indications and the remaining cesareans were performed for obstetric indications.

Eleven percent of pregnancies (9 of 80) occurred in women receiving anticoagulation therapy; 4 women received subcutaneous unfractionated heparin and 5 women received subcutaneous low molecular weight heparin. Indications for anticoagulation included atrial fibrillation (n = 2), history of cerbrovascular events (n = 2), deep venous thrombosis (n = 3), placental thrombosis (n = 1), and the presence of an atrial clot (n = 1). No obstetric bleeds were observed in women who received anticoagulation therapy.

Significant univariate predictors that were entered into the multivariate model included history of cardiac events, moderate or severe MS (mitral valve area ≤ 1.5 cm^2), presence of pulmonary hypertension, and history of valvotomy or valvuloplasty. Moderate or severe MS, as determined at the time of the first antenatal echocardiogram (odds ratio 3.4, 95% confidence interval 1.2 to 10.0), and a history of cardiac events before pregnancy (odds ratio 6.8, 95% confidence interval 1.8 to 25.9) were independent predictors of cardiac complications.

Seventeen women underwent serial echocardiographic assessment. There was no significant difference in the mitral valve area measured by the pressure half-time method during pregnancy compared with that measured after pregnancy. However, a significant decrease occurred in mitral valve mean gradient and right ventricular systolic pressure after pregnancy. Mean change in right ventricular systolic pressure primarily reflects the changes seen in patients with increased pressures in the antepartum period (>60 mm Hg; Figure 2).

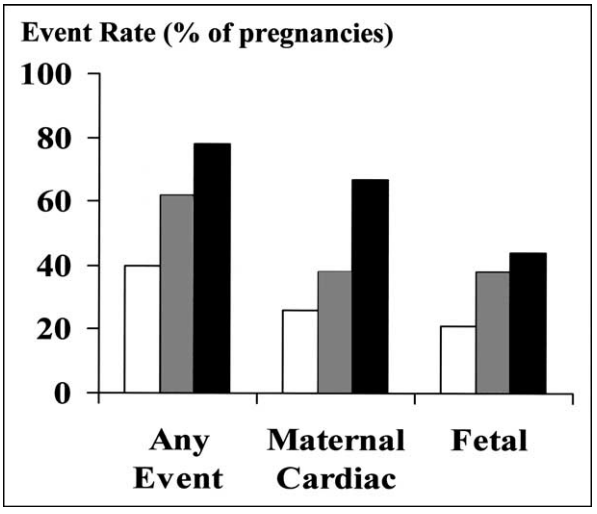

FIGURE 1. Relation between severity of MS and frequency of adverse maternal cardiac, fetal, or neonatal events. Any event refers to cardiac, neonatal, or fetal events. *White bars* indicate pregnancies in women with mild MS; *gray bars* indicate women with moderate MS; and *black bars* indicate women with severe MS.

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There were no maternal deaths during pregnancy in this investigation of a contemporary cohort of Canadian women with rheumatic MS. However, pulmonary edema, cardiac arrhythmia, and fetal and/or neonatal complications continued to be frequent. Moderate or severe MS and a history of cardiac events before pregnancy were independent predictors of maternal cardiac complications during pregnancy. Most women received some form of medical therapy during pregnancy, although

TABLE 3 Maternal Cardiac and Fetal and/or Neonatal Outcomes (functional class before pregnancy)

	Degree of MS					
	Mild		Moderate		Severe	
	I* (n = 39)	II* (n = 3)	I* (n = 24)	II* (n = 5)	I* (n = 8)	II* (n = 1)
Maternal cardiac event†	11 (28%)	0	8 (33%)	3 (60%)	6 (75%)	0
Pulmonary edema	10	0	7	3	5	0
Arrhythmias	3	0	2	1	3	0
Fetal and/or neonatal event†	8 (21%)	1 (33%)	8 (33%)	3 (60%)	3 (38%)	1 (100%)
Premature birth	6	0	5	3	2	1
Small for gestational age	1	1	3	1	0	0
Respiratory distress	3	0	2	0	0	0
Intraventricular hemorrhage	0	0	0	0	0	0
Fetal and/or neonatal death	1	0	0	0	1	0

*New York Heart Association functional class before pregnancy.
†Events are not mutually exclusive.
Abbreviation as in Table 2.

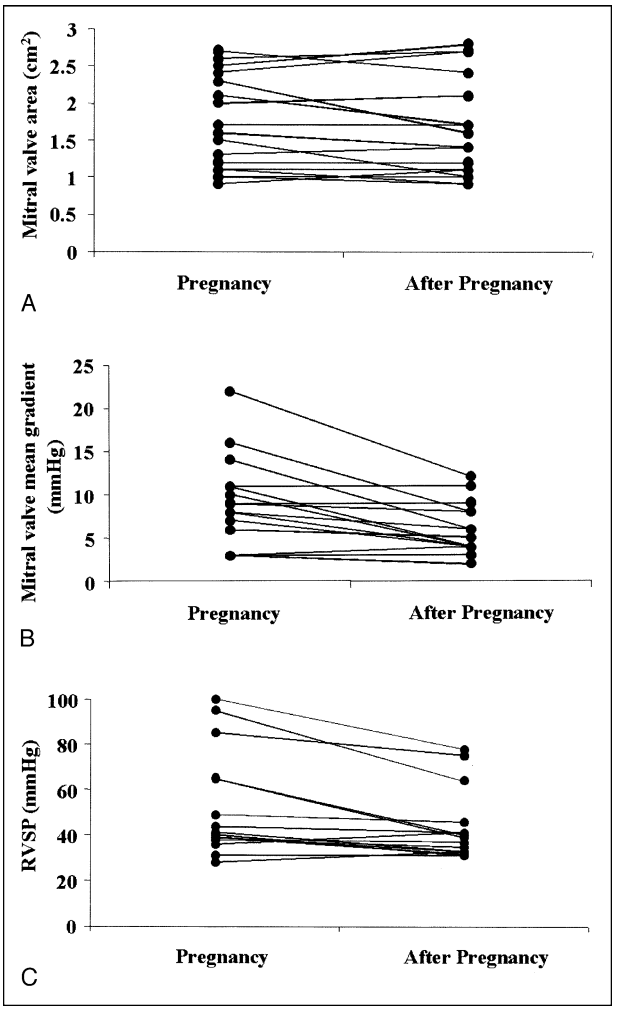

FIGURE 2. Changes in echocardiographic measurements in 17 patients during and after pregnancy. *(A)* mitral valve area as measured by the pressure halftime method during and after pregnancy (1.7 ± 0.6 vs 1.6 ± 0.7 cm^2, p = 0.30); *(B)* mitral valve mean gradient (9.3 ± 5.0 vs 6.2 ± 3.0 mm Hg, p = 0.003); *(C)* right ventricular systolic pressure (RVSP) (51 ± 22 vs 42 ± 15 mm Hg, p = 0.004).

surgical or percutaneous valvuloplasty was not performed. Because of the substantial rate of complications in this population of mostly asymptomatic women with less advanced forms of MS who are receiving modern antenatal care, it may be time to define the role of medical therapy (such as β-adrenergic blockade) and percutaneous valvuloplasty in preventing cardiac and neonatal complications in pregnant women with MS. Echocardiographic assessment of the mitral valve area calculated by the pressure halftime method remained constant during and after pregnancy, suggesting that this measure can be used during pregnancy to assess the severity of MS, whereas assessing the severity of MS by the mitral valve gradient alone may be misleading.

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