Pregnancy in Cyanotic Congenital Heart Disease
Outcome of Mother and Fetus

Patrizia Presbitero, MD; Jane Somerville, MD, FRCP, FACC; Susan Stone; Erio Aruta, MD; David Spiegelhalter, PhD; Filippo Rabajoli, MD

Abstract In a series of 416 women with congenital heart disease seen in the Royal Brompton National Heart and Lung Hospital, London, and the Hospital Giovanni Bosco, Torino, Italy, there were 822 pregnancies. The outcomes of 96 pregnancies in 44 patients with cyanotic congenital heart disease were studied. Patients with the Eisenmenger reaction were excluded. Patients were divided arbitrarily into groups according to the type of maternal congenital cardiac anomaly, and factors influencing maternal and fetal outcome were evaluated. The incidence of maternal cardiovascular complications was high (32%), with one death from endocarditis 2 months after delivery. Forty-one (43%) of 96 pregnancies resulted in a live birth; 15 (37%) were premature. Mean weight of full-term infants was 2575 g.

The prevalence of pregnancies complicated by rheumatic heart disease has decreased in North America and Western Europe in the last two decades, but pregnancies in patients with congenital heart disease, often with complex anomalies, are occurring more frequently. This is due to the increased number of women with congenital heart anomalies now surviving to adulthood because of successful cardiac surgery and improved care during infancy and childhood. Previous studies of series and case reports suggest that cyanotic congenital heart disease adds a greater risk to pregnancy than other lesions, but information from more patients is required to make useful recommendations.

There are a number of conditions deemed unsuitable for radical repair because of the basic anatomy but nevertheless are compatible with survival. Such lesions as complex pulmonary atresia with aortopulmonary collaterals, defects complicated by the Eisenmenger reaction, and single-ventricle hearts (with and without earlier palliation) are in this category. Some cyanotic patients reach adulthood without serious symptoms necessitating surgery, such as those with mild tetralogy of Fallot, Ebstein's anomaly, and some cases of corrected transposition with pulmonary stenosis and ventricular septal defect.

Univariate analysis suggested that maternal disease, Ability Index, hemoglobin, and arterial oxygen saturation before the pregnancy were factors that discriminated between successful and unsuccessful fetal outcome, with hemoglobin and arterial oxygen saturation being the most important predictors.

Women with cyanotic congenital heart disease can go through pregnancy with a low risk to themselves, with frequent treatable complications, but there is a high incidence of miscarriage, premature births, and low birth weights. An incidence of congenital heart disease in the fetus of 4.9% (2 of 41 live births) is higher than that found in the normal population. (Circulation. 1994;89:2673-2676.)

Key Words • congenital heart disease • pregnancy • cyanosis

The purpose of this study was to identify the main factors influencing the successful outcome of pregnancy in women with cyanotic congenital heart defects.

Methods

Selection of Patients

The data were collected in two centers specializing in the care of patients with adult congenital heart disease: the Royal Brompton National Heart and Lung Hospital (RBNLH), London, and the Hospital Giovanni Bosco (HGB), Torino, Italy. The RBNLH is a supraregional center with a specific unit dealing with adult congenital heart disease, established since 1975. Patients are referred from many different regions nationwide, and there is considerable variation in obstetric practice and supervision of pregnancy where the delivery takes place. At the HGB there is a regional center for adult congenital heart disease, and most of the patients with congenital heart disease who are pregnant are followed in the obstetric hospital, which collaborates with the HGB.

This was a retrospective study. A limitation of this was that the first and early second trimester losses were difficult to assess, as in the normal population. From this population of 416 women who had 822 pregnancies, there were 44 patients with cyanotic congenital heart disease who had 96 pregnancies. Their ages ranged from 15 to 41 years (mean, 24) at the time of pregnancy. Twenty-eight patients were from the RBNLH and 16 were from the HGB. The HGB patients were referred to the regional obstetric hospital, and 6 were directly supervised by one of the authors (P.P.) during the pregnancy.

Patients in the following categories were excluded: (1) patients with previous surgical repair who were no longer cyanotic, (2) pregnancies intentionally interrupted, (3) patients with the Eisenmenger reaction, and (4) patients whose notes had been destroyed or lost.

Cyanotic heart disease was diagnosed when patients had been noted to have central cyanosis on effort and/or at rest, had established clubbing of fingernails and toes with measured systemic arterial desaturation, and had the appropriate anatomy to explain this. At cardiac catheterization or when the
patient was at rest, the systemic arterial oxygen saturation was measured as 90% in 5 pregnancies, 91% in 4 pregnancies, 92% in 4 pregnancies, and <90% in 39 pregnancies. The arterial oxygen saturation was unknown in 44 pregnancies, but the patients were obviously clinically cyanotic, which meant that their systemic arterial oxygen saturation was likely to be <85%.

The study population was divided into four groups according to the basic anatomic abnormality in the mother to make discussion and analysis easier: Group 1 was single-ventricle and/or tricuspid atresia (10 patients with 26 pregnancies); group 2, tetralogy of Fallot or pulmonary atresia with aortopulmonary collaterals (21 patients with 46 pregnancies); group 3, Ebstein's anomaly and atrial septal defect (8 patients with 14 pregnancies); and group 4, corrected transposition of the great arteries, ventricular septal defect, and pulmonary stenosis (5 patients with 10 pregnancies). Twenty-two patients (50%) had undergone previous palliative shunts and remained cyanotic.

The following problems were considered: maternal death; cardiovascular complications during pregnancy, during delivery, or in the month afterward; prematurity; type of delivery; state of the fetus; and whether or not there were congenital cardiac or other obvious skeletal anomalies recognized and reported in the first 3 months of life. No subsequent examination or request for information about the child was sought.

The following factors were examined in terms of their influence on fetal outcome: (1) basic anomaly in the mother according to the groups already specified, (2) hemoglobin at the time pregnancy first was reported (unknown in 2 pregnancies), (3) resting arterial oxygen saturation (unknown in 44 pregnancies), (4) age of mother at delivery (exact age unknown in 4 pregnancies), (5) previous surgical shunt, and (6) Ability Index, which assesses the symptomatic state of the patient, including the patient's perception of normality.

**Statistical Analysis**

With regard to fetal outcome, each potential risk factor was considered individually with respect to observed rates of live birth. Since many women contributed more than 1 pregnancy to the series, the set of 96 pregnancies cannot be considered independent. Statistical significance of risk factors is adjusted for this dependence using a random-effects logistic regression procedure using the statistical package EGRET (Statistical and Epidemiological Research Corporation). Multivariate risk factor analysis was carried out using the same procedure.

**Results**

**Maternal Outcome**

**Mortality**

One patient with tetralogy of Fallot and an open Blalock anastomosis died from *Streptococcus faecalis* endocarditis 2 months after a vaginal delivery by forceps without antibiotic prophylaxis. She presented with hemoptyses related to an aneurysm at the pulmonary artery end of the shunt and positive blood cultures and died in the hospital from a massive hemoptysis from rupture of the aneurysm.

**Cardiovascular Complications**

Cardiovascular complications occurred in 14 patients (32%). Eight patients developed heart failure, 3 requiring hospital admission and intravenous diuretics at 32 to 36 weeks of gestation.

Two patients had thrombotic complications. One woman with multiple pulmonary artery stenoses in whom a duct had been ligated in childhood developed occlusion of the right pulmonary artery some time at the end or around delivery of the second pregnancy, which led to progressive symptomatic deterioration over the postpartum 2 years. Emergency dilatation and stenting of the only remaining patent left lower pulmonary artery produced clinical improvement. A left cerebral infarct in a woman aged 27 years with complex pulmonary atresia developed during the 10th week of her third pregnancy. She recovered, with residual, very mild hemiparesis.

Supraventricular tachycardia recurred during two pregnancies in the second and third trimesters in one patient with tricuspid atresia and a Glenn shunt and the other with Ebstein's anomaly and atrial septal defect. The arrhythmia was controlled with digoxin and class I antiarrhythmic drugs (quinidine sulfate and propranolone) in both patients.

Peripartum bacterial endocarditis occurred in two patients (4.5%), both with palliated tetralogy of Fallot. Neither had antibiotic prophylaxis during labor. Both had a forceps delivery, and one had a long labor.

Elective cesarean section was performed in 10 patients, in 6 (14%) because of the maternal cardiovascular problems and in 4 for obstetric reasons. The exact details of delivery, outcome, complications, and specific indications were unknown when they occurred in outside regional hospitals, and the notes were no longer available. The status of the patients after the delivery was worse than before in only 4 patients (Table 1).

**Fetal Outcome**

Forty-one live births (43%) occurred, at term in 26 (27% of all pregnancies) and premature in 15 at 26 to 37 weeks. There were 49 spontaneous abortions at 6 weeks to 5 months and 6 stillbirths at 26 to 38 weeks. Birth weights of those born at term were 2100 to 3600 g (mean, 2575).

Congenital heart disease was documented in 2 of 41 live infants, causing death at age 2 days from a large ventricular septal defect in an infant from a mother with palliated Fallot and at age 6 years from dilated cardiomyopathy in an infant with fibroelastosis from a mother with Ebstein's anomaly. Two infants from one mother were stillborn at 8 months and had congenital heart disease. No further investigation into other living children or anomalies in aborted fetuses was made.

The percentage of live births for each category of the potential risk factors studied is shown in Table 2. The type of maternal disease was somewhat predictive of successful outcome ($P=.07$), with groups 3 and 4 (Ebstein's anomaly with atrial septal defect, corrected

<table>
<thead>
<tr>
<th>Maternal Ability Index</th>
<th>Before Delivery</th>
<th>After Delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>31</td>
<td>31</td>
</tr>
<tr>
<td>2</td>
<td>62</td>
<td>57</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>(4)</td>
</tr>
<tr>
<td></td>
<td>(1)</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>96</td>
<td>96</td>
</tr>
</tbody>
</table>
transposition of the great arteries, ventricular septal defect, and pulmonary stenosis) having an increased chance of live birth in comparison to groups 1 and 2 (single-ventricle and/or tricuspid atresia, tetralogy of Fallot, or pulmonary atresia with aortopulmonary collaterals). Both hemoglobin (P=.003) and arterial oxygen saturation (P=.01) displayed a strong and systematic relation to the chance of live birth.

The maternal age had little predictive power (P=.45), in contrast with ability indexes, which showed some discriminating evidence of the successful and unsuccessful outcomes (P=.10). There was little evidence that those with a palliative shunt fared better than those without (P=.35). Multivariate analysis, using logistic regression adjusted for nonindependent pregnancies, showed that once arterial oxygen saturation was taken into account, no other factor added significantly to the prediction of a live birth. The outcome of pregnancies according to the maternal cardiac anomaly is shown in Table 3.

Discussion

It has been suggested that pregnancy in patients with cyanotic congenital heart disease has high risks for both mother and fetus, but the views have been based mostly on case reports and small series that include different patients from ours, making direct comparison difficult. For instance, 8 of 22 cyanotic patients in Whittemore’s series had Eisenmenger syndrome, which itself has special risks. In our series, Eisenmenger patients are excluded because it is considered that elevated pulmonary vascular resistance is a greater hazard than the presence of cyanosis. The absence of the Eisenmenger patients probably accounts for the lower incidence of maternal deaths and serious complications in our series.

Table 3. Outcome of Pregnancies According to Maternal Cardiac Anomaly

<table>
<thead>
<tr>
<th>Disease Group</th>
<th>No. of Mothers</th>
<th>No. of Pregnancies</th>
<th>Cardiovascular Complications</th>
<th>Live Birth</th>
<th>Premature</th>
<th>Spontaneous Abortion</th>
<th>Stillbirth</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>26</td>
<td>2</td>
<td>8 (31%)</td>
<td>3</td>
<td>17</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>21</td>
<td>46</td>
<td>8</td>
<td>15 (33%)</td>
<td>9</td>
<td>26</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>14</td>
<td>3</td>
<td>12 (86%)</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>10</td>
<td>1</td>
<td>6 (60%)</td>
<td>2</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>44</td>
<td>96</td>
<td>14</td>
<td>41 (43%)</td>
<td>15</td>
<td>49</td>
<td>6</td>
</tr>
</tbody>
</table>

Disease groups are group 1, single-ventricle and/or tricuspid atresia; group 2, tetralogy of Fallot or pulmonary atresia with aortopulmonary collaterals; group 3, Ebstein’s anomaly and atrial septal defect; and group 4, corrected transposition of the great arteries, ventricular septal defect, and pulmonary stenosis.
There is a limitation of this study in it being retrospective. However, it is the largest experience of cyanotic congenital heart patients and allows reasonable predictions about outcome of pregnancy in this group of patients. It shows what can go wrong and defines factors that can guide physicians concerning outcome, possible complications, and advice that should be given to prospective parents. There is, for the mother, a likelihood of right ventricular failure, which should be anticipated by increased rest in the second and third trimesters. Medical treatment is effective, and early administration of diuretics with good cardiologic supervision should prevent the need for emergency admissions. Over-treatment with diuretics must be avoided because of the risk of hemococoncentration and abnormal renal function in the adult cyanotic patient.

In the two patients with thrombotic complications (pulmonary and cerebral), the hemoglobin level was only slightly elevated (17 and 18 g/dL), so the incidents should not be attributed to polycythemia. The patient with pulmonary arterial stenoses and thrombosis had generalized vascular disease involving the pulmonary arteries, and local pathologic changes close to the stenoses can occur with or without pregnancy. The value of anticoagulants is questionable because it is known that polycythemia predisposes to bleeding problems, and childbirth is a potentially hemorrhagic event. Proper hydration throughout pregnancy and labor, elastic stockings to prevent deep-vein thrombosis, and early mobilization are more important. We do not recommend anticoagulation in the cyanotic patient who is pregnant unless there is a specific indication such as deep-vein thrombosis or valve prosthesis, in which case subcutaneous heparin, which can be easily controlled once labor starts, should be given.

In our series, 3 patients had bacterial endocarditis, resulting in 1 death. This is 3% of pregnancies, or 7% of patients, which is extremely high and supports the absolute need for prophylactic treatment. Thus, we do not agree with the current American Heart Association recommendations that no prophylaxis is necessary for an uncomplicated delivery, since it is difficult to predict accurately whether the delivery will be complicated or uncomplicated. We consider it better to give antibiotic coverage intravenously as soon as labor begins, thus being prepared for any subsequent complication that might be associated with bacteremia.

The clinical state in most of the patients during and after the pregnancy was good if they were Ability Index 1 or 2 before pregnancy. Some deteriorated for 1 to 2 years after the birth. Whether this was due to the natural worsening of the disease or to an increased demand on a disabled woman from caring for a baby is unknown. It is advisable during the course of the pregnancy, and if possible before, to have full discussion with the family, drawing attention to the need for extra support and help for the years after delivery.

A low percentage of live babies (43% to 65%) with a high incidence of fetal loss occurs in this series as in other series; 34% of the live babies were premature in Whittemore’s group compared with 37% in this series. It is difficult to know whether fetuses born after 20 weeks did not live because of prematurity, abnormality, or other causes, but such a course was more frequent in women with cyanotic congenital heart disease than in the normal population. The incidence of congenital anomalies in those who miscarried early is unknown, but it might be higher than in the normal population and perhaps plays a role in determining fetal outcome of the mother with cyanotic congenital heart disease. It has already been emphasized that the prematurity and the low birth weight for gestational age are related to the high level of hemoglobin and the low arterial oxygen saturation of the mother. From our univariate analysis, hemoglobin and arterial oxygen saturation just before or at the beginning of pregnancy were found to be the main determinants for fetal loss. Hemoglobin falls at the end of pregnancy because of hemodilution, so arterial oxygen saturation is a better predictor of fetal outcome, particularly later in pregnancy, and it should be measured regularly throughout the pregnancy. We also have shown that the nature of the maternal disease is important in determining the outcome of the pregnancy; this is easily understood if we consider the wide spectrum of physiopathological conditions in the various cyanotic congenital heart conditions. All of these variables are highly related.

The incidence of congenital heart disease in the newborn in our study group is lower than Whittemore’s (4.9% versus 13.5%), and a possible explanation is her longer and more careful follow-up of the offspring until 3 years of age. The different incidence of congenital and genetic anomalies in different diseases or the use of teratogenic substances in the different series may be an explanation of the wide variations of the incidence of congenital heart disease in newborns reported in the literature.

This study shows that women with cyanotic congenital heart disease can go through pregnancy with a low risk to themselves but with a high incidence of maternal cardiac complications, premature birth, and spontaneous abortion. The likelihood of a live birth can be predicted from the arterial oxygen saturation at rest when it is >85% and when hemoglobin at the beginning of pregnancy is <20 g/dL. Risks can be reduced by careful, integrated care by the informed cardiologist and obstetrician throughout the pregnancy, delivery, and postpartum period.

References
P Presbitero, J Somerville, S Stone, E Aruta, D Spiegelhalter and F Rabajoli

Circulation. 1994;89:2673-2676
doi: 10.1161/01.CIR.89.6.2673

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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World Wide Web at:
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