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Pregnancy Outcomes in Women With Dilated Cardiomyopathy

Jasmine Grewal, MD,* Samuel C. Siu, MD, SM,*† Heather J. Ross, MD,‡ Jennifer Mason, RN,* Olga H. Balint, MD,* Mathew Sermer, MD,* Jack M. Colman, MD,* Candice K. Silversides, MD, SM*

Toronto and London, Ontario, Canada

Objectives The objectives of this study were to determine adverse outcomes during pregnancy in women with dilated cardiomyopathy (DCM) and to compare their cardiac outcomes with those of nonpregnant women with DCM.

Background Women with DCM are at risk for complications during pregnancy, but few studies have examined outcomes in this specific population.

Methods This was a substudy of a larger prospective cohort study of outcomes in women with heart disease. Maternal cardiac, obstetric, and fetal outcomes in pregnancy in women with DCM were examined. For comparison, cardiac outcomes in nonpregnant women with DCM ($n = 18$) matched by age and left ventricular (LV) systolic function were examined. A matched-pair survival analysis was used to compare groups.

Results Thirty-six pregnancies in 32 women with DCM were included. Thirty-nine percent (14 of 36) of the pregnancies were complicated by at least 1 maternal cardiac event. In the multivariate analysis, moderate or severe LV dysfunction and/or New York Heart Association functional class III or IV ($p = 0.003$) were the main determinants of adverse maternal cardiac outcomes during pregnancy. In the subset of women with moderate/severe LV dysfunction, 16-month event-free survival was worse in pregnant women compared with nonpregnant women ($28 \pm 11\%$ vs. $83 \pm 10\%$, $p = 0.02$). The adverse neonatal event rate was highest among women with obstetric and cardiac risk factors (43%).

Conclusions In pregnant women with DCM the risk of adverse cardiac events is considerable, and pre-pregnancy characteristics can identify women at the highest risk. Pregnancy seems to have a short-term negative impact on the clinical course in women with DCM. (J Am Coll Cardiol 2010;55:45–52) © 2010 by the American College of Cardiology Foundation

Women with dilated cardiomyopathy (DCM) are at risk for complications during pregnancy if they are unable to adapt to the hemodynamic changes of pregnancy. In the Confidential Enquiries into Maternal Death in the United Kingdom, maternal cardiac deaths during pregnancy, although rare, were frequently related to ventricular dysfunction (1). However, little is known about cardiac morbidity or risk stratification in this population. Although the literature generally advises against pregnancy in women with significant left ventricular (LV) systolic dysfunction (left ventricular ejection fraction [LVEF] <30%), there are minimal data to support this recommendation (2). Counseling about the safety of pregnancy can have a major impact on prospective mothers, and it is therefore important that more data be available to help provide appropriate advice about pregnancy risks to women with a DCM. Therefore, the purposes of this study were: 1) to examine adverse maternal cardiac, obstetric, and fetal and/or neonatal events in a contemporary group of women with DCM undergoing pregnancy; and 2) to determine the impact of the pregnancy on the clinical course of the disease by comparing adverse cardiac events in pregnant versus nonpregnant women with DCM and significant LV systolic dysfunction.

Methods

Study population. Women with previously documented idiopathic or doxorubicin-induced DCM were enrolled in our ongoing prospective pregnancy outcomes study between De-

From the *University of Toronto Pregnancy and Heart Disease Research Program, University Health Network, and Mount Sinai Hospital, Toronto, Ontario, Canada; †Division of Cardiology, Department of Medicine, University of Western Ontario, London, Ontario, Canada; and the ‡University of Toronto Heart Function Program, Division of Cardiology, University Health Network, Toronto General Hospital, Peter Munk Cardiac Centre, Toronto, Ontario, Canada. Supported by operating grants from Canadian Institutes of Health Research (53130 and 93722), Heart and Stroke Foundation of Canada (NA 5662 and 5927), the Ramsay Gunton Professorship in Cardiology from the Schulich School of Medicine and Dentistry (to Dr. Siu), and a generous donation from Mrs. Josephine Rogers. Dr. Grewal is the recipient of the Gordon B. and Shannon D. Allan Fellowship in Adult Congenital Heart Disease, Toronto, Canada.

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Abbreviations and Acronyms

DCM = dilated cardiomyopathy

LV = left ventricle/ventricular

LVEF = left ventricular ejection fraction

NYHA = New York Heart Association

cember 1994 and July 2008 (3,4). A DCM was defined as a dilated ventricle with reduced LVEF in the absence of coronary, valvular, congenital, or any systemic diseases known to cause myocardial dysfunction (5). Women with cardiomyopathies from other causes, including peripartum cardiomyopathy, were excluded. Peripartum cardiomyopathy was defined by: 1) the development of heart failure in the last month of pregnancy or within 5 months of delivery; 2) an LVEF <45% by echocardiography; 3) absence of an identifiable cause for the cardiac failure; and 4) absence of recognizable heart disease before the last month of pregnancy. Nonpregnant women were matched with pregnant women by age, diagnosis, degree of LV systolic dysfunction, and year of pregnancy (year of initial clinic visit) and followed up over 16 months to ascertain event rates. For the purpose of this comparison, only women with moderate or severe LV dysfunction (LVEF <45%) were included. This study received institutional ethics approval.

Baseline data and follow-up. Details pertaining to data collection in women with heart disease followed up in our Pregnancy and Heart Disease Research Program at University Health Network and Mount Sinai Hospitals have been described elsewhere (3). All pregnant women were followed up prospectively from the start of pregnancy until 6 months post-partum. Clinical, electrocardiographic, and echocardiographic data were collected at the time of clinic visits. These baseline data were recorded: age, comorbid medical conditions (pulmonary disease, thyroid dysfunction, hypertension, diabetes mellitus), smoking history, New York Heart Association (NYHA) functional class, prior cardiac events (heart failure, transient ischemic attack, arrhythmias, or stroke), prior cardiac interventions, use of cardiac medications, and anticoagulation. In the group of pregnant women, these additional baseline data were recorded: gestational age and parity status. Medication use was recorded at the time of the first antenatal visit among pregnant women. In many instances, cardiac medications recorded at the first antenatal visit were not representative of the medications used before pregnancy because medications such as angiotensin-converting enzyme inhibitors had already been discontinued by an alternate care provider or were stopped before conception. Obstetric risk factors associated with adverse fetal and/or neonatal events were also recorded for the pregnant group of women and included history of premature delivery or rupture of membranes, incompetent cervix, and cesarean section, and during the present pregnancy included intrauterine growth retardation, antepartum bleeding >12 weeks gestation, febrile illness, or uterine/placental abnormalities (3,6–9).

Echocardiographic assessment included left and right ventricular systolic function, valvular function, and systolic pulmonary artery pressure (4,10). Left ventricular systolic function was given a functional grade assessment: normal (LVEF >55%), mild (45% to 54%), moderate (30% to 44%), or severe (<30%) (11). The modified Quinones method was used to calculate LVEF (12), with subsequent visual estimation if endocardial definition was suboptimal. An experienced echocardiographer interpreted all echocardiograms.

Nonpregnant and pregnant women were followed up for an equal length of time (16 months). The beginning of follow-up in the nonpregnant group was at the time of their first visit to the heart failure clinic at our institution. Baseline clinical, electrocardiographic, and echocardiographic data as described earlier were recorded. Medication use at the time of first heart failure clinic visit was recorded.

Outcomes. Adverse events during the antepartum, peripartum, and post-partum periods were classified as cardiac, fetal and/or neonatal, and obstetric. Two physicians blinded to the women's baseline characteristics independently verified adverse events. Adverse cardiac events for both pregnant women and nonpregnant control subjects were defined as pulmonary edema (documented by chest radiograph or by crackles heard over at least one-third of posterior lung fields); sustained symptomatic tachyarrhythmia or bradyarrhythmia requiring treatment; stroke, angina, or myocardial infarction; cardiac arrest; or cardiac death. Fetal and neonatal complications were defined as premature birth (<37 weeks gestation), small-for-gestational-age birth weight (<10th percentile for gestational age), respiratory distress syndrome, intraventricular hemorrhage, fetal death (20 weeks gestation and before birth), or neonatal death (from birth to age 28 days). Obstetric complications were maternal death from noncardiac causes, pregnancy-induced hypertension (increase of 30 mm Hg in systolic blood pressure and 15 mm Hg in diastolic blood pressure compared with baseline values), or post-partum hemorrhage (blood loss >500 ml after vaginal delivery or >1,000 ml after cesarean section, requiring transfusion or accompanied by a decrease in hemoglobin level ≥20 g/l).

Statistics. All data were analyzed using SPSS version 16.0 (SPSS Inc., Chicago, Illinois). Data are presented as median value with interquartile range, and in some instances ranges are also provided. Univariate predictors of maternal cardiac complications during pregnancy in women with DCM were determined using univariate logistic regression analysis. A multivariate logistic regression model was then created to identify predictors of adverse maternal cardiac events during pregnancy based on the univariate analysis. Variables identified in the univariate analysis with a value of $p < 0.1$ were included in the multivariate model. Because of the correlation between NYHA functional class and LV systolic function, a single variable was created for the multivariate model combining NYHA functional class III or IV and moderate or severe LV dysfunction.

The second analysis consisted of a comparison of outcomes in pregnant versus nonpregnant women with DCM and moderate or severe LV systolic dysfunction. Baseline characteristics between groups were determined using McNemar or

Mann-Whitney *U* tests as appropriate. Adverse cardiac events in pregnant women were compared with those in nonpregnant women. Survival in both groups was depicted using Kaplan-Meier curves, and comparison between groups was performed using a matched-pair survival analysis. A value of $p < 0.05$ (2-sided) was considered statistically significant.

Results

Between December 1994 and July 2008, 906 women with heart disease undergoing pregnancy were prospectively followed up and enrolled in our larger cohort study. Of these, 36 pregnancies occurred in women with DCM (32 women); 84% (n = 27) with idiopathic DCM and 16% (n = 5) with doxorubicin-induced cardiomyopathy. Baseline characteristics of pregnant women and control subjects are summarized in Table 1. Of the 4 women who had an episode of heart failure before pregnancy, 2 had mild, 1 had moderate, and 1 had severe LV systolic dysfunction at the time of enrollment. One woman with severe LV dysfunction had an implantable cardioverter-defibrillator implantation. Her ventricular function had improved before pregnancy, and the lead was subsequently explanted because of a manufacturer's recall. At the time of post-partum discharge, 3 (9%) women were in NYHA functional class II, 1 (3%) was in class IV, and the remainder were in class I.

Maternal cardiac outcomes. Fourteen of 36 (39%) pregnancies (up to 6 months post-partum) in women with a DCM were complicated by at least 1 adverse maternal cardiac event (Table 2). One woman experienced heart failure at 13 weeks gestation followed by nonsustained ventricular tachycardia at 15 weeks gestation, necessitating a therapeutic abortion. Twenty-four weeks after the procedure she presented again with ventricular tachycardia. Atrial fibrillation or flutter occurred in 4 women during the antepartum period (17, 23, 28, and 36 weeks gestation), and in 1 woman during labor and delivery. Heart failure occurred in 3 pregnancies during the antepartum period (20, 28, and 38 weeks gestation), 1 during labor and delivery, and 4 during the post-partum period (2 days, 5 days, 12 weeks, and 16 weeks after delivery). A transient ischemic attack occurred in 1 woman at 19 weeks gestation. All adverse maternal cardiac events were successfully managed with medical therapy.

Characteristics predictive of an adverse cardiac event during pregnancy in univariate analysis are shown in Table 3. In multivariate analysis, moderate or severe LV systolic dysfunction and/or NYHA functional class III or IV were the main determinants of adverse maternal cardiac events during pregnancy (Table 3). A history of cardiac events before pregnancy showed a trend toward significance for predicting pregnancy-related maternal cardiac outcomes. After excluding multiple pregnancies in the same individual, the univariate and multivariate analyses were repeated (n = 4), and the results remained unchanged.

Table 1 Baseline Characteristics of Pregnant Women (n = 36)

Clinical	
Pregnancies	36
Women	32
Nulliparity	16 (44)
Age at enrollment, yrs	32 (27–35)
Other cardiac defects	
Secundum ASD*	3 (8)
MVP (>mild MR)	3 (8)
History of cardiovascular events	
Heart failure	4 (11)
Transient ischemic attack	1 (3)
Supraventricular tachycardia	2 (6)
Atrial fibrillation/flutter	2 (6)
Other medical conditions	
Hypertension	3 (8)
Hyperlipidemia	1 (3)
Smoking history	4 (11)
Epilepsy	1 (3)
Cancer†	5 (14)
Prior cardiac intervention	1 (3)
NYHA functional class	
I	24 (67)
II	6 (17)
III or IV	6 (17)
Cardiac medications at first antenatal visit	
ACE inhibitors	4 (11)
Beta-blockers	13 (36)
Digoxin	8 (22)
Diuretic	7 (19)
Echocardiographic	
Left ventricular systolic dysfunction	
Mild	18 (50)
Moderate	8 (22)
Severe	10 (28)
Moderate/severe MR	10 (28)
Moderate/severe TR	7 (19)

Data are n, n (%), or median (interquartile range). *The atrial shunt was classified as small by color Doppler and the absence of right ventricular dilation in all 3 patients. †Breast cancer in 2 patients, leukemia in 2 patients, and Wilms tumor in 1 patient.

ACE = angiotensin-converting enzyme; ASD = atrial septal defect; MR = mitral regurgitation; MVP = mitral valve prolapse; NYHA = New York Heart Association; TR = tricuspid regurgitation.

The frequency of adverse maternal cardiac events over the 16-month follow-up varied according to the severity of LV systolic dysfunction. Only 1 woman with mild LV systolic dysfunction and in baseline NYHA functional class II had an adverse cardiac event; however, she also had a history of cardiac events before pregnancy. The frequency of adverse cardiac events was similar between women with moderate or severe LV systolic dysfunction (75% [6 of 8] moderate and 70% [7 of 10] severe, p = 0.81). All women with moderate LV systolic dysfunction also had 1 other high-risk characteristic; 50% (4 of 8) had a prior cardiac event, 25% (2 of 8) were NYHA functional class III or IV, and 25% (2 of 8) had moderate or severe mitral regurgitation.

All women with adverse cardiac events during pregnancy (n = 14) had either moderate or severe LV dysfunction, NYHA functional class III or IV, and/or a previous cardiac

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Table 2 Maternal Adverse Cardiovascular Outcomes During Pregnancy

	Any Cardiac Event	Cardiac Arrest or Death	Heart Failure	Arrhythmia	Stroke/TIA	Angina or MI
Total	17	0	9	7	1	0
Timing of events						
Antepartum	10	0	4	5	1	0
Labor and delivery	2	0	1	1	0	0
Post-partum (6 months)	5	0	4	1	0	0

Events are not mutually exclusive. Fourteen pregnancies complicated by 1 or more event.
MI = myocardial infarction; TIA = transient ischemic attack.

event. There were no adverse events in women with none of these 3 clinical parameters (moderate or severe LV dysfunction, NYHA functional class III or IV, and/or a previous cardiac event). If any 1 of these 3 risk factors was present, the risk of an adverse cardiac event was 64% (14 of 22) (Fig. 1).

Obstetric and fetal/neonatal outcomes. The 36 pregnancies resulted in 37 live births, including 1 twin and 1 triplet pregnancy (Table 4). There was 1 therapeutic abortion at 20 weeks and 1 fetal death. Among the live births, the median gestational age at delivery was 38 weeks (range 28 to 41 weeks), and the median birth weight was 3,060 g (range 1,230 to 4,045 g). The most frequently used method of anesthesia was an epidural in 86% of deliveries. Eighty-one percent (29 of 36) of the deliveries were vaginal, and were induced in 11% of cases. Cesarean deliveries occurred in the remaining 7 pregnancies for these indications: previous cesarean delivery (n = 3), failure to progress (n = 1), fetal distress (n = 1), breech presentation (n = 1), and coexistent medical condition (n = 1). Cesarean delivery was not performed for cardiac indications in any of the women. The length of hospital stay was a median of 3 days (interquartile range 3 to 6 days). Adverse obstetric outcomes are shown in Table 4.

Seven of 35 (20%) pregnancies (not including the pregnancy that ended in therapeutic abortion) were complicated by an adverse fetal and/or neonatal event (Table 4). Even when the 2 multiple-gestation pregnancies (1 twin and 1 triplet) were excluded from the analysis, the fetal and/or neonatal event rate remained high at 15% (5 of 33). Fifty-three percent (19 of 36) of women had at least 1 risk factor for adverse fetal and/or neonatal events. Obstetric risk factors associated with adverse fetal and/or neonatal events included any prior history of premature delivery or rupture of membranes (n = 1), incompetent cervix (n = 0), or cesarean deliveries (n = 2). During the current pregnancy, any of these variables was also considered an obstetric risk factor: intrauterine growth retardation (n = 1), antepartum bleeding >12 weeks gestation (n = 1), febrile illness (n = 0), or uterine/placental abnormalities during the present pregnancy (n = 3). Nonobstetric risk factors included smoking (n = 4), anticoagulation use (n = 3), multiple gestation (n = 2), and maternal age <20 or >35 years (n = 11). Neonatal complications were most common in women with more severe DCM (moderate or severe LV systolic dysfunction and/or NYHA functional class III or IV) if they had concomitant obstetric risk factors (Fig. 2).

Comparisons of cardiac outcomes in pregnant versus nonpregnant women with significant LV systolic dysfunction. Because the 16-month event rate was low among pregnant women with mild LV systolic dysfunction, these women were not included in this analysis. The baseline characteristics of the 18 nonpregnant women and 18 preg-

Table 3 Predictors of Adverse Cardiac Events in Pregnant Women With Dilated Cardiomyopathy

	Adverse Cardiac Event (n = 14)	No Adverse Cardiac Events (n = 22)	OR (95% CI)	p Value
Univariate analysis				
Age, yrs	34 (24–36)	31 (29–35)	1.0 (0.9–1.1)	0.98
Nulliparity	6 (43)	10 (45)	1.1 (0.3–4.3)	0.88
Prior adverse cardiac events	6 (43)	3 (14)	4.7 (1.1–23.8)	0.05
Baseline NYHA functional class III or IV	5 (36)	1 (4)	11.7 (1.2–114.6)	0.03
Moderate or severe LV systolic dysfunction	13 (86)	5 (23)	44.2 (4.6–421.2)	0.001
Severe mitral regurgitation	5 (36)	1 (5)	11.7 (1.2–114.6)	0.04
Severe tricuspid regurgitation	4 (29)	3 (14)	2.5 (0.4–13.6)	0.28
Comorbid medical conditions	5 (36)	10 (45)	0.67 (0.17–2.6)	0.56
Moderate or severe LV dysfunction and/or NYHA functional class III or IV	13 (93)	6 (27)	16.0 (2.7–93.6)	<0.0001
Multivariate analysis				
Moderate or severe LV dysfunction and/or NYHA functional class III or IV			42.6 (3.5–517.1)	0.003
Prior adverse cardiac events			7.0 (0.6–78.8)	0.08

Values are median (interquartile range) or n (%).
CI = confidence interval; LV = left ventricle; NYHA = New York Heart Association; OR = odds ratio.

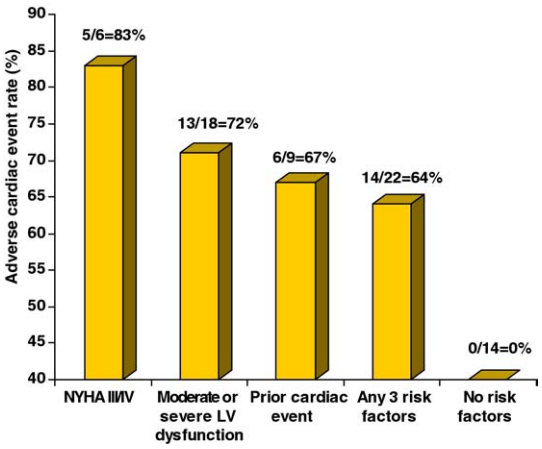

Figure 1 Incidence of Adverse Cardiac Events According to Maternal Risk Factors

The first 3 risk categories are not mutually exclusive. Any risk factor refers to the presence of any 1 of the 3 risk factors (moderate or severe left ventricular [LV] dysfunction, New York Heart Association [NYHA] functional class III or IV, previous cardiac events).

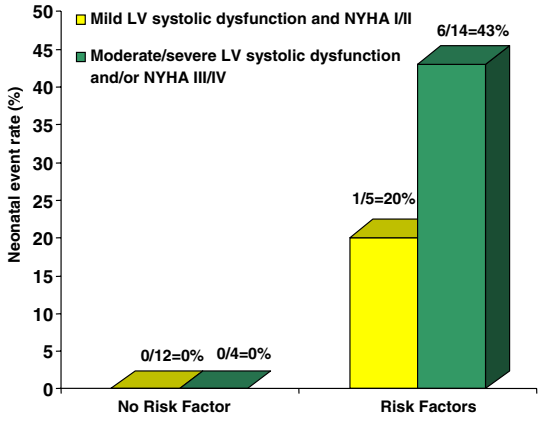

Figure 2 Frequency of Neonatal Events in Women With and Without Risk Factors

Yellow bars represent women with both mild LV systolic dysfunction and NYHA functional class I or II. **Green bars** represent women with moderate or severe LV systolic dysfunction and/or NYHA functional class III or IV. Risk factors of adverse fetal and/or neonatal events included both obstetric and nonobstetric parameters. Obstetric risk factors include a history of premature delivery or rupture of membranes, incompetent cervix, cesarean delivery, and during the present pregnancy, intrauterine growth retardation, antepartum bleeding >12 weeks gestation, febrile illness, and uterine/placental abnormalities. Nonobstetric risk factors include smoking, anticoagulation use, multiple gestation, and maternal age <20 and >35 years. Abbreviations as in Figure 1.

nant women with a DCM who had moderate or severe LV dysfunction are shown in Table 5. Significantly more nonpregnant women were taking cardiac medications during the 16-month follow-up period when compared with the pregnant women. Three nonpregnant women (17%) had events during the 16-month follow-up period: cardiac transplantation caused by refractory heart failure (n = 1), death secondary to ventricular tachycardia (n = 1), and syncope secondary to ventricular tachycardia (n = 1). In women with moderate or severe LV systolic dysfunction, adverse cardiac events were more common in pregnant women compared with nonpregnant women with a DCM (72% [13 of 18] vs. 17% [3 of 18]). The 16-month event-free survival was worse in pregnant women compared with nonpregnant women (28 ± 11% vs. 83 ± 10%, p = 0.02) (Fig. 3).

Table 4 Obstetric and Fetal Outcomes

	Pregnancies, n (%)
Adverse obstetric outcomes	
Total events*	5/36 (14)
Pre-eclampsia	3 (8)
Post-partum hemorrhage	2 (5)
Noncardiac death	0 (0)
Adverse fetal outcomes	
Total events†	7/35 (20)
Live birth weight <2,500 g	5 (14)
Pre-term delivery (<37 weeks)	5 (14)
Intraventricular hemorrhage	0 (0)
Respiratory distress	1 (3)
Fetal death‡	1 (3)
Neonatal death	0 (0)
Intrauterine growth retardation	1 (2)

*Percentage of total 36 pregnancies that had an obstetric complication. †Percentage of 35 pregnancies that had a neonatal complication (36 pregnancies minus the therapeutic abortion). Each twin and triplet pregnancy was counted as a single pregnancy: the twins and triplets all had low birth weight (<2,500 g), and the triplets were also premature (<37 weeks). ‡Occurred at 28 weeks of gestation in a woman who developed pulmonary edema.

Table 5 Characteristics of Pregnant Women Compared With Nonpregnant Women

	Pregnant Women (n = 18)	Nonpregnant Women (n = 18)	p Value
Clinical			
Nulliparity	8 (44)	18 (100)	0.002
Age at enrollment, yrs	32 (20–35)	35 (26–38)	0.15
Other medical conditions			
Hypertension	2 (11)	1 (6)	1.0
Smoking history	2 (11)	1 (6)	1.0
Hyperlipidemia	1 (5)	1 (6)	0.48
NYHA functional class III or IV	5 (28)	7 (39)	0.14
Moderate to severe LV dysfunction	18 (100)	18 (100)	1.0
Moderate dysfunction	10	10	
Severe dysfunction	8	8	
Cardiac medications*			
Any cardiac medication	11 (61)	18 (100)	0.02
ACE inhibitors	2 (11)	17 (94)	<0.0001
Beta-blockers	6 (33)	16 (89)	0.006
Digoxin	7 (39)	7 (39)	1.0
Diuretic	3 (17)	12 (67)	0.004

Values are n (%) or median (interquartile range). *Cardiac medications recorded at the first antenatal visit among pregnant women and at the time of the first heart failure clinic visit among nonpregnant women.

ACE = angiotensin-converting enzyme; LV = left ventricle; NYHA = New York Heart Association.

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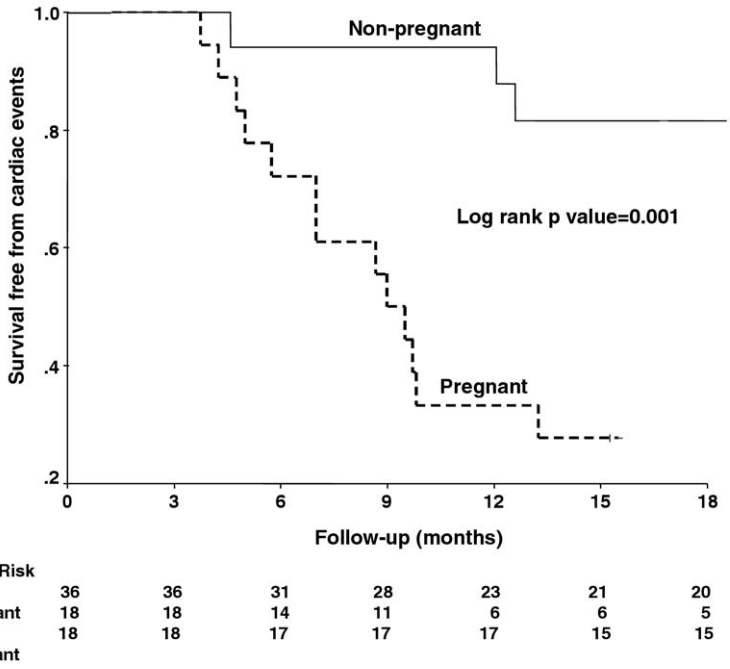

Figure 3 **Comparisons of Cardiac Outcomes in Pregnant Versus Nonpregnant Women With Significant Left Ventricular Systolic Dysfunction**

Sixteen-month survival free from adverse cardiac events in pregnant women **(dashed line)** compared with nonpregnant women **(solid line)**. Time zero is defined as: 1) the first antenatal visit for pregnant women; and 2) the index visit to the heart failure clinic for nonpregnant women.

Discussion

This is the first study to examine in detail the risks of pregnancy in women with DCM. In this cohort of pregnant women with DCM, we found that maternal cardiac complications were considerable in women with moderate or severe LV systolic dysfunction and/or NYHA functional class III or IV symptoms. In our study, women with no history of cardiac events, mild LV systolic dysfunction, and good functional class did well and did not have any cardiac complications during pregnancy. Adverse fetal and/or neonatal events were highest in women with moderate or severe LV systolic dysfunction and/or NYHA functional class III or IV if they had concomitant obstetric risk factors. Pregnancy seemed to have a negative impact on the clinical course of DCM because adverse cardiac events were more common over a 16-month period in pregnant women compared with nonpregnant women with DCM.

Cardiac complications during pregnancy in our series were high (39% of pregnancies). The most common complication was heart failure, and this typically occurred late in the pregnancy or post-partum. In 1 small prior retrospective series of women with DCM (8 women), 25% of pregnancies were complicated by adverse events; 1 woman with an LVEF of 16% required transplantation after termination of pregnancy, and in another, heart failure developed at 28 weeks of gestation (13). However, 50% of the women (4 of 8) had only mild LV systolic dysfunction. In another larger series of women with heart disease (43 women with cardiomyopathy, 18 with idiopathic DCM), adverse events occurred in 42% of pregnancies in the subset of patients with cardiomyopathy. However, the specific event rate in women with DCM was not reported (10). Furthermore, there were 3 maternal deaths in the cardiomyopathy group, but again it was not reported whether any of these deaths occurred in the setting of DCM. In our series, despite the high risk of complications in this group of women, all complications were successfully managed with medical therapy and there were no maternal deaths. This is a reassuring experience, but certainly maternal mortality is possible in high-risk women with DCM, and this possibility needs to be considered when counseling an individual. Furthermore, the late effects of pregnancy on the diseased heart are not well understood, and the effects on long-term ventricular function and prognosis require further study.

A number of prior studies have identified risk factors for adverse maternal outcomes during pregnancy, including NYHA functional class (4,14). Independent of functional status, LVEF <40% also has been shown to predict adverse events in pregnancy (4,14,15). Our findings in women with DCM are similar, although it is important to note that only a small number of women were in NYHA functional class III or IV in our study. The rate of adverse maternal cardiac events is high in this group of women, and approaches 65% if one or more of these risk factors were present: moderate

or severe LV systolic dysfunction, NYHA functional class III or IV, and/or a history of an adverse cardiac event. Alternatively, if none of these factors were present, women did not experience adverse events. These disease-specific findings are incremental to previous work and will be important in the counseling and follow-up during pregnancy in women with DCM.

Results of this study also show that pregnancy in women with DCM directly impacts the natural course of the disease, at least over the short term. We showed that cardiac complications in pregnant women were significantly more common compared with those in nonpregnant women during a 16-month follow-up period. The increased incidence of adverse cardiac events among pregnant women seems to begin in the third trimester at the time of maximal hemodynamic change, supporting the idea that it is the hemodynamic load that leads to cardiac decompensation. Some studies have shown a transient decrease in LV contractility during pregnancy (16), and this may also play a role in cardiac decompensation in women with abnormal LV function. Although many of the baseline characteristics were similar between the 2 groups, the authors acknowledge that an important difference between groups was that nonpregnant women were more likely to receive angiotensin-converting enzyme inhibitors, beta-blockers, and diuretic agents over the 16-month follow-up when compared with their pregnant counterparts. Although many pregnant women were optimally managed on heart failure therapy before pregnancy, medications were discontinued early in pregnancy because of contraindications and/or patient preference. This factor may also explain some of the observed differences in event rates between the 2 groups. In addition to increased cardiac complications during pregnancy, discontinuing cardiac medications for the duration of pregnancy may also have late negative effects on ventricular function.

In the population of pregnant women with DCM described in this study, we observed a high rate (20%) of adverse fetal and/or neonatal events. Previous studies examining pregnant women with other forms of heart disease have also reported high rates of neonatal complications (14,15,17–21). Specifically, in a prospective study from our center of neonatal outcomes in pregnant women with all forms of heart disease, adverse neonatal outcomes occurred in 18% of pregnancies in the heart disease group, compared with 7% of healthy pregnant control subjects (2). Previous work and this study showed that these complications are more common in women with advanced LV dysfunction and poor functional class (3). In addition, we found there to be an important interaction between maternal cardiac and obstetric risk factors and fetal and/or neonatal outcomes (2). Fetal and/or neonatal event occurrences were high in women with moderate or severe LV systolic dysfunction and/or NYHA functional class III or IV if there were concomitant obstetric risk factors. The mechanism for this finding is not known and requires further study. Finally, although many risk factors cannot be modifiable, those that can, such as smoking, could certainly be addressed in an attempt to reduce the risk of fetal complications.

Study limitations. Because all women included in this prospective study were receiving care at a tertiary care cardiac center, a referral bias may exist. Women with less severe heart disease or those doing well during pregnancy may not have been referred to our center. However, a substantial proportion of women had only mild LV dysfunction, suggesting that milder forms of disease were indeed included in the cohort. Because of the small sample size, this study was not powered to identify multiple predictors of outcomes. Larger sample sizes would be needed to identify additional determinants of outcome. Newer echocardiographic measures of ventricular function and mechanics as well as serum markers such as brain natriuretic peptide were not obtained, but may serve as useful prognostic markers in the future. Longer-term follow-up was not the focus of this study, but would be valuable in understanding the long-term effects of pregnancy on the diseased heart.

Conclusions

In pregnant women with DCM, clinical parameters, including NYHA functional class and LV systolic function, can be used to identify women at highest risk for cardiac complications during pregnancy. When compared with nonpregnant women, pregnancy seems to have a negative impact on the clinical course for women with DCM, at least over the short term. Fetal and/or neonatal complications are also increased in mothers with DCM, and the risk is magnified by the presence of both cardiac and obstetric risk factors.

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Reprint requests and correspondence: Dr. Candice K. Silversides, University of Toronto, Toronto General Hospital, 585 University Avenue, 5N-521, Toronto, Ontario M5G 2N2, Canada. E-mail: candice.silversides@uhn.on.ca.

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