

Pregnancy in women with congenital heart disease

Embarazo y cardiopatía congénita

Lucelli Yáñez-Gutiérrez,* Carmen Emma Cerrud-Sánchez,* Diana López-Gallegos,*
Horacio Márquez-González,* Marlenne Berenice García-Pacheco,*
Moisés Jiménez-Santos,** Jaime Alfonso Santiago-Hernández,***
Homero Alberto Ramírez-Reyes,*** Carlos Riera-Kinkel****

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ABSTRACT

Advances in the diagnosis and treatment of heart disease have enabled patients to reach adulthood thus reproductive age. In this matter, when women with congenital heart disease get pregnant, it is vital that the multidisciplinary health team includes –of course– an obstetrician, but also a cardiologist and a geneticist. Such teamwork will be able to provide a comprehensive care hence increase the chances of reaching term delivery and, moreover, the probability of reducing the rate of complications for both the mother and the fetus. It is therefore important to acknowledge the physiological changes that occur during pregnancy and the possible complications according to the type of heart disease that the mother presents. It is also responsibility of this multidisciplinary group to provide advice and guidance to terminate the pregnancy when the risk is high.

RESUMEN

Los avances en el diagnóstico y tratamiento de las cardiopatías han permitido que los pacientes lleguen a la edad adulta. La mitad son mujeres y llegarán a la edad reproductiva. Es de vital importancia que el equipo médico incluya tanto al obstetra, como al cardiólogo y al genetista. Esta labor de equipo otorga atención integral y de calidad que incrementa las posibilidades de llevar a término un embarazo con un porcentaje bajo de complicaciones tanto para la madre como para el feto. Por tanto, se debe conocer desde los cambios fisiológicos que ocurren durante el embarazo como las posibles complicaciones de acuerdo al tipo de cardiopatía ya sea de reciente diagnóstico como aquellas reparadas quirúrgicamente o con cardiología intervencionista. También es responsabilidad de este grupo multidisciplinario brindar consejo y orientación para interrumpir el embarazo cuando el riesgo sea alto.

INTRODUCTION

Heart disease is the leading cause of maternal death during pregnancy; this includes several cases of congenital heart disease. Due to advances in treatment options (surgery, cardiological intervention, drugs) the natural history of all congenital heart defects has been modified¹ thus, currently, 8-9 out of 10 children with congenital heart disease reach adulthood; from these, half are women who reach reproductive age.² It is therefore important to provide counseling prior to pregnancy, explain the alternatives for contraception and provide optimal care before, during and after pregnancy.^{1,2}

**PREGESTATIONAL ASSESSMENT
AND CONTRACEPTION**

Ideally, preventive and orientative enforces should begin in adolescence and young women of reproductive age, preparing both patients who have been diagnosed with congenital heart disease, and their parents. Communication between the pediatric cardiologist, the gynecologist, the geneticist and psychologists should interact and perform collaborative work in order to provide the necessary support. These sessions should clarify all doubts and include clear aspects about the morbidity and mortality of procedures, the inherent risk of congenital heart disease complications, in-

* Servicio de
Cardiopatías
Congénitas.
** Servicio de
Tomografía.
*** Servicio de
Hemodinamia.
**** División de
Cirugía Cardiorrástica.

UMAE Hospital de
Cardiología Centro
Médico Nacional Siglo
XXI.

dicating life expectancy in the case of congenital heart disease, as well as discussing the need for additional surgeries and future disabilities and hospitalizations.¹

The issue of contraception should be addressed by the specialist, however, all team members must keep in mind that several alternatives exist, all with a margin of error or undesirable side effects; therefore the case should be individualized in order to choose the safest option for patients. Hormonal treatments have an increased risk of thromboembolic events and, in the case of patients with anticoagulants, it must be remembered that these modify the metabolism of warfarin and lose their effectiveness when using antibiotics or bosentan. The intrauterine device is safe, although it has been reported in some groups to cause risk of bacteremia and infectious endocarditis, in addition to the fact that about 5% of patients may have a vasovagal reaction to manipulating the cervix during insertion; in addition, replacement must take place at least every 5 years. Barrier methods are definitely not first choice because of the high probability of failure. The best options include definitive treatments such as ligation of the fallopian tubes or recently, *stent* implants.³⁻⁶

As mentioned before, in order to assess a pregnant patient with congenital heart disease, the physiological changes that occur both at circulatory level (*Table I*) as well as those to the respiratory system (*Table II*), structural changes (*Table III*) and some special considerations at the moment of delivery, such as hemodynamic changes secondary to pain and anxiety, the fact that with each uterine contraction there is a 50% increase in heart rate and cardiac output (approximately 300-400 mL of intravascular volume) and that decompression of the inferior vena cava causes a transfer of blood from the contracted uterus must be considered.^{7,8}

RISK ASSESSMENT

Based on cohort studies such as the CARPREG study, conducted in 13 Canadian hospitals from 1994-1999, including 546 patients and a total of 599 pregnancies, from which 74% had congenital heart disease and 22% developed heart disease.

Of all the patients with congenital heart disease, at least 46% had been intervened. Further, predictors of both maternal and fetal events were established. Maternal ones included: history of cardiac events, the presence of arrhythmia, functional classification (FC) of the New York Heart Association (NYHA) above II, the presence of cyanosis, left obstruction data and systemic ventricular dysfunction. Fetal ones included: NYHA functional classification above II, cyanosis in the mother, using heparin or warfarin in the peripartum period, history

Table I. Circulatory changes during pregnancy.

- ↑ Cardiac output 30-50%
- ↑ Blood flow 18-25%
- ↓ O₂ venous-artery difference
- ↑ Cardiac contraction
- ↑ Heart rate 20% (10-20 bpm)
- ↑ Plasmatic volume 40-50%
- ↓ Systemic blood pressure
- ↑ Pulse pressure
- ↓ Diastolic pressure > ↓ Systolic pressure
- ↑ Regional flow (uterus, mammary gland, kidney, skin)
- ↓ Vascular resistances (systemic, pulmonary)
- ↔ Central venous pressure
- ↔ Wedge pressure
- Hypercoagulable

Table II. Respiratory changes during pregnancy.

- ↑ Ventilation per minute 45%
- ↑ Oxygen consumption 20%
- ↑ PaO₂
- ↑ PaCO₂
- ↓ Functional residual capacity 40%

Inspiratory capacity

- ↑ Tidal volume
- ↔ Vital capacity
- ↔ Total capacity
- ↔ Lung compliance
- ↓ Airway resistance
- Compensated respiratory alkalosis

of maternal smoking, multiple gestation and evidence of left obstruction. Upon analysis of arterial hypertension, it was apparent that nulliparity, lupus erythematosus and a history of coarctation of the aorta are the most important risk factors. Regarding postpartum hemorrhage, only the use of oral anticoagulant (warfarin) or heparin during peripartum are risk factors. Another important fact to consider is that cyanosis in the mother obviously disrupts hemostasis and was a significant factor.

Another published paper specifies that left obstruction will be in either the left mitral valve (area less than 2 cm²), aortic (area less than 1.5 cm²) or gradient of the left ventricular outflow tract greater than 30 mmHg. Events of arrhythmias, stroke, transient ischemic attack and acute pulmonary edema before pregnancy were other variables to consider and it is noteworthy that age was analyzed as a risk factor, concluding that if you are under 18 or over 35 you are more at risk, as well as taking into account fitness and whether a smoker.^{9,10}

The Zahara study, published in 2010, perhaps the largest published to date, included 1,802 women, 1,302 pregnancies, 336 spontaneous abortions and 58 who chose abortions, aged 27.4 + 2.6 years. This included almost all congenital heart diseases and the most common cardiac complications were arrhythmias and heart failure, whereas the most frequent obstetric complications were arterial hypertension and low birth weight or prematurity.¹¹

From these works, maternal and neonatal risk factors were proposed (Table IV), together with the amended classification from the World Health Organization (WHO) for maternal cardiovascular risk (Table V).^{9,11,12}

SPECIAL TOPICS

Risk of Inheritance

It is a frequently asked question within the assessment of women of reproductive age, due to the fact that overall risk is increased when the mother presents cardiopathy (up 6.7%); however, the fact that the father presents heart disease can also incur risk (2.1%). The type of cardiopathy also modifies such risks: atrioventricular defects in the mother incur a risk of 11.6%, but if it is the father, the risk is 4.3%; aortic stenosis 8 versus 3.8%, respectively; aortic coarctation 6.3 versus 3%, interventricular communication 6 versus 3.6%, pulmonary stenosis 5.3 versus 3.5% and Tetralogy of Fallot 2 versus 1.4%, again, respective to mother/father. Therefore it is imperative that all patients with congenital heart disease are provided with genetic counseling.^{9,10,13}

Cardiovascular drugs

It is well known that congenital cardiopathies will affect embryonic development and organ, thus both angiotensin converting enzyme inhibitors and antagonists of angiotensin II receptors are contraindicated due to the potential renal injury that may result. Likewise, amiodarone is also contraindicated because of the risk of neonatal hypothyroidism, prematurity or neurodevelopmental problems. Spironolactone is not recommended because of genital abnormalities; oral anticoagulants

Table III. Structural changes during pregnancy.

Can be poorly tolerated in cardiac patients	Other complications to consider
<ul style="list-style-type: none"> • Myocardial hypertrophy • Dilatation of cardiac cavities • Valvular insufficiency • Contractility is slightly reduced • Dilation of diameter of aortic root 	<ul style="list-style-type: none"> • Proarrhythmic phenomena • Thrombosis

Table IV. Maternal and neonatal risk factors.

Maternal risk factors	Neonatal risk factors
<ul style="list-style-type: none"> • History of arrhythmias • Cardiovascular drugs • Functional classification • Left obstruction • Severe valvular regurgitation • Pulmonary or systemic AV • Mechanical prosthesis • Cyanotic heart disease 	<ul style="list-style-type: none"> • Twin or multiple gestation • Smoking • Cyanotic heart disease • Mechanical prosthesis • Cardiovascular drugs

(warfarin and acenocumarine) because of their inherent embryopathy and the risk of bleeding.^{14,15}

However, the following drugs are considered relatively safe: aspirin, diuretics, beta blockers (although there are reports show-

Table V. WHO risk table.

Risk classification	Risk to pregnancy by disease	Diseases	Mortality %
I	No detectable increased risk of maternal mortality and without any increase or slightly higher morbidity	<ul style="list-style-type: none"> • PVS, PDA, MVP • Successfully repaired simple lesions (ASD, VSD, PDA, APVC) • Isolated atrial or ventricular ectopic beats 	0.1
II	Slightly increased risk of maternal mortality or moderate increase in morbidity	<ul style="list-style-type: none"> • Unoperated ASD or VSD • Repaired Tetralogy of Fallot • Most arrhythmias <p><i>Can be WHO II or III:</i></p> <ul style="list-style-type: none"> • Mild left ventricular dysfunction • Hypertrophic cardiomyopathy • Native valvular heart disease or tissue that is not considered to be WHO I or IV • Marfan syndrome WITHOUT aortic dilatation • Aorta < 45 mm in aortic disease associated with bicuspid aortic valve • Repaired coarctation 	0.5
III	Significantly increased risk of maternal death or serious morbidity. Guidance from a specialist is required. If the decision is taken to continue with the pregnancy, cardiac and obstetric intensive monitoring by specialists is required throughout pregnancy, childbirth and postpartum	<ul style="list-style-type: none"> • Mechanical valve • Systemic right ventricle • Fontan circulation 	5.5
IV	Extremely high risk of maternal mortality or serious morbidity; pregnancy is contraindicated. If pregnancy occurs, its discontinuation should be considered. If the pregnancy is continued it should be dealt with as classification III.	<ul style="list-style-type: none"> • Pulmonary hypertension of any etiology • Severe systemic ventricular dysfunction (LVEF < 30%, NYHA III-IV) • Previous peripartum cardiomyopathy, with any residual impairment of left ventricular function • Severe mitral stenosis, severe symptomatic aortic stenosis • Marfan syndrome with dilated aorta > 45 mm • Aortic dilatation > 50 mm in aortic disease associated with bicuspid aortic valve • Serious native coarctation 	6

PVS = Pulmonar valvular stenosis, PDA = Patent ductus arteriosus, MVP = Mitral valve prolapse, ASD = Atrial septal defect, VSD = Ventricular septal defect, APVC= Anomalous pulmonary venous connection.

ing that they stunt growth), digoxin, calcium channel blockers, adenosine, procainamide (although pseudo-lupus syndrome must be considered), lidocaine, and flecainide.¹⁶

Oral anticoagulation

A controversial aspect concerning embryopathy and the risk of thrombosis, is the use of oral anticoagulants for any therapeutic indication, e.g., prosthesis, history of thrombus, atrial arrhythmias, etc. Guidelines state that the use of oral anticoagulation (OAC) can be prescribed during the second and third trimester to the 36th week; in the first trimester, unfractionated heparin (UFH) or low molecular weight heparin (LMWH) was used, adjusting for APTT > 2 times control or anti Xa 4-6 hours weekly, after administration of 0.8-1.2 U/mL, as appropriate. This change in anticoagulation regimen during pregnancy should be implemented within hospital settings; if labor starts while still in treatment with OAC, caesarean section is indicated. LMWH should be suspended 36 hours before delivery and changed to UFH, which is then suspended 4-6 hours before the planned delivery and restarted after 4-6 hours if there is no complication from hemorrhaging. An echocardiogram is obviously indicated for those women with mechanical prostheses who present sudden dyspnea or an embolic event during the aforementioned regime change between anticoagulant and heparin.^{12,16}

Classification IIA, could consider continuing with OAC during the first trimester if the dose required to maintain therapeutic anticoagulation is < 5 mg/day of warfarin or < 2 mg/day acenocumarine. If doses are > 5 or 2 mg respectively, suspension of OAC between weeks 6 to 12 should be considered and further replaced with UFH or LMWH, among high-risk patients. The use of LMWH is considered within classification III, if the level of antiXa cannot be controlled.¹⁶

Severe arrhythmias

In case of severe arrhythmia, antiarrhythmic drugs can be used with some confidence re-

garding the product. Cases where vagal maneuvers have been used safely have been reported, as well as the introduction of an implantable cardioverter defibrillator or a pacemaker guided by echocardiography in pregnant women with serious arrhythmias or conduction disorders that compromise their lives and that of the product.¹⁶⁻¹⁸

Interventionist cardiology

It is known that interventionist procedures must be postponed as far as possible because of the teratogenic risk from radiation (limit is 50 mGy), although common procedures do not involve a very high dose (e.g., both mitral valvuloplasty and coronary angioplasty produce 20mGy). Nevertheless, if it is necessary to undergo a procedure, security measures should be taken in order to protect the abdomen with a lead vest, and should be postponed at least until the second trimester when the uterus is still small and can be perfectly covered and dye should be used; the latter, even if not considered teratogenic, has been reported to be related to neonatal hypothyroidism. E.g., a conventional X-ray causes < 0.01 mGy of fetal exposure and 0.1 mGy for the mother, a CT scan irradiates 0.3 mGy to the fetus and 7 mGy to the mother, coronary angiography yields 1.5 mGy to the fetus and 7 mGy to the mother, and a percutaneous intervention or radiofrequency ablation gives 3 mGy to the fetus and 15 mGy to the mother.^{12,19,20}

Cardiac surgery

Although mortality is reported to be similar to that of the general population, surgery is usually reserved only for cases resistant to medical treatment, due to > 30% fetal loss.^{19,21}

Cardiopulmonary resuscitation

Should this be necessary, it is suggested that resuscitation is performed with the mother discreetly placed on the left lateral decubitus position 15-30°, compressions are made slightly higher than usual and the femoral route should not be used for delivering drugs. A C-section should be urgently scheduled.²²

Unresolved lesions

Obstructive lesions of the pulmonary valve with maximum gradient > 64 mmHg must be resolved before pregnancy. Ebstein's anomaly with symptoms of cyanosis and/or heart failure must be resolved prior to pregnancy or strong advice to desist from getting pregnant should be given. Patients with severe enlargement of the right ventricle because of insufficient pulmonary valve should be referred for pulmonary valve replacement with biological prosthesis before pregnancy. All women with bicuspid aorta should have an echocardiogram and other imaging studies in order to assess the ascending aorta and surgical treatment will be proposed if the aorta is > 50 mm. In patients with Fontan surgery, oral anticoagulation will be proposed during pregnancy, as well as for patients with PAH and suspected pulmonary embolism.

Finally, women are contraindicated and advised to terminate the pregnancy if they have PAH, with saturation of < 85%, women with transposition of the great arteries and impairment of right ventricular function, those with an univentricular heart who have undergone the Fontan operation or who have deterioration in the systemic ventricular function or moderate failure of the atrioventricular, or those with cyanosis or protein losing enteropathy.²³

CONCLUSIONS

Improvements in medical and surgical treatments have enabled women with congenital heart disease to reach adulthood. Awareness of the need for pregnancies to be programmed and monitored by a multidisciplinary team and necessarily include genetic counseling should be initiated in adolescence. It is the duty of health personnel to promote an echocardiogram for both mother and fetus. We must insist that patients with lower risk of complications are those in FC I-II with resolved heart disease or simple lesions and we must suggest that cyanotic patients or classification III-IV patients should not become pregnant because they present high risk for both the mother and fetus.

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Correspondence to:

Dra. Lucelli Yáñez Gutiérrez
Cuahtémoc Núm. 330,
Col. Doctores, Delegación Cuahtémoc,
06725, México, D.F.
Tel. (55) 56-27-69-00, ext. 22203
E-mail: lucelli.yanez@imss.gob.mx

www.medigraphic.org.mx