Adverse Neonatal and Cardiac Outcomes Are More Common in Pregnant Women With Cardiac Disease

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Background—Pregnant women with heart disease (HD) are at increased risk for cardiac (CV) complications. However, the frequency of neonatal (NE) complications in pregnant women with HD relative to pregnant women without HD has not been examined.

Methods and Results—Pregnant women with HD were prospectively monitored during 302 pregnancies. The frequency of NE and CV complications was compared with those in a control group without HD during 572 pregnancies. The frequency of NE complications was higher in the HD group (18% versus 7%; HD versus controls). The NE complication rate was lowest in pregnancies of women age 20 to 35 years who did not smoke during pregnancy, did not receive anticoagulants, and had no obstetric risk factors: 4% in control patients, 5% in HD patients with no cardiac risk factors for NE complications (left heart obstruction, poor functional class, or cyanosis), and 7% in HD patients with ≥1 such risk factor. In contrast, the event rate in pregnancies of controls age <20 or >35 years who had obstetric risk factors or multiple gestation or who smoked was 11%. In the HD group, women age <20 or >35 years who had obstetric risk factors or multiple gestation, who smoked, or who received anticoagulants experienced an even higher NE complication rate (27% with no cardiac risks for NE events and 33% in the presence of ≥1 cardiac risk factors). The frequency of CV complications was higher in the HD group (17% versus 0%; HD versus controls).

Conclusion—Pregnant women with HD are at increased risk for both NE and CV complications. The risk for NE adverse events in pregnant women with HD is highest in those with both obstetric and cardiac risk factors for NE complications.

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Key Words: pregnancy ■ heart disease ■ prognosis

In the presence of maternal heart disease, the circulatory changes of pregnancy may result in adverse consequences, including death of the mother or fetus.1–5 Previous studies examining pregnancy outcomes in women with heart disease have focused on maternal cardiac outcomes.1–11 Although neonatal outcomes were reported in previous studies, it is difficult to interpret their findings in the absence of a control group.1,2,4,6,8 The frequency of neonatal complications was likely underestimated because most outcome studies were retrospective.2–4,6,7,9–11 In view of the association between neonatal complications, structural brain abnormalities, and neurocognitive impairment,12–14 it is important to establish the relative risk of neonatal complications in pregnant women with heart disease, as this will help determine the intensity of antepartum surveillance and follow-up of offspring. In the present study, we prospectively examined the frequency of neonatal, obstetric, and cardiac complications in pregnant women with and without heart disease.

Methods

The present study was a preplanned substudy of a multicenter study that examined cardiac outcomes in pregnant women with heart disease.3 The heart disease group consisted of patients prospectively enrolled in the multicenter study from Toronto General, Mount Sinai, and Women’s College hospitals in Toronto (1994 to 1999), meeting the following criteria: pregnant women with structural cardiac lesions or with symptomatic cardiac arrhythmias requiring treatment before pregnancy. Women with isolated mitral valve prolapse (mild mitral regurgitation) were excluded.

The control group consisted of pregnant women prospectively recruited from the general obstetric clinics of the same 3 hospitals during the same time period as the cardiac patients, who received their care from the same obstetricians who cared for the pregnant women with heart disease. For the first 4 years of the study, 2 consecutive controls were recruited for every pregnant woman with heart disease recruited into the study; controls were recruited within 2 weeks of the recruitment of each woman with heart disease. During the last 12 months of the study, funding reduction resulted in the recruitment of 1 control for every woman with heart disease. This study received institutional ethics approval, and subjects gave written informed consent.

Each patient was monitored from the first antenatal visit (baseline) until the sixth postpartum month, using a standardized follow-up

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schedule and prespecified definitions for data collection. Adverse events were independently verified by 2 physicians unrelated to the study, who were blinded to patient baseline characteristics or group assignment.

The following baseline data were recorded in all patients: age, gestational age, parity status, comorbid conditions (pulmonary disease, thyroid dysfunction, hypertension, diabetes mellitus, or systemic lupus erythematosus), maternal smoking and/or alcohol consumption, maternal educational status (surrogate for socioeconomic status), and recognized obstetric risk factors for neonatal complications (history of premature delivery or rupture of membranes, incompetent cervix, or caesarean section; or intraterine growth retardation, antepartum bleeding >12 weeks gestation, febrile illness, or uterine/placental abnormalities during present pregnancy).15–18

In the heart disease group, the following additional baseline data were recorded: New York Heart Association (NYHA) functional class, prior cardiac events (heart failure, transient ischemic attack, or stroke before present pregnancy; for those who had undergone prior cardiac intervention, only events after the intervention were considered), nature of cardiac lesion or arrhythmia, nature of cardiac intervention, presence of cyanosis (oxygen saturation <90%), use of cardiac medications and anticoagulants, and 12-lead ECG. As previously described, the heart disease group underwent echocardiographic assessment of ventricular systolic function, inflow or outflow obstruction, valvular regurgitation, and systolic pulmonary artery pressure.4,5

Follow-up data were obtained at clinical visits during the second trimester (<28 weeks), third trimester (28 to 37 weeks), peripartum period (onset of labor until hospital discharge), and then at 6 weeks and 6 months postpartum. Newborns of mothers with congenital heart disease were examined for heart disease; pediatric echocardiography was performed in all infants with abnormal cardiac examinations.

Adverse events during the ante-, peri-, and postpartum periods were classified as neonatal, obstetric, or cardiac complications. Neonatal complications were defined as: premature birth (<37 weeks gestation), small-for-gestational-age birth weight (<10th percentile for gestational age), respiratory distress syndrome, intra-ventricular 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, or postpartum hemorrhage. Pregnancy-induced hypertension was defined as an increase of ≥30 mm Hg in systolic blood pressure and ≥15 mm Hg in diastolic blood pressure compared with baseline values. Postpartum hemorrhage was defined as blood loss >500 mL after vaginal delivery or >1000 mL after caesarean section. Repairing of cardiac defects was considered to be accompanied by a drop in hemoglobin level of ≥20 g/L. Cardiac complications 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, cardiac arrest, or cardiac death.

Data Analysis
Each pregnancy was treated as a separate data unit. Baseline characteristics and complication rates in pregnancies not ending in miscarriage were compared between heart disease and control groups by χ2, Fisher’s exact, and t tests wherever appropriate. Comparative risk for neonatal events between heart disease and control groups was adjusted for baseline differences in clinical, socioeconomic, and obstetric characteristics by multivariate logistic regression analysis, which accounted for the fact that some women underwent >1 pregnancy.19

To examine the relationship between baseline maternal characteristics and neonatal event rate, the total patient sample was divided into 2 groups by the presence or absence of major noncardiac maternal factors previously shown to be associated with increased neonatal risk (including the recognized obstetric characteristics as defined earlier and maternal age <20 or >35 years, use of anticoagulation during pregnancy, smoking, and multiple gestation).15–18

Within each group, neonatal event rates were compared between the control women and the women with heart disease. The women with heart disease were further subdivided into those with and without cardiac risk factors shown by us and others to be associated with neonatal complications (maternal NYHA functional class III/IV, cyanosis, or left heart obstruction as defined by mitral valve area <2 cm2, aortic valve area <1.5 cm2, or peak left ventricular outflow tract gradient >30 mm Hg).1,2,4–6,20

Results
Follow-up was completed in all patients in March 2000. Three hundred one pregnant women with heart disease were enrolled during 334 pregnancies, and simultaneously, 572 pregnant women without heart disease were enrolled during 578 pregnancies. The frequency of miscarriage and termination was significantly higher in the heart disease group (Figure 1). To adjust for differences in baseline gestational age, the miscarriage rate was also compared for those pregnancies in which the patient presented at >12 weeks gestation. When only pregnancies meeting this criterion were analyzed, there was still a trend to increased miscarriage in the heart disease group (P=0.09). The proportion of terminations performed for cardiac, medical, or genetic indications in the HD and control groups were 68% and 100%, respectively (P=0.46).

Overall, 90% and 99% of pregnancies in the heart disease and control groups, respectively, progressed beyond 20 weeks of gestation (completed pregnancies); the age distribution and parity status of the heart disease and control groups were comparable (Table 1). The number of pregnancies with comorbid conditions, obstetric risk factors for neonatal complications, or in which the mother continued to smoke during pregnancy was higher in the heart disease group. A higher proportion of women in the control group had attained college, university, or a trade certificate as their highest educational level (Table 1).

In the heart disease group, the principal maternal cardiac lesion was congenital in 194 (64%), acquired in 85 (28%), and arrhythmic in 23 (8%) pregnancies. Nature of the principal maternal cardiac lesion and baseline cardiac status are summarized in Table 2. In 123 pregnancies (41%), the mother had undergone ≥1 of the following surgical interventions before conception: closure of cardiac shunts (n=46), coarctation repair (n=19), repair of complex congenital lesion (tetralogy of Fallot or double outlet right ventricle...
TABLE 1. Characteristics of Completed Pregnancies in Heart Disease and Control Groups

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Heart Disease</th>
<th>Control</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of pregnancies (women)</td>
<td>302 (280)</td>
<td>572 (566)</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–35</td>
<td>240 (80)</td>
<td>451 (79)</td>
<td>0.83</td>
</tr>
<tr>
<td>&lt;20 or &gt;35</td>
<td>62 (20)</td>
<td>121 (21)</td>
<td></td>
</tr>
<tr>
<td>Parity status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>163 (54)</td>
<td>295 (52)</td>
<td>0.50</td>
</tr>
<tr>
<td>1</td>
<td>96 (32)</td>
<td>193 (34)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>27 (9)</td>
<td>65 (11)</td>
<td></td>
</tr>
<tr>
<td>≥3</td>
<td>16 (5)</td>
<td>19 (3)</td>
<td></td>
</tr>
<tr>
<td>Baseline gestational age, wk</td>
<td>17±9</td>
<td>14±5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Multiple gestations</td>
<td>10 (3)</td>
<td>14 (2)</td>
<td>0.46</td>
</tr>
<tr>
<td>Highest educational level</td>
<td>166 (55)</td>
<td>421 (74)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Comorbid conditions†</td>
<td>45 (15)</td>
<td>34 (6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Obstetric high-risk characteristics‡</td>
<td>93 (28)</td>
<td>119 (21)</td>
<td>0.012</td>
</tr>
<tr>
<td>Smoking during pregnancy</td>
<td>36 (12)</td>
<td>42 (7)</td>
<td>0.033</td>
</tr>
</tbody>
</table>

Values are mean±SD or n (%). Significant correlations are in bold.
*College, university, or trade certificate
†Hypertension, diabetes mellitus, pulmonary or thyroid disorders, or systemic lupus erythematosus.
‡History of premature delivery or rupture of membranes, incompetent cervix, or caesarean section; or intrauterine growth retardation, antepartum bleeding after 12 weeks’ gestation, febrile illness, or uterine placental abnormalities during present pregnancy.

[23], Mustard repair [n=12], Rastelli repair [n=3], or Fontan repair [n=3]), valve repair (n=14), prosthetic valve replacement (mechanical [n=8], tissue [n=11], or pulmonary autograft [n=3]), reimplantation of left coronary artery (n=1), resection of subaortic stenosis (n=1), heart-lung transplantation (n=1), or resection of atrial myxoma (n=1).

The caesarean rate was higher in the heart disease group (Table 3). Six caesarean deliveries were performed for a cardiac indication in the heart disease group, in contrast to none in the control group. There were no significant differences between the 2 groups in the proportion of caesarean deliveries performed as a result of failure to progress, fetal distress, breech presentation, or prior caesarean section.

The frequency of neonatal complications in the heart disease group was more than twice that of controls (Table 3). For each type of neonatal event (premature birth, small for gestational age birth weight, respiratory distress syndrome or intraventricular hemorrhage, fetal/neonatal death) the event rate was higher in the heart disease group (Figure 2 and Table 3). Five of 6 neonatal deaths were in premature newborns; the other death was in a newborn with small-for-gestational-age birth weight.

Maternal heart disease was associated with an increased risk of neonatal complications, even when baseline differences in clinical, cardiac, socioeconomic, and obstetric risk profile between the 2 groups were accounted for (odds ratio, 2.3; 95% confidence interval, 1.4 to 4.0; P=0.006). The frequency of the most serious NE complications (intraventricular hemorrhage, delivery before 34 weeks, or neonatal/fetal death) was also higher in the heart disease (6%) group than in the control (2%) group (P=0.002).

The frequency of neonatal complications was lowest in singleton pregnancies in women age 20 to 35 years who did not smoke during pregnancy, did not receive anticoagulants during pregnancy, and had no obstetric risk factors: 4% in control patients, 5% in heart disease patients with no cardiac risk factors for NE complications (left heart obstruction or poor functional class/cyanosis), and 7% in heart disease patients with ≥1 such risk factor (P=0.41). In contrast, the event rate in pregnancies of controls age <20 or >35 years who had obstetric risk factors or multiple gestation or who smoked was 11%. In the heart disease group, women <20 or >35 years of age who had obstetric risk factors, who had multiple gestation, who smoked, or who received anticoagulants demonstrated a neonatal complication rate even higher (27% with no cardiac risks for NE events and 33% with ≥1 of these cardiac risk factors; P<0.001) (Figure 3).

Congenital heart disease was seen in the offspring in 8% of the 183 live births resulting from pregnancies in mothers with congenital heart disease but not part of a recognized genetic syndrome (atrial or ventricular septal defect [n=14], pulmonic stenosis [n=1]).

The frequency of postpartum hemorrhage and pregnancy-induced hypertension was not significantly different between heart disease and control groups (Table 3). There was no significant difference between the groups when a more recent criterion for pregnancy-induced hypertension (blood pressure ≥140/90 after 20 weeks of gestation) was used (5% and 3%.

TABLE 2. Antenatal Characteristics of Completed Pregnancies in Heart Disease Group

<table>
<thead>
<tr>
<th>Principal Cardiac Lesion</th>
<th>Total</th>
<th>NYHA Class III or IV or Cyanosis</th>
<th>Left Heart Obstruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shunts</td>
<td>62</td>
<td>...</td>
<td>2</td>
</tr>
<tr>
<td>Coarctation</td>
<td>22</td>
<td>...</td>
<td>8</td>
</tr>
<tr>
<td>AS/BAV</td>
<td>27</td>
<td>1</td>
<td>17</td>
</tr>
<tr>
<td>Pulmonic stenosis</td>
<td>20</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Complex</td>
<td>53</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Miscellaneous*</td>
<td>10</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Acquired valvular</td>
<td>57</td>
<td>2</td>
<td>33</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>20</td>
<td>5</td>
<td>...</td>
</tr>
<tr>
<td>Acquired other†</td>
<td>8</td>
<td>2</td>
<td>...</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>23</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

*Marfan syndrome (6), fibroelastosis of left ventricle (1), dextrocardia with situs inversus (2), repaired anomalous origin of left coronary artery from pulmonary artery (1), or repaired truncus arteriosus (1).
†Pulmonary hypertension (2) or ischemic heart disease (6).
Arhythmias were supraventricular tachycardia, ventricular tachycardia, or sick sinus syndrome; AS/BAV, congenital aortic stenosis or bicuspid aortic valve; cardiomyopathy, dilated (16) or hypertrophic (4) cardiomyopathy; complex, tetralogy of Fallot, double outlet right ventricle, transposition complexes, Ebstein anomaly, or univentricular circulation; and shunts, left to right shunt at atrial, ventricular, or arterial level.
There was 1 noncardiac death (postpartum depression and suicide in a woman with atrial septal defect).

Fifty-two completed pregnancies (17%) in the heart disease group were complicated by a cardiac event (Table 3); heart failure or cardiac arrhythmia accounted for most of the cardiac outcomes (94%). Embolic strokes complicated pregnancy in 3 women; 1 each with dilated cardiomyopathy, mechanical valve replacement with suboptimal anticoagulation, and transposition of the great arteries with Mustard procedure with severe systemic ventricular systolic dysfunction. The woman with Mustard procedure who had a stroke succumbed because of postpartum heart failure. The other postpartum cardiac death occurred in a mother with severe pulmonary hypertension. Maternal stroke or cardiac death complicated 4 pregnancies (1%). The maternal cardiac complications have been reported previously in detail as part of the larger national study.5 There were no cardiac complications in the control group (P<0.001 versus heart disease group).

**Discussion**

In this contemporary cohort of pregnant women receiving comprehensive perinatal care, pregnant women with heart disease are at increased risk for neonatal and cardiac complications. In women without obstetric risk factors for neonatal adverse events, the incremental risk of neonatal complications associated with the presence of maternal heart disease was small. However, in those with heart disease and concurrent obstetric risk factors, the risk of neonatal complications was considerably higher than that in controls with similar obstetric risk factors.

Previous studies examining pregnant women with heart disease have reported high rates of neonatal complications in the control group (P<0.001 versus heart disease group).

**TABLE 3. Outcomes of Completed Pregnancies in Heart Disease and Control Groups**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Heart Disease</th>
<th>Controls</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of pregnancies</td>
<td>302</td>
<td>572</td>
<td></td>
</tr>
<tr>
<td>Caesarean section</td>
<td>88 (29)</td>
<td>129 (23)</td>
<td>0.032</td>
</tr>
<tr>
<td>Any neonatal event</td>
<td>54 (18)</td>
<td>40 (7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Birth at &lt;37 weeks’ gestation</td>
<td>46 (15)</td>
<td>29 (5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Birth weight &lt;10th percentile for gestational age</td>
<td>11 (4)</td>
<td>9 (2)</td>
<td>0.059</td>
</tr>
<tr>
<td>Respiratory distress syndrome</td>
<td>7 (2)</td>
<td>1 (0.2)</td>
<td>0.003</td>
</tr>
<tr>
<td>Intraventricular hemorrhage</td>
<td>1 (0.3)</td>
<td>. . .</td>
<td>0.35</td>
</tr>
<tr>
<td>Fetal or neonatal death</td>
<td>10 (3)</td>
<td>4 (0.7)</td>
<td>0.003</td>
</tr>
<tr>
<td>Birth at &lt;37 weeks’ gestation from premature onset of labor</td>
<td>31 (10)</td>
<td>23 (4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pregnancy-induced hypertension</td>
<td>16 (5)</td>
<td>21 (4)</td>
<td>0.26</td>
</tr>
<tr>
<td>Postpartum hemorrhage</td>
<td>8 (3)</td>
<td>9 (2)</td>
<td>0.28</td>
</tr>
<tr>
<td>Maternal cardiac complications*</td>
<td>52 (17)</td>
<td>. . .</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Noncardiac death</td>
<td>1 (0.3)</td>
<td>. . .</td>
<td>0.35</td>
</tr>
</tbody>
</table>

Values are n (%).

*Cardiac death, stroke, pulmonary edema, tachyarrhythmia, or bradyarrhythmia. Significant correlations are in bold.

**Neonatal event rate (% pregnancies)**

**Figure 2.** Event rates in heart disease (solid bars) and control (empty bars) groups subdivided into specific type of neonatal complications. Prem birth indicates delivery at <37 weeks of gestation; SGA, small-for-gestational-age birth weight; RDS or IVH, respiratory distress syndrome or intraventricular hemorrhage; and death, fetal or neonatal death. *P<0.005, heart disease vs controls.

**Figure 3.** Frequency of neonatal complications when patients are divided into 2 groups by the presence or absence of maternal noncardiac risk factors (obstetric high-risk characteristics as defined in the text: smoking, use of anticoagulation, multiple gestation, maternal age). Control group is represented by empty bars. Heart disease group with neither left heart obstruction nor poor functional class/cyanosis is represented by shaded bars. Heart disease group with left heart obstruction or poor functional class/cyanosis is represented by solid bars.
tions,\textsuperscript{1,2,4,6,8,20} It is difficult to apply their findings, however, because they examined patients from an earlier era and/or used data collected retrospectively. In virtually all these previous studies, the increase in neonatal risk associated with pregnancy in women with heart disease was assumed. In the single study in which outcomes from retrospectively selected controls were examined, pregnant women with valvular heart disease had a significantly higher neonatal complication rate than that of controls.\textsuperscript{20} Our study extends the results of previous studies by quantifying the relative risk associated with heart disease in a large group of pregnant women with a wide spectrum of cardiac lesions who were receiving modern obstetric and cardiac care, while adjusting for the effects of baseline cardiac and obstetric characteristics. Prospective enrollment of both the heart disease and control groups, who received obstetric care in the same hospitals and during the same time period, minimized the potential confounding influence of local practice patterns or changes in practice patterns over time. Unlike previous studies that have focused only on fetal death, premature birth, or small-for-gestational-age birth weight,\textsuperscript{1,2,4,6,8} we were able to prospectively assess all clinically important neonatal complications, including respiratory distress syndrome and intraventricular hemorrhage.

Previous studies have reported that poor maternal functional class, cyanosis, and left heart obstruction were associated with neonatal complications in pregnant women with heart disease.\textsuperscript{1,2,4,6} The present study unifies prior study findings by demonstrating the interaction between baseline cardiac and obstetric characteristics in determining neonatal complications. For example, even in the presence of cardiac risk factors such as left heart obstruction, poor functional class, or cyanosis, the neonatal complication rate in the heart disease group was only minimally increased from that of controls if the mother did not have other maternal risk factors. On the other hand, if the mother had concurrent maternal risk factors, the neonatal complication rate in the heart disease group was more than twice that of controls with similar maternal risk factors. Women in this group with maternal cardiac risk factors for neonatal events experienced the highest neonatal complication rate.

There are several possible reasons for the increased rate of neonatal complications in pregnant women with heart disease. The relationship between maternal cyanosis and fetal growth has been well defined; maternal oxygen saturation is inversely related to birth weight and fetal mortality.\textsuperscript{6,23} The effect of functional class and left heart obstruction on perinatal delivery, fetal death, and growth retardation is likely mediated by uteroplacental insufficiency. Indeed, fetal cardiac contractility and output are adversely affected by hypoxic academia resulting from uteroplacental insufficiency.\textsuperscript{22,23} The increased rate of premature birth in the heart disease group cannot be attributed to a more aggressive strategy of preterm induction in this group, as the rate of spontaneous premature onset of labor resulting in preterm delivery was also significantly higher in the heart disease group than in control groups. Thus, the effect of both obstetric and cardiac risk factors may be manifested as a higher risk of premature labor. Indeed, we previously observed an association between antenatal cardiac complications and the onset of premature labor.\textsuperscript{4} The higher rate of small-for-gestational-age birth weight infants did not reach statistical significance, perhaps as a result of the overriding effects of preterm births; a higher frequency might have been observed if more pregnancies had progressed toward term. Alternatively, provision of modern antenatal care and universal access to obstetric care may have resulted in a lower incidence of intrauterine growth retardation than previously reported.

We examined other neonatal outcomes such as respiratory distress syndrome and intraventricular hemorrhage in addition to prematurity, low birth weight, and death. The relationship between prematurity and small-for-gestational age birth weight, and neurocognitive abnormalities is well described.\textsuperscript{12–14,24} However, respiratory distress syndrome and intraventricular hemorrhage are also associated with developmental delay and cognitive impairment.\textsuperscript{25–28} By more completely assessing the risk of neonatal complications, the present study identified those neonates who are at risk for neurocognitive impairment and are therefore candidates for more intensive follow-up and therapeutic strategies.

A key study finding was that the deleterious effects of maternal heart disease on neonatal outcomes were amplified by the presence of concurrent obstetric risk factors for neonatal complications. This relationship between maternal status and neonatal outcomes has not been previously reported, likely because previous studies have either not examined obstetric risk factors or lacked sufficient patient numbers. Future investigations will need to define the mechanisms underlying our observations, analogous to the approach used in analyzing the relationship between maternal diabetes and congenital cardiac malformations.\textsuperscript{29–30} Furthermore, clinicians will be reminded of the need to optimize obstetric and cardiac status in pregnant women with heart disease. The importance of smoking cessation may need special emphasis in women with heart disease who are considering pregnancy.

Our study was not designed to provide lesion-specific comparisons of risk. However, in previous studies from our center and others, left heart obstruction, poor functional class, and cyanosis have predicted neonatal complications.\textsuperscript{1,2,4,7} Only by examining patients with a spectrum of cardiac lesions and risk profiles have we been able to define the interaction between maternal cardiac status, obstetric risk factors, and neonatal complications. Selection bias was minimized by the fact that participating centers provide primary and referral obstetric care for the metropolitan Toronto area.

We chose to adjust for baseline differences between heart disease and control groups at the time of analysis, as it was not possible to match the groups in all baseline characteristics. However, the 2 groups were similar in regard to maternal age and parity status. Universal access to obstetric care and the use of a standardized obstetric follow-up schedule in the province of Ontario likely reduced the effect of socioeconomic status on neonatal outcomes.

In conclusion, the increased risk of neonatal complications in pregnant women with heart disease is amplified by the presence of obstetric risk factors. Women with heart disease who are age <\textasciitilde{}20 or >35 years or who exhibit maternal
obstetric or cardiac risk factors require increased intensity of antepartum surveillance. These women likely will benefit from referral to a regional center for care during their pregnancy. Conversely, women with heart disease without cardiac or obstetric risk factors are at minimally increased risk compared with pregnant women without heart disease and likely do not require increased intensity of antepartum surveillance.

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References
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