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Pregnancy in Patients with Heart Disease: Experience with 1,000 Cases

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Summary

Background: Previously, the high maternal mortality in cardiac patients who became pregnant prompted the assertion: Women with an abnormal heart should not become pregnant. This long-standing notion needs to be revised today.

Hypothesis: The study was undertaken to ascertain the experience with a large series of pregnant women with cardiac disease cared for in the same referral center.

Methods: From 1989 to 1999, 1,000 pregnant women with heart disease were followed by the same clinical and obstetric team. The cardiac diseases included rheumatic heart disease (55.7%), congenital heart disease (19.1%), Chagas' disease (8.5%), cardiac arrhythmias (5.1%), cardiomyopathies (4.3%), and others (7.3%).

Results: Of the pregnant women studied, 765 (76.5%) experienced no cardiovascular events during the study; 235 (23.5%) patients had the following cardiovascular complications: congestive heart failure (12.3%), cardiac arrhythmias (6%), thromboembolism (1.9%), angina (1.4%), hypoxemia (0.7%), infective endocarditis (0.5%), and other complications (0.7%). Clinical treatment allowed adequate management in 161 (68.8%) patients; however, 46 (19.6%) patients underwent interventional procedures because of refractory complications. The general maternal mortality rate was 2.7%. Of the 915 (91.5%) infants who were discharged, 119 (13%) were premature.

Conclusion: Pregnancy in women with heart disease is still associated with considerable morbidity and mortality rates, which strongly correlate to maternal underlying disease. Strict prenatal care and early risk stratification during gestation are fundamental measures to improve the prognosis of pregnancy in women with heart disease.

Key words: pregnancy, heart disease, maternal outcome, fetal outcome, cardiac complication

Introduction

Previously, the high maternal mortality in cardiac patients who became pregnant prompted the assertion: Women with an abnormal heart should not become pregnant.[1] This long-standing notion needs to be revised today. Perloff[2] reported a progressive and substantial reduction in maternal death and improved fetal outcome in pregnant women with heart disease. Nevertheless, heart disease remains a leading cause of nonobstetric maternal death during pregnancy.[3]

With increasing experience, it has become clear that not all clinical situations carry the same ominous prognosis. While pregnancy remains prohibitive under some conditions (e.g., pulmonary vascular disease) or associated with significant maternal morbidity (e.g., mitral stenosis), other conditions, such as mitral valve prolapse, have a benign course during gestation. In addition, medications used during pregnancy may influence outcome. Therefore, patients should be evaluated for underlying cardiac disease to select appropriate management.

Clearly, risk stratification influences therapeutic decisions during pregnancy as does counseling about future gestations. The present study is a report of experience with the largest published series of pregnant women with cardiac disease cared for by the same team of physicians in one institution.

Materials and Methods

From 1989 to 1999, 1,000 pregnant women with heart disease were followed at the Heart Institute of the University of

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TABLE I Underlying diseases — 1,000 cases

Cardiac lesion	Total No. / %	No intervention	Previous intervention
Rheumatic valvular disease	557/55.7	326/58.5	231/41.5
Surgical repair			107/19.2
Bioprostheses			87/15.6
Mechanical prostheses			22/3.9
Percutaneous balloon valvoplasty			15/2.7
Congenital heart disease	191/19.1	91/47.6	79/41.4
Acyanotic	121/63.3	81	40
Left-to-right shunts defects		41	29
Valvular or vascular obstructive lesions		40	11
Cyanotic	49/25.6	10	39
Tetralogy of Fallot		1	25
Double-outlet right ventricle		2	1
Ebstein's anomaly		7	6
Transposition of the great arteries		0	7
Eisenmenger's syndrome			21/11
Chagas' disease			85/8.5
Conduction disorders		53/62.4	
Dilated cardiomyopathy		19/22.3	
Indeterminate		13/15.3	
Cardiac arrhythmias			51/5.1
Supraventricular and/or ventricular rhythm disturbances		34/66.7	
Pre-excitation syndrome		12/23.5	
Congenital total heart block		5/9.8	
Cardiomyopathy			43/4.3
Dilated		27/62.8	
Idiopathic		18/41.9	
Peripartum		9/21.0	
Hypertrophic		15/34.8	
Restrictive		1/2.3	
Miscellaneous			73/7.3

São Paulo. Rheumatic and congenital heart disease accounted for approximately 75% of all cardiac abnormalities, with the remaining causes of cardiac anomalies evenly distributed (Table I). Miscellaneous conditions included 32 cases with mitral valve prolapse (8 with cardiac arrhythmia and 24 with valve regurgitation); 14 cases with coronary artery disease (all with coronary stenosis of > 70% proven by coronary angiogram and 7 with prior myocardial infarction); 13 presented with pulmonary vascular disease (in 8 associated with schistosomiasis); 7 had Takayasu's arteritis; 3 patients had thoracic aortic aneurysm, 3 had Marfan's syndrome, and 1 patient had undergone cardiac transplantation.

All patients were followed up monthly by the same clinical and obstetric team for up to 8 months of gestation, weekly thereafter until delivery, and up to 3 months after delivery. Electrocardiogram and Doppler echocardiography studies were performed in all patients. The infants were examined before discharge, and echocardiograms were performed if congenital heart disease was suspected.

Routine prophylaxis management of specific cardiac events such as rheumatic fever and infective endocarditis was performed according to conventional strategies.[4,5]

The routine strategy adopted against thromboembolic episodes was as follows: (1) In patients with mechanical prostheses, coumadin was stopped and heparin was used instead in two periods: during the first trimester of gestation and from Week 34 of gestation until 2 days after delivery; in the remaining period coumadin was maintained. Daily doses of subcutaneous unfractioned heparin was used: either 30,000 U to achieve 1½ to 2 times of activated partial thromboplastin time (APTT), or low-molecular weight heparin doses at 1 mg/kg t.i.d. (2) In atrial fibrillation, pulmonary hypertension or cyanotic heart disease, subcutaneous unfractioned heparin or low-molecular weight heparin was employed from Week 24 of gestation until 2 days after delivery, at daily doses of 20,000 U or 40 mg, respectively. In both situations, coumadin was introduced 2 days after delivery, adjusted to a target International Normalized Ratio (INR) of 2.0 to 3.5.

Cardiac complications were managed as follows: heart failure was treated with bed rest, salt restriction, digoxin, furosemide, hydralazine, with or without nitrates. Hydralazine, recognized as not associated with harmful fetal effects,[6] was selected to replace the angiotensin-converting enzyme inhibitors that are contraindicated during pregnancy.[7] Ther-

apy for patients with pulmonary congestion associated with mitral stenosis included propranolol (60–80 mg/day) and furosemide.[8] In clinical emergencies, such as a severe pulmonary congestion and/or low cardiac output, dobutamine and/or sodium nitroprusside (for no more than 3 h to avoid the potential of cyanogen fetal toxicity) were used. Emergency treatment of arrhythmias with hemodynamic impairment included electrical cardioversion, intravenous verapamil, or adenosine. Low doses of propranolol, verapamil, quinidine, or digoxin were subsequently administered for maintenance therapy, while life-threatening ventricular arrhythmias were managed with amiodarone.

Treatment of patients with cyanotic congenital heart disease or pulmonary vascular disease included hospitalization from the second trimester of pregnancy until delivery, subcutaneous heparin in cases of Eisenmenger's syndrome, and intermittent long-term oxygen therapy.

In general, heart disease was not considered an indication to induce labor, essentially for obstetrical reasons. Therapeutic abortion was recommended in situations such as Eisenmenger's syndrome, ventricular dysfunction with heart failure, and diseases of the aorta (aortic aneurysms, Takayasu's arteritis, Marfan's syndrome).

Results

Maternal Outcome

Of 1,000 pregnant women, 765 (76.5%) had no cardiovascular complications during the study; the remaining 235 (23.5%) patients experienced cardiovascular events, shown in Table II in decreasing order of frequency.

In patients with rheumatic heart disease, there were 119 (21.4%) complications (Table III). Congestive heart failure and pulmonary congestion occurred in 54 (63.5%) patients with moderate or severe mitral stenosis (mitral valve area below 1.5 cm^2 assessed by Doppler echocardiogram), 19 (22.3%) with valve regurgitation, 12 (14.1%) with bioprostheses, related in 10 patients to bioprosthesis dysfunction (7 detected before gestation). Among the 20 patients with cardiac arrhythmias, 16 were in atrial fibrillation associated with mitral valve disease. Eight episodes of thromboembolism occurred in native mitral valves (five associated with atrial fibrillation, with three of these following a regimen of anticoagulation recommended in the protocol), and four in mechanical prostheses. Infective endocarditis was observed in one patient with aortic regurgitation during Week 19 of

TABLE II Complications relative to underlying disease

Cardiac diseases	No. of cases	Complications (No. / %) Total No. / %	CHF/PC	Arrhy	Thromb	Angor	Hyp	IE	Others
Rheumatic valvular	557	119/21.4	85/71.4	20/16.8	12/10.1	0	0	2/1.7	0
Congenital	191	44/23.0	22/50.0	4/9.1	1/2.8	5/11.4	7/15.9	1/2.8	4/2.0
Chagas' disease	85	21/24.7	4/19.0	16/76.2	1/4.8	0	0	0	0
Arrhythmias	51	11/21.5	2/18.2	9/818	0	0	0	0	0
Cardiomyopathy	43	18/41.8	7/38.9	4/22.2	2/11.1	5/27.7	0	0	0
Others	73	22/30.1	3/13.6	7/31.8	3/13.6	4/18.2	0	2/9.1	3/13.6
Total	1,000	235/23.5	123/12.3	60/6.0	19/1.9	14/1.4	7/0.7	5/0.5	7/0.7

Abbreviations: Angor = angina, Arrhy = cardiac arrhythmias, CHF/PC = congestive heart failure/pulmonary congestion, Hyp = hypoxemia, IE = infective endocarditis, Thromb = thromboembolism.

TABLE III Maternal outcome—overview of 1,000 cases

Cardiac diseases No. (%) cases	Total No. / % 1,000	RHD 557	CHD 191	Chagas 85	Arrhy 51	CM 43	Others 73
No complications	765/76.5	438/78.6	147/76.9	64/75.3	40/78.5	25/58.2	51/69.9
Complication	235/23.5	119/21.4	44/23.1	21/24.7	11/21.5	18/41.8	22/30.1
Medical treatment [a]	161/68.8	82/68.9	29/65.5	14/66.7	10/90.9	15/83.3	11/50.0
Intervention [b]	47/20.0	28/23.5	8/18.2	4/16.7	1/9.1	0	6/27.2
Mortality	27/2.7	9/1.6	7/3.6 [c]	3/3.7	0	3/6.9	5/6.8

[a] Successful medical treatment.

[b] Interventional procedures during gestation.

[c] Six of them with Eisenmenger's syndrome.

Abbreviations: RHD = rheumatic valve disease, CHD = congenital heart disease, Chagas = Chagas' disease, Arrhy = arrhythmia, CM = cardiomyopathy, Others = miscellaneous conditions.

gestation, and in another patient with bioprosthesis during Week 33 of gestation. Both patients survived, although the first required aortic valve replacement. Maternal deaths were caused by heart failure in patients with severe mitral valve diseases and thrombosis of mechanical prostheses.

In patients with congenital heart disease, 44 (23.0%) complications were documented (Table II). Of the 22 patients with congestive heart failure, 20 had unrepaired defects; 13 patients had aortic valve stenosis, 3 had aortic coarctation, and the remaining patients had shunt lesions. Paroxysmal supraventricular arrhythmias were observed in three patients with atrial septal defects and in one after surgical repair of tetralogy of Fallot. Angina was reported in two patients with aortic stenosis and in three with Eisenmenger's syndrome. Hypoxemia was reported in five patients with unrepaired cyanotic congenital heart disease and in two with Eisenmenger's syndrome; these patients had refused therapeutic abortion during the first trimester of gestation. Infective endocarditis was observed in one patient with an uncorrected ventricular septal defect. Among other complications, recurrent syncope was documented in two patients with Eisenmenger's syndrome and in one with aortic valve stenosis.

Cardiac arrhythmias were the most frequent complications in the group with Chagas' disease (Table II), including six cases of complex ventricular arrhythmias. All cases of congestive heart failure were associated with dilated cardiomyopathy.

Of patients with cardiac arrhythmias without structural cardiac lesions, 11 (21.5%) experienced clinical worsening of a previous arrhythmia, with induction of concomitant congestive heart failure in two patients who presented with intermittent paroxysmal atrial tachycardia (Table II).

In the cardiomyopathy group, there was a high complication rate (41.8%), involving 18 patients (Table II): 5 of 7 patients with congestive heart failure had hypertrophic cardiomyopathy; there were 4 cases of cardiac arrhythmias including 3 of acute atrial fibrillation and 5 of angina, also in patients with hypertrophic cardiomyopathy. Both patients who presented with thromboembolic complications had dilated cardiomyopathy. Recurrent syncope was recorded in one woman with dilated cardiomyopathy. No patient developed the disease during gestation; peripartum cardiomyopathy had been diagnosed in previous pregnancies. All maternal deaths occurred in dilated form of disease.

Finally, 22 (30.1%) patients in the miscellaneous group experienced complications, including the following (Table II): congestive heart failure in 3 patients with pulmonary vascular disease; cardiac arrhythmias in 3 patients with pulmonary vascular disease and in 4 with coronary arterial disease; thromboembolic episodes in 3 patients with pulmonary vascular disease; angina in 4 patients with coronary arterial disease; and infective endocarditis in 2 patients: 1 with a previously normal aortic valve and another with mitral valve prolapse with chordae rupture.

Only 7 (53.8%) of the 13 patients in the pulmonary vascular disease had an uneventful pregnancy; the remaining experienced various events including 2 cases of maternal bleeding after delivery and 1 case of hemorrhage due to ruptured esophageal varices.

Conversely, 13 (92.8%) women with coronary arterial disease achieved full-term gestation, including 7 (50%) who were free of cardiovascular events. Four patients, however, developed unstable angina, two requiring coronary angioplasty and one needing surgical revascularization. Coronary artery dissection was not observed in any patient.

Of the 235 patients who experienced cardiovascular events during the study, 161 (68.5%) could be clinically managed. Nevertheless, 46 (19.6%) patients were refractory to medical therapies, requiring interventional procedures (Table III).

Twenty-five patients underwent heart surgery as follows: valve surgery in 10 patients; prosthesis-valve repeat surgery in 8 patients; surgical repair of congenital cardiac defects in 5 patients. Heart surgical procedures resulted in 1/25 (4.0%) maternal death and 4 (16.0%) stillbirths. Other cardiac intervention procedures undertaken in 18 patients (Table III) included percutaneous balloon mitral valvuloplasty (10 cases), coronary angioplasty (2 cases), and pacemaker implantation (6 cases).

Overall maternal mortality, underlying disease, and complications are presented in Table III. The main clinical situations associated with death were rheumatic heart disease in nine (1.6%) cases; congenital heart disease in seven (3.5%) cases (six of them with Eisenmenger's syndrome), Chagas' disease in three (3.7%) cases, dilated cardiomyopathy in three (6.9%) cases, and pulmonary vascular disease in five (38%) cases.

Obstetrical and Fetal Data

Vaginal delivery occurred in 613 (65%) patients and cesarean section in 331(35%) women, mostly for obstetrical indications. The main obstetrical reasons were fetal growth retardation, fetal distress, and labor induction failure. In < 5% of the cases, cesarean section was indicated by heart disease, such as diseases of the aorta and severe impairment of maternal hemodynamics, as in cases of cardiomyopathy, Eisenmenger's syndrome, severe left ventricular obstructive outflow diseases, or pulmonary vascular disease.

Of the 915 (91.5%) infants who were discharged, 796 (79.6%) were full term (Table IV). Neonatal weight was 2,926 ± 654 g. Twins were born in five cases. Of 29 (2.9%) stillbirths, 5 occurred immediately after the onset of acute atrial fibrillation. Among 22 (2.2%) cases of fetal pathology correlating with maternal cardiac disease, there were 4 cases of congenital Chagas' disease; an infant with neurological disease, whose mother had undergone aortic valve replacement during the second trimester of gestation; and the remaining were cases of cardiac disease.

Discussion

This observational study, one of the most extensive ever undertaken in the same Institution on follow-up of gestation in women with heart disease, documented a 23.5% incidence of cardiovascular complications, a 2.7% overall mortality rate, and 7.7% spontaneous abortion and stillbirth in 1,000 cases

TABLE IV Fetal outcome—overview of 1,000 pregnancies

Cardiac diseases No. (%) cases	Total No. / % 1,000	RHD 557	CHD 191	Chagas 85	Arrhy 51	CM 43	Others 73
Infants discharged	915/91.5	528/94.8	159/83.2	78/91.7	50/98.0	36/83.7	64/87.6
Abortions [a]	56/5.6	23/4.1	22/11.5	3/3.5	0	3/6.9	5/6.8
Stillbirths	29/2.9	6/1.1	10/5.2	4/4.7	1/1.9	4/4.3	4/5.5
Prematurity	119/11.9	57/10.2	31/16.2	13/15.3	—	5/11.6	13/17.8
CHD	22/2.2	2/0.3	11/5.8	4/4.7	—	3/6.9	2/2.7

[a] Therapeutic abortion in 8 (0.8%) cases.
Abbreviations as in Table III.

studied. The adherence to a carefully conducted protocol allowed an uneventful course of pregnancy in most patients (76.5%). Furthermore, appropriate medical therapy and interventional procedures in the management of complications also permitted successful pregnancy in severe clinical conditions (Table III). Considering the varying prognoses and characteristics of the underlying diseases, each situation will be addressed individually.

Rheumatic heart disease, which was present in more than half of patients (Table I), remains the most frequent cause of valve disease. Although a significant number of patients with rheumatic heart disease had serious valve lesions, they showed favorable characteristics to prognosis of gestation such as young age, sinus rhythm, and normal myocardial function. Besides medical treatment, surgical interventions or percutaneous balloon valvuloplasty were frequently effective, resulting in satisfactory maternal outcome (Table III).

Pulmonary congestion was the most frequent complication in patients with mitral stenosis; notwithstanding, all of them were in New York Heart Association (NYHA) functional class I/II at the beginning of pregnancy. In fact, according to our previous report, functional class I/II at the beginning of gestation does not assure an uneventful pregnancy in mitral stenosis.[8] In these cases, the use of furosemide and propranolol allowed clinical control in most patients up to delivery, a fact that favors medical therapy as the first option for managing such patients. Propranolol was selected to reduce heart rate, improve hemodynamics, and to prevent atrial fibrillation. Adverse effects attributed to propranolol in newborns, such as bradycardia, birth apnea, polycythemia, and hyperbilirubinemia,[9] are related to doses and have not been observed at doses up to 80 mg/day.

In cases of paroxysmal atrial fibrillation, also a common complication, electrical cardioversion should be considered the first alternative for reverting to sinus rhythm because it is effective, shortens the period of low cardiac output, and avoids potential danger to the fetus by the use of high doses of antiarrhythmic drugs. Atrial fibrillation apparently increased the risk of thromboembolism, since it occurred in five cases of rheumatic disease despite anticoagulation with heparin.

The significant incidence of cardiac complications in mitral stenosis induces some authors to perform "prophylactic" percutaneous balloon mitral valvuloplasty before gestation.[10] However, this is a controversial issue; we tend to avoid preventive intervention because this procedure is associated with 0.5% mortality, 1% cerebral embolic events, 1% cardiac perforation, 2% mitral regurgitation requiring valve replacement, and 15% mild and moderate mitral regurgitation.[11] Moreover, percutaneous balloon mitral valvuloplasty, if necessary, can be performed safely and effectively during pregnancy.[12]

Among 26 patients with mechanical prostheses, 4 (15.4%) had thromboembolic episodes, with 3 occurring during heparin treatment, causing one maternal death and two emergency valve replacements. These data are consistent with those of many others,[13, 14] who emphasize adverse pregnancy outcomes in women with mechanical prosthetic valves, particularly during heparin use.

Conversely, heart failure rate (13.7%) in bioprosthesis cases, most of them due to prosthetic dysfunction, suggest that dysfunction of bioprostheses implies a worse clinical and hemodynamic prognosis during gestation. Nevertheless, these data do not support the hypothesis that pregnancy accelerates the degeneration of bioprosthesis,[15–16] because in the majority of these cases some dysfunction was recognized before gestation. Indeed, the results of a contemporary prospective and comparative 5-year study did not indicate that pregnancy contributes to bioprosthesis deterioration,[17] consistent with findings in other studies.[18–20] The conflicting conclusions concerning the role of pregnancy in accelerating structural bioprosthetic failure may be due to differences in study population and data collection.

Although there were insufficient data for comparative statistical analyses, absence of maternal mortality in bioprotheses without dysfunction, low rate of fetal demise, and dispensable anticoagulation prompt us to recommend bioprostheses rather than mechanical prostheses in pregnant women.

In congenital heart disease, pregnancy was well tolerated by women with cardiac shunts without pulmonary hypertension, the most common form of congenital heart disease (Table I). Supraventricular arrhythmias, frequent in patients with atrial septal defects and heart failure in patent ductus arteriosus, were controlled by medical therapy with favorable maternal and fetal outcomes.

In contrast, shunt lesions associated with pulmonary hypertension, chiefly in Eisenmenger's syndrome, are dangerous because of increased thromboembolism risk and right heart failure.[21] In addition, long-term prevention with use of

anticoagulants frequently leads to hemorrhagic complications.[22] Although controversial, the use of heparin in this setting was based on the high incidence of maternal death related to thromboembolism during gestation.

The high maternal mortality (33%) and fetal demise (47%) rates in Eisenmenger's syndrome correlated with congestive heart failure, sudden death, thromboembolism, and infection emphasize the obstetrical and fetal risks of pregnancy in this group of patients. Indeed, of 21 pregnancies of women with Eisenmenger's syndrome, only 7 were discharged with both mother and infant alive. This result supports the notion[23, 24] that patients with Eisenmenger's syndrome should avoid pregnancy and, if pregnant, should be advised to have an elective abortion without delay.

Among obstructive lesions, pulmonary stenosis, even in patients with significant right ventricular outflow obstruction, was not associated with complications. In contrast, pregnancy in patients with moderate to severe aortic valve stenosis was associated with 68.5% maternal morbidity, including one sudden death and the need for aortic valve replacement due to congestive heart failure and recurrent syncope in two cases.

These data confirm the adverse prognosis of pregnancy in women with significant symptomatic aortic stenosis, specifically with an aortic gradient > 70 mmHg.[25] Although surgical intervention can be performed during pregnancy at refractory heart failure or syncope, it must be recommended before pregnancy.

Tetralogy of Fallot was the most common cyanotic malformation; most of these had been surgically corrected in early childhood, allowing a favorable maternal and fetal outcome. Ebstein's anomaly, the most frequent uncorrected type of cyanotic malformation (Table I), presented a wide variation in the severity of lesions that determined its clinical manifestation; however, paroxysmal tachycardia caused cyanosis in two patients, probably due to an increase the right-to-left shunting.

In Brazil, the prevalence of Chagas' disease in pregnant women infected by *Trypanosoma cruzi* ranges from 2.0 to 16.4%, two-thirds of them without heart injury;[26] however, in the present study, 85% of patients with Chagas' disease had heart impairment due to a selection bias, explaining the high complication and mortality rates of 24.7 and 3.7%, respectively (Table II).

Patients with an indeterminate form of disease, defined as the absence of apparent cardiac damage, but with serum-positive tests, experienced uneventful courses during gestation. Conversely, in patients with conduction disorders that were or were not associated with myocardial dysfunction, there were 76.2% of cardiac arrhythmia and 19.0% of congestive heart failure (Table II). In addition, some complications were refractory to medical treatment, including 4 of the 16 patients with complex cardiac arrhythmias who required pacemaker implantation. Despite specific treatment for cardiac arrhythmias and congestive heart failure, the maternal mortality rate was 3.7% including one case of sudden death, representing the fourth cause of overall maternal mortality (Table III); moreover, congenital transmission of Chagas' disease in four cases adds further reason for restricting pregnancy in this group of patients.

Cardiomyopathy had complication and mortality rates of 30 and 10%, respectively; this underscores the harmful maternal prognosis specifically associated with left ventricular dysfunction.[27] The small number does not permit comparison of pregnancy outcome between peripartum and idiopathic cardiomyopathy; furthermore, peripartum diagnosis was established in previous gestation. Poor prognosis was related to cardiovascular events before gestation, such as heart failure, thromboembolism episodes, and cardiac arrhythmias in both causes. These data confirm that dilated cardiomyopathy with left ventricular dysfunction is a contraindication for pregnancy, independent of its etiology.

In hypertrophic cardiomyopathy, the high (73.3%) incidence of congestive heart failure, angina, and atrial fibrillation depended on the clinical form of disease. These data are in agreement with some reports that indicate a poor maternal outcome in obstructive forms of these conditions or when there are symptoms of atrial fibrillation before gestation.[28] The clinical management, including bed rest, prolonged hospitalization, and use of verapamil (240 mg/day) plus propranolol (160 mg/day) did not assure good maternal outcome even in patients with previous surgical myectomy or pacemaker implantation; in addition, high doses of drugs can be hazardous to the fetus. The high complication rate and relative lack of effective therapeutic measures prompt us to advise women with symptomatic hypertrophic cardiomyopathy to avoid pregnancy.

Cardiac arrhythmias without structural lesions usually present favorable maternal and fetal outcomes and generally require no antiarrhythmic drugs;[29] however, this study was limited to patients with significant and symptomatic cardiac arrhythmias that required treatment with antiarrhythmic drugs during pregnancy, guided by careful clinical and Holter monitoring for 24 h. Drugs such as cardiac glycosides, verapamil, quinidine, and propranolol, at doses tailored to the gestational age, were not associated with obstetrical or fetal side effects. Drugs such as amiodarone, propafenone, and procainamide were employed less frequently, being restricted to specific clinical situations. In particular, the reported analyses of amiodarone use during gestation indicate that it is associated with neonatal bradycardia, prolonged QT interval, small size of the fetus in view of its gestational age, prematurity, and prenatal hypothyroidism.[30] Despite this, in the present study maternal or fetal adverse effects were not observed in the small number of women who used amiodarone during gestation. Therefore, amiodarone use during pregnancy should be reserved for treatment of drug-refractory, symptomatic, and/or potentially lethal arrhythmias.

Miscellaneous

This study was limited to women with mitral valve prolapse associated with cardiac arrhythmias and/or valve incompetence, the outcome of which depended on the degree of mitral regurgitation and/or the presence and type of cardiac arrhythmias. Our results were similar to a previous report document-

ing an uneventful course of pregnancy in women with mitral valve prolapse,[31] except for one (0.2%) case of ruptured chordae due to infective endocarditis.

Coronary arterial disease was infrequent (0.014%) and was associated with cigarette smoking and oral contraceptive, findings that are in agreement with the literature.[32] Although no deaths occurred in patients with coronary arterial disease, almost half of them experienced some complications, including unstable angina in 28.6% and congestive heart failure in 21.4%; these patients required intensive medical therapy and eventually intervention procedures (percutaneous coronary angioplasty in two cases, surgical myocardial revascularization in one) to achieve a successful maternal outcome.

Pulmonary vascular disease was associated with complication and mortality rates of 86 and 38%, respectively, data that confirm an extreme risk of pregnancy in this setting. In addition, in patients with pulmonary hypertension secondary to schistosomiasis, maternal bleeding after delivery occurred in two patients and hemorrhage due to ruptured esophageal varices in another two. These observations are similar to the study by Weiss and Hess[33] that showed a maternal mortality of 56% for secondary pulmonary hypertension compared with 36% for primary pulmonary hypertension. These differences were attributable to additional adverse factors such as hepatitis, systemic connective tissue, or vascular inflammatory disease. In spite of strict current management protocol, pulmonary vascular disease is associated with an ominous maternal prognosis, independent of the underlying cause,[34] and pregnancy is absolutely contraindicated in women with pulmonary vascular disease.

Obstetrical and Fetal Considerations

In the majority of patients, the delivery method was determined by obstetric reasons or fetal demands. The high rate of 37.5% of cesarean sections was related to the peculiarity inherent in pregnancy in patients with severe heart disease, associated with retardation of fetal growth, fetal distress, and labor induction risks. In heart disease situations, in which cesarean section was indicated, the aim was to improve the maternal and fetal prognosis in those very dangerous clinical settings by reducing the gestational period. In this event, the procedure must be carried out as soon as fetal maturity was established.

In this study, 91% of pregnancies resulted in healthy infants, comparable with those in the general population; this was rewarding considering the high incidence of severe cardiac disease in this cohort. The occurrence of 4.8% of spontaneous abortion is included in the actual rate of abortion in women with cardiac disease since most patients were referred from the first trimester of gestation.

Furthermore, the high incidence of fetal pathologies in groups with congenital heart disease, hypertrophic cardiomyopathy, and Chagas' disease (Table I) was very strongly associated with its genetic or infectious nature and is consistent with other reports.[35, 36] Thus, during prenatal care, a detailed cardiac examination including serial fetal ultrasound studies and eventually fetal echocardiography should be performed.

Study Limitations

This study has no control group, because the number of clinical situations is so large that obtaining controls is virtually impossible. We do acknowledge that this fact limits interpretation and extrapolation of the data. In addition, the study covers a long observational period during which therapeutic advances that occurred in the field were incorporated gradually into the study protocols. Nevertheless, we believe that this large number of patients followed in the same institution by the same team of physicians offers insight into the pathophysiology, complications, and outcome of these broad clinical problems.

Conclusions

Our data support the fact that the prognosis of pregnant women with heart disease has improved, leading frequently to successful outcomes. However, pregnancy is contraindicated in patients with Eisenmenger's syndrome, severe cardiomyopathies, and pulmonary vascular disease in view of ominous gestational evolution and scarcity of effective medical resources. Proper evaluation of maternal prognosis prior to conception, and adequate clinical follow-up during pregnancy, are both fundamental measures for obtaining a satisfactory outcome in these patients.

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