Pregnancy and Congenital Heart Disease

Begoña Manso, Ferran Gran, Antonia Pijuan, Gemma Giralt, Queralt Ferrer, Pedro Betrián, Dimpna Albert, Ferran Rosés, Núria Rivas, Montserrat Parra, Josep Girona, Inmaculada Farran, and Jaume Casàliglia

Introduction and objectives. Since the creation of the Adult Congenital Heart Disease Units and of the High Obstetric Risk Units, there has been increasing interest in hemodynamic and obstetric outcomes in pregnant woman with congenital heart disease.

Methods. Retrospective descriptive study of 56 women with congenital heart disease aged (mean [range]) 25 (18-40) years, who experienced a total of 84 pregnancies between January 1992 and August 2006. The women were divided into 3 pregnancy risk groups: A, low-risk; B, moderate-risk; and C, high-risk.

Results. The incidence of complications during pregnancy was 1.6%, 15%, and 20% in groups A, B, and C, respectively; the incidence during the puerperium was 2%, 23%, and 50%, respectively; and maternal mortality was 0%, 7.6%, and 25%, respectively. Overall, 69 children were born, and the prematurity rates in the 3 groups were 11%, 15%, and 100%, respectively. The following risk factors were studied: pulmonary hypertension, cyanosis, arrhythmia, left ventricular outflow tract obstruction, right ventricular dilatation, systemic right ventricle, and anticoagulation therapy. The risk factor most significantly associated with maternal or fetal morbidity, or mortality was found to be pulmonary hypertension.

Conclusions. Risk stratification in pregnant women with congenital heart disease provides prognostic information that can help multidisciplinary teams to target care to achieve the best results.

Key words: Congenital heart disease. Pregnancy. Risk factor.

Embarazo y cardiopatías congénitas

Introducción y objetivos. Desde la creación de las Unidades de Cardiopatías Congénitas (CC) del Adulto y las Unidades Obstétricas de Alto Riesgo Cardiológico, ha habido creciente interés por la evolución hemodinámica y obstétrica de embarazadas con CC.

Métodos. Estudio descriptivo retrospectivo de 56 mujeres con CC y media de edad de 25 (18-40) años, que iniciaron 84 gestaciones entre enero de 1992 y agosto de 2006. Se las distribuyó en 3 grupos de riesgo gestacional: A, bajo; B, moderado y C, alto.

Resultados. Las incidencias de complicaciones durante la gestación fueron del 1,6, el 15 y el 20%, y durante el puerperio, el 2, el 23 y el 50%; la mortalidad materna fue 0, del 7,6 y del 25% de los grupos A, B y C respectivamente. Nacieron 69 niños y las tasas de prematuridad fueron del 11, el 15 y el 100% respectivamente. Los factores de riesgo principales fueron: la hipertensión pulmonar (HTP), la cianosis, la arritmia, la obstrucción del tracto de salida del ventrículo izquierdo, el ventrículo derecho (VD) dilatado, el VD sistémico necesidad de y la anticoagulación. La HTP fue el factor más importante asociado a morbimortalidad maternofetal.

Conclusiones. La estratificación por riesgo en las gestantes con CC ofrece información pronóstica que permite adecuar la atención de equipos multidisciplinarios para conseguir resultados exitosos.

Palabras clave: Cardiopatía congénita. Embarazo. Factor de riesgo.

INTRODUCTION

The overall incidence in our setting of pregnant women with congenital heart disease is estimated at 1.5% to 2%. Since 1960, treatment advances in congenital heart diseases (CHD) have dramatically decreased mortality and more than half the females who have surgical repair since then have now reached childbearing age. The most important nonobstetric cause of maternal death during pregnancy is cardiac disease. This has
meant that pregnancy is routinely discouraged among women with congenital heart disease.

Pregnancy involves a series of hemodynamic changes: increased blood volume (higher in multiple gestations), increased heart rate, decreased peripheral resistances, and proaggregant effect; moreover, uterine enlargement leads to compromise of venous return by the inferior vena cava.

During labor, cardiac output increases 10% to 40%, with variations in circulating volume with each uterine contraction. There is considerable adrenergic discharge due to pain and anxiety, as well as loss of blood volume that varies according to the bleeding that occurs.

In the first 2 weeks of puerperium, the excess blood volume is progressively lost.

Various studies of pregnant women with CHD have identified risk factors to help provide adequate preconception and prognostic counseling. However, due to the broad spectrum of anatomical and pathophysiological characteristics of the various CHDs, there are no specific guidelines for each condition, thus requiring an individual approach for each patient.

The purpose of this study was to investigate the complications of pregnancy, delivery, and puerperium in 3 risk groups, as well as to assess the newborns according to gestational age, weight, and whether or not they had any CHD.

RESULTS

The study included 56 women born between 1959 and 1983 who had a pregnancy at a mean age of 25 (range, 18-40) with a total of 84 pregnancies between January 1992 and August 2006.

Pregnancy Outcome (Table 2)

Group A

Two patients from this group had twin pregnancy, but complications were observed in only 1 of them. The patient with repaired double mitral lesion and atrial septal defect as well as severe residual mitral regurgitation and twin pregnancy presented heart failure in the third trimester and, therefore, labor was induced at 33 weeks. The other twin pregnancy in a patient with repaired ostium secundum atrial septal defect was normal.

In this group, 16 (25%) patients presented severe pulmonary insufficiency secondary to previous surgeries: Fallot’s tetralogy (7), pulmonary stenosis either alone (4), or associated with shunting (5). Of these, 11 had dilated right ventricle, but with no clinical repercussions. None had complications during pregnancy.

Group B

Three patients of this group presented complications: 2, heart failure; and 1, prosthetic thrombosis. Heart failure occurred in 1 patient with cyanosis and palliated univentricular physiology who required early delivery at 33 weeks and 1 mother with unoperated moderate aortic stenosis that resolved with medical treatment. The other complication consisted of 1 prosthetic thrombosis at week
TABLE 1. Distribution of Conditions

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Patients, No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Low-risk group (n=37)</td>
<td></td>
</tr>
<tr>
<td>Aortic coarctation, operated</td>
<td>5</td>
</tr>
<tr>
<td>Mild aortic regurgitation, unoperated</td>
<td>1</td>
</tr>
<tr>
<td>Mild mitral regurgitation, unoperated</td>
<td>2</td>
</tr>
<tr>
<td>Partial and abnormal venous drainage, unoperated</td>
<td>1</td>
</tr>
<tr>
<td>Ostium secundum atrial septal defect, operated</td>
<td>3</td>
</tr>
<tr>
<td>Ostium secundum atrial septal defect and pulmonary stenosis, operated</td>
<td>2</td>
</tr>
<tr>
<td>Ostium primum atrial septal defect and mitral regurgitation, operated</td>
<td>2</td>
</tr>
<tr>
<td>Restrictive ventricular septal defect, unoperated</td>
<td>1</td>
</tr>
<tr>
<td>Ventricular septal defect and ductus, operated</td>
<td>1</td>
</tr>
<tr>
<td>Ventricular septal defect and pulmonary stenosis, operated</td>
<td>2</td>
</tr>
<tr>
<td>Persistent arterial duct, operated</td>
<td>1</td>
</tr>
<tr>
<td>Severe pulmonary stenosis, operated</td>
<td>4</td>
</tr>
<tr>
<td>Severe pulmonary stenosis, unoperated</td>
<td>1</td>
</tr>
<tr>
<td>Double right ventricular outflow, surgically repaired</td>
<td>4</td>
</tr>
<tr>
<td>Fallot’s tetralogy, surgically repaired</td>
<td>7</td>
</tr>
</tbody>
</table>

| B. Moderate-risk group (n=15)                                             |              |
| Moderate aortic stenosis, unoperated                                      | 2            |
| Mild mitral stenosis and residual moderate recoarctation                 | 1            |
| Residual moderate aortic stenosis after valvulotomy                      | 1            |
| Mechanical mitral valve                                                  | 2            |
| Mechanical aortic valve                                                  | 1            |
| Double atroventricular and ventriculoarterial discordance, unoperated    | 2            |
| Transposition of great arteries, repaired by atrial switch               | 5            |
| Single ventricle with right ventricular outflow tract obstruction, palliated with S-P shunt | 1 |

| C. High-risk group (n=4)                                                  |              |
| Pulmonary atresia and ventricular septal defect, palliated with S-P shunt | 1            |
| Ventricular septal defect, unoperated, with PH                           | 1            |
| Endocardial cushion defect, operated late, with mild residual mitral stenosis and PH | 1 |
| Imbalanced endocardial cushion defect, unoperated, with PH               | 1            |

PH indicates pulmonary hypertension; S-P, systemic-to-pulmonary.

TABLE 2. Overall Results of Groups A, B, and C

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n (%)</td>
<td>37 (64)</td>
<td>15 (29)</td>
<td>4 (7)</td>
<td>56</td>
</tr>
<tr>
<td>Pregnancies, n</td>
<td>59</td>
<td>20</td>
<td>5</td>
<td>84</td>
</tr>
<tr>
<td>Induced abortions, n (%)</td>
<td>3 (6)</td>
<td>3 (23)</td>
<td>2 (50)</td>
<td>8</td>
</tr>
<tr>
<td>Spontaneous abortions</td>
<td>4</td>
<td>4</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Newborns (Twins), n</td>
<td>54 (4)</td>
<td>13 (0)</td>
<td>2 (1)</td>
<td>69 (4)</td>
</tr>
<tr>
<td>Premature, n (%)</td>
<td>6 (11)</td>
<td>2 (15)</td>
<td>2 (100)</td>
<td>10</td>
</tr>
<tr>
<td>Complications, n/N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td>1/59 (1.6)</td>
<td>3/20 (15)</td>
<td>2/5 (40)</td>
<td>5/84</td>
</tr>
<tr>
<td>Delivery</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1/87</td>
</tr>
<tr>
<td>Puerperium, n/N (%)</td>
<td>1/52 (2)</td>
<td>3/13 (23)</td>
<td>1/2 (50)</td>
<td>5/87</td>
</tr>
<tr>
<td>Maternal deaths, n (%)</td>
<td>0</td>
<td>1 (7.6)</td>
<td>1 (25)</td>
<td>2</td>
</tr>
<tr>
<td>Deliveries, n</td>
<td>52</td>
<td>13</td>
<td>2</td>
<td>67</td>
</tr>
<tr>
<td>Caesarea, n (%)</td>
<td>14 (27)</td>
<td>3 (23)</td>
<td>1 (50)</td>
<td>18</td>
</tr>
<tr>
<td>Instrument-aided, n (%)</td>
<td>10 (20)</td>
<td>5 (38)</td>
<td>0</td>
<td>15</td>
</tr>
<tr>
<td>Normal, n (%)</td>
<td>28 (53)</td>
<td>5 (39)</td>
<td>1</td>
<td>34</td>
</tr>
</tbody>
</table>

16 of pregnancy and occurred in a patient with a mechanical mitral valve who was receiving heparin and experienced acute pulmonary edema. Following echocardiographic diagnosis of the prosthetic dysfunction due to thrombus, fibrinolysis was performed on this patient, with clinical, and echocardiographic resolution of the symptoms. There were no repercussions on the course of the pregnancy or the fetus.
Three patients from this group were receiving anticoagulant therapy before pregnancy due to mitral (2) and aortic (1) prosthesis. In all 3 patients, coumarin derivatives were substituted between weeks 16 and 36 of the pregnancy. Two of them had spontaneous abortions, 1 early and 1 late. The third was the previously described patient with successful thrombolysis.

No anatomical pathology study was available for the aborted fetuses, except for 1 autopsy from a late spontaneous abortion (at 23 weeks) in which embryopathy was ruled out.

Four patients from this group had moderate left ventricular outflow tract obstruction: aortic recoarctation (1), unoperated aortic stenosis (1), residual aortic stenosis (1), and aortic prosthesis with stenosis (1). The first 2 had successful outcomes with no complications. The third experienced heart failure in the second trimester and premature delivery at 35 weeks. The last patient had a spontaneous abortion (she was on anticoagulant therapy).

In this group, there were 7 (46%) women with systemic right ventricle: 5 with transposition of the great arteries repaired by atrial switch and 2 with congenitally corrected transposition. None of the women showed any signs of heart failure. There were no complications during the pregnancy and each woman had at least 1 live newborn.

Except for 1 caesarean birth indicated at 28 weeks for hemodynamic decompensation in the patient with PH, all other caesarean deliveries were done for obstetrical reasons.

In group A, there was only 1 complication during delivery consisting of self-limiting, well-tolerated supraventricular tachycardia in a patient with uncorrected severe pulmonary stenosis, and a history of previous arrhythmias. Groups B and C had no complications.

Newborn Outcome

A total of 69 children were born with a weight of 2830 (range, 1000-4250) g. Of these, 10 were premature births, 4 were twins, and 1 had a low birth for the gestational age.

The only low-weight infant of the series belonged to group A and was born to a woman with an ostium primum atrial septal defect and epilepsy under therapy. The incidence of prematurity was 11% (6), with this associate with a hemodynamic cause in 2 newborns who were also twins.

In group B, the incidence of prematurity was 15%, not being severe. One case was related to cyanosis and heart failure in the mother.

In group C, the 2 live births were premature in association with maternal heart disease. One of these had significant neurological sequelae.

Puerperium Outcome

In our series, maternal mortality was only observed during the puerperium and occurred in 1 patient in group B and 1 in group C.

One patient in group A who was pregnant with twins presented cardiac decompensation that resolved with medication.

Three patients in group B presented complications: 1 mother with a single ventricle palliated by a shunt continued to experience heart failure after delivery; another patient with surgical aortic valvuloplasty and residual moderate stenosis presented subdural hematoma; and 1 patient with transposition of the great...
arteries, repaired by the Mustard technique, who died due to ventricular fibrillation after supraventricular tachycardia with rapid conduction. This last patient had presented previous arrhythmias, and her usual amiodarone therapy had been switched to beta-blockers during the pregnancy.

In group C, there was 1 cardiorespiratory arrest resistant to resuscitation in a patient with ventricular septal defect and PH who, after emergency caesarean birth for hemodynamic decompensation, was given bromocryptin to suppress lactation.

All patients with congenital heart disease considered to be at risk spent the puerperium in the cardiologic intensive care unit.

**DISCUSSION**

As observed in longer series, in our series, complications and mortality were directly related to the risk groups. Mortality ranged from 25% among the high-risk patients to 1.6% in those at low risk.

In our experience, risk classification based only on an anatomic diagnosis is misleading because multiple hemodynamic states (cyanosis, PH) are themselves important risk factors. For methodological purposes, we adopted a risk stratification based on the anatomy of the CHD and included certain hemodynamic states:

- Low risk (mortality <1%): mild-to-moderate pulmonary valve stenosis, mild aortic stenosis, small septal defects, small ductus, valve regurgitation, and repaired heart disease with no residual lesions
- Moderate risk (mortality, 1%-10%): patients with a right ventricle functioning as systemic, patients with mechanical valves, cyanotic patients without PH, moderate outflow tract obstruction in both ventricles, univentricular repairs
- High risk (mortality >10%): PH, systemic ventricular dysfunction, severe left ventricular outflow tract obstruction, and aortic aneurysm

The incidence of induced abortions in our series was related to the gestational risk stratification, which was higher in the high-risk group. The decision may have been the result of pre-pregnancy prognostic information offered during reproductive counseling. In the low-risk groups, the incidence of abortion was similar to that of the general population (10%). In all, the incidence of complications was noticeably higher in the high-risk group, which perhaps justifies this methodological classification.

However, the outcomes should perhaps be viewed in light of these risk “modulators” that represent certain hemodynamic states.

Twin pregnancy is an added risk factor, it is known that blood volume is proportionally higher in the case of multiple gestations. Certain hemodynamic states can deteriorate because large preloads are managed, as occurred in the patient with double mitral lesion. The other multiple pregnancy progressed without difficulties, with a virtually normal hemodynamic status.

Arrhythmias are frequent during pregnancy due to hormonal, emotional, and hemodynamic changes and can appear in patients with no history or increase in those who have already had them. In our series, 2 patients had a prior history of arrhythmias, both of them presenting complications, although of very different severity: 1, very mild in the delivery, and the other, eventually causing death in the puerperium. It is difficult to stratify risk in pregnancy based on the arrhythmias, although they are events that could justify the inclusion of patients with this history in the highest risk group. We did not observe arrhythmias in patients who had never experienced this condition.

Previous studies have reported on pregnancies among women with pressure overload due to systemic right ventricle; however, dilatation and irreversible deterioration of contractile function after pregnancy was observed. It is known that the complications most commonly observed in these cases are arrhythmias and right ventricular insufficiency. In our patients, the right ventricle was assessed only by echocardiography. All had right ventricular function subjectively classified by an experienced observer as acceptable and were asymptomatic. The pregnancies occurred without complications, although 1 of the 2 deaths in the series occurred during the puerperium of a patient with systemic right ventricle associated with another related risk factor: arrhythmia. There were no cases of progressive dilatation of the right ventricle after pregnancy in our series.

Right ventricular volumetric overload due to massive regurgitation of the pulmonary valve is usually well-tolerated during pregnancy, as demonstrated in certain studies and in our series. The risk in this case would be the onset of heart failure or arrhythmias. In our series, pulmonary insufficiency was not corrected in any patient before pregnancy because it did not cause right ventricular dysfunction. However, the risk involved was assumed and there were no complications.

The functional class has traditionally been considered an important risk factor, and the New York Heart Association (NYHA) classes III-IV are the least favorable for a successful outcome. In our series, none of the women were class III-IV, possibly because of the preconception counselling discouraging pregnancy in adverse functional stages.

Heart disease that produces cyanosis with hemoglobin saturations < 85% involve a high rate of complications and maternal and fetal death. Although pregnancy is not advisable for women with hypoxia, in our series there were 2 women with a hemoglobin saturation of 75% and...
81% (both had PH); none of them had live newborns, which corroborates the risk that hypoxia poses for the fetuses. However, the other 6 pregnancies of 3 mothers with hemoglobin saturation between 85% and 90% (2 of them also with PH and another with univentricular physiology without PH) ended in 3 spontaneous abortions and 3 live newborns, all premature. We observed a slight decrease in saturation during pregnancy in the patient with univentricular physiology and pulmonary flow dependent on systemic-pulmonary fistulae, although this did not lead to metabolic or hemodynamic complications in the mother.

PH is another major risk factor and known to have the high mortality rate for both mother and fetus. The inability to modify the pulmonary resistances according to the changes of blood volume, risk of thrombosis or bleeding, or increased right-to-left shunting (due to decreased systemic resistances) explain the high probability of maternal complications.22,23 Our unit discourages pregnancy in women with this condition, although there were 4 cases, all with very poor clinical progress for both the fetus (3 abortions, 2 premature births) and mother (puerperal death). Although the literature contains reports that the risk factors of cyanosis and PH independently imply prematurity, abortions, and low weight, it was difficult in our series to separate the importance of each one because they were simultaneously present in a few patients.

Severe left ventricle dysfunction (ejection fraction <35%) is another known risk factor that advises against pregnancy. In our series, this did not occur in any patients, although there were women in good clinical condition in whom the systemic right ventricle function was imprecisely assessed.

It is known that oral anticoagulant therapy administered to patients with mechanical valves is highly teratogenic in the first trimester of pregnancy,24 whereas heparin increases the risk of prosthetic thrombosis25,26 and maternal mortality. When coumarin derivative doses below the equivalent of 20 mg warfarin are used, the risk of fetal malformations is lower.27 This information was provided to the mothers so they could decide on the pregnancy, although our approach was to advise against it. If patients decided to continue, they were asked to consider replacing coumarin derivatives with heparin between weeks 6 and 16, and after week 36 of the pregnancy. In our series, 4 women required anticoagulation, 3 from group B, and 1 from group C. All of them had maternal morbidity (prosthetic thrombosis) and fetal morbidity (3 abortions). Thrombosis during heparin administration and thrombolysis was performed.28 The teratogenicity of the coumarin derivative could not be confirmed, since autopsy was only performed in 1 of the 3 abortions, ruling out embryopathy.

Of the 4 pregnancies with moderate left ventricular outflow obstruction, 3 had a successful outcome to pregnancy, although 1 presented heart failure and the other, spontaneous abortion (she had been taking anticoagulants because of the prosthesis). In case of severe stenosis, correction before pregnancy has been recommended.29 In our series, all of such patients had hemodynamically well-tolerated moderate stenosis before pregnancy: 1 had not received treatment before and the other 3 presented restenosis (1 of aortic prosthesis, 1 of recoarctation, and 1 after surgical valvuloplasty). In 3 of them, valve replacement was considered preferable after completion of the pregnancy.

Other risk factors not observed in our series were aortic aneurysms and dilatations of the aortic root in collagenopathies.30

The complications described during pregnancy are: heart failure, thromboembolism, arrhythmia, and death.25,27,31-33 In our series, only the first 2 were observed: 1 case of thrombosis associated with the risk factor of anticoagulation-mechanical valve and 2 who developed heart failure with the same risk factor (left ventricular outflow tract obstruction), although 1 of these patients had the added factor of twins.

The deliveries were scheduled electively as indicated by the clinical guidelines.34,35 Vaginal birth was the preferred form of delivery, with instruments used if required to shorten the expulsion period. All caesarean births in our series were performed for obstetrical reasons, except for hemodynamic instability in 1 patient with PH. In our series, we found no significant complications in this phase.

In the puerperium, described as a high-risk period risk for the mother, particularly for those with PH,36 we observed the only cases of death of our series, which were triggered by arrhythmia and PH crises. Although no published cases were found, bromocryptin may be related to the death of the patient with PH, since one of its adverse effects is systemic hypotension, which could produce a crisis of severe hypoxia in the context of Eisenmenger syndrome. The patient with a puerperal arrhythmic complication had 2 risk factors already mentioned: previous arrhythmia and dilated systemic right ventricle. Careful monitoring of the mothers during the puerperium is important, particularly if there are risk factors such as PH or arrhythmia.

Our series was unable to confirm known fetal complications, such as the inheritability of CHD, with a reported risk of 2 to 20-fold that of the general population, according to the maternal heart disease.37,38 This may be explained by the fetal echocardiography done on all mothers with CHD. In our setting, pregnancy is usually terminated when there is a fetal diagnosis of complex CHD. All spontaneous abortions occurred in the first trimester, except for 1 late fetal death at 23 weeks that was apparently directly related to the use of oral anticoagulants, but did not affect the fetus. Prematurity occurred in our series in direct relation to gestational risk; its incidence in groups A
and B was equal to that of the general population (8%-9%). Intrauterine growth retardation, reported very often in relation to maternal cyanosis, was observed in only 1 patient in our series who had had low-risk heart disease and was receiving antiepileptic medication. Based on our results, we do not know whether or not maternal cyanosis is an important risk factor for low birth weight, since our series only had 1 infant with this factor, born slightly premature but with an adequate weight.

PH, which also appears to be related to low birth weight, was not observed in our series as a risk factor because no infants were born from these mothers at term.

CONCLUSIONS

Due to advances made in the treatment of CHD, there is a growing population of women who reach the childbearing years and consider vital needs such as the desire for offspring.

In our series, there was a high percentage of pregnancies, deliveries, and puerperium without complications, particularly in the groups with lower gestational risk, allowing us to conclude that pregnancy is possible with adequate management. However, certain clinical and hemodynamic conditions that represent major risk factors should be assessed.

Among the risk factors, PH showed the worst results for mother and fetus, whereas moderate left ventricular outflow tract obstruction was most closely associated with maternal morbidity during pregnancy and the use of oral anticoagulants was primarily related to abortions and maternal morbidity.

Arrhythmia is another risk factor that was closely correlated to complications, although these had variable repercussions. The risk factors of dilated right ventricle, systemic right ventricle, or cyanosis were not evident in our series. Although complications have been described at all stages, the puerperium was the most life-threatening in our series.

It is extremely important for the medical team involved (cardiologists, obstetricians, anesthetists) to provide adequate follow-up and a fair estimate of the risks to these potential mothers. Once the patients have been appropriately informed, the objective of the medical team should be to ensure the best outcome for the patient’s decision. Based on the recommendations of other authors, the following approach should be taken with each group:

- Low risk: could receive the usual obstetric care
- Moderate risk: should be controlled by a multidisciplinary team at a third-level referral hospital
- High risk: should be advised against pregnancy, but closely monitored by an expert team at a third-level referral hospital if it occurs

REFERENCES

24. Roberts N, Ross D, Flint SK, Arya R, Blott M. Thromboembolism in pregnant women with mechanical prothetic heart valves