TITLE: PREGNANCY IN PATIENTS WITH HEART DISEASE: EXPERIENCE WITH 1000 CASES

Short title: PREGNANCY AND HEART DISEASE

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Condensed abstract:

Heart disease remains a leading cause of non-obstetric maternal death during pregnancy. We report the outcome of 1000 pregnant women with rheumatic, congenital, Chagas’ disease, cardiac arrhythmia, cardiomyopathy or other heart diseases. Whereas 765 (76.5%) patients had no cardiovascular events, 235(23.5%) experienced cardiovascular complications associated with a maternal mortality rate of 2.7%. Of the 915 (91.5%) infants discharged, 796 (86.9%) were full term. The outcome of pregnancy in women with heart disease is related to the maternal underlying heart disease, and its prognosis improves with a strict clinical follow-up during prenatal care and a careful evaluation prior conception.
Summary

Objective: To report the experience with a large series of pregnant women with cardiac disease cared in the same referral center.

Methods and Results: From 1989 to 1999, 1000 pregnant women with heart disease were followed by the same clinical and obstetric team. The cardiac diseases consisted of 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%). Seven hundred sixty-five (76.5%) pregnant women 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 owing to refractory complication. The general maternal mortality rate was 2.7%. Of the 915 (91.5%) infants who were discharged, 119 (13%) were premature babies.

Conclusion: Pregnancy in women with heart disease is still associated with considerable morbidity and mortality rates which are strongly correlated to maternal underlying disease. The 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[1]: *Women With an Abnormal Heart Should Not Become Pregnant.* 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 non-obstetric maternal death during pregnancy[3].

With increasing experience, it has become clear that not all clinical situations carry the same ominous prognosis. Whereas there are conditions in which pregnancy remains prohibitive (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 well as counseling about future gestations. The present study is a report of experience with the largest published series of pregnant women with cardiac disease cared by the same team of physicians in one institution.
MATERIAL and METHODS

From 1989 to 1999, 1000 pregnant women with heart disease were followed at Heart Institute of the University of São Paulo. Rheumatic heart disease 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 (eight with cardiac arrhythmia and 24 with valve regurgitation); 14 cases with coronary artery disease (all of them with coronary angiogram study proven coronary stenosis of >70% and seven with prior myocardial infarction); 13 presented pulmonary vascular disease (eight of them associated to schistosomiasis); seven had Takayasu’s arteritis; three cases with thoracic aortic aneurysm, three with Marfan’s syndrome and one patient who suffered cardiac transplantation.

All patients were followed-up by the same clinical and obstetric team monthly for up to eight months of gestation, weekly thereafter until delivery and up to three months after delivery. Electrocardiogram and Doppler echocardiography studies were performed in all patients. The babies were examined before discharge and echocardiogram 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 the conventional strategies.[4,5]

The routine strategy against thromboembolic episodes adopted was: a) in patients with mechanical prosthesis, coumadin was stopped and heparin used instead, in two periods: during the first trimester of gestation and between 34th week of gestation up to two days after delivery; in the remaining period coumadin was maintained. Daily doses of subcutaneous unfractioned heparin was used, from 30.000 units to achieve one and half to two times of...
APTT (activated partial thromboplastin time) or low molecular weight heparin doses at 1mg/kg/t.i.d., and b) in atrial fibrillation, pulmonary hypertension or cyanotic heart disease, subcutaneous unfractioned heparin or low molecular weight heparin was employed from 24th week of gestation until two days after delivery, at daily doses, of 20.000 units or 40mg, respectively. Coumadin was introduced two days after delivery, adjusted to a target INR (international normalized relation) of 2.0 to 3.5, in both situation.

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 to harmful fetal effects, was selected to replace the enzyme angiotensin-converting inhibitors, that are contraindicated during pregnancy. Therapy for patients with pulmonary congestion associated with mitral stenosis included propranolol (60-80 mg/day) and furosemide. In clinical emergencies, such as a severe pulmonary congestion and/or low cardiac output, dobutamine and/or sodium nitroprusside (no more than 3 hours to avoid the potential of cyanogen fetal toxicity), were used. Emergency treatment of arrhythmias with hemodynamic impairment included electrical cardioversion, intravenous verapamil or adenosine. A low dose of propranolol, verapamil, quinidine, or digoxin were subsequently employed 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 2nd 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, that was
managed essentially by 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:** Seven hundred sixty-five (76.5%) out of 1000 pregnant women had no cardiovascular complications during the study; the remaining 235 (23.5%) patients experienced cardiovascular events, shown in Table II in order of decreasing 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%) cases with moderate or severe mitral stenosis (mitral valve area below 1.5 cm$^2$ assessed by echodopplercardiogram), 19 (22.3%) with valve regurgitation, 12 (14.1%) cases with bioprosthesis, ten of them related to bioprosthesis dysfunction (seven detected before gestation). Among the 20 cases of cardiac arrhythmias 16 were atrial fibrillation associated with mitral valve disease. Eight episodes of thromboembolism occurred in native mitral valves (five associated with atrial fibrillation, three of them upon regimen of anticoagulation recommended in the protocol), and four in mechanical prosthesis. Infective endocarditis was observed in one patient with aortic regurgitation during the 19$^{th}$ week of gestation; and the other case in a patient with bioprosthesis, during the 33$^{rd}$ week of gestation. Both patients survived, although the first required aortic valve replacement. The maternal deaths corresponded to 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 cases of congestive heart failure, 20 occurred in unrepaired defects, 13 with aortic valve stenosis, three with aortic coarctation and the remaining patients with shunt lesions. Paroxysmal supraventricular arrhythmias were observed in three patients with atrial septal defects and one after surgical repair of tetralogy of Fallot. Angina was reported in two patients with aortic stenosis and three with Eisenmenger’s syndrome. Hypoxemia was reported in five patients with unrepaired cyanotic congenital heart disease and two with Eisenmenger’s syndrome who had refused therapeutic abortion during the 1st trimester of gestation. Infective endocarditis was observed in one case with an uncorrected ventricular septal defect. Among other complications recurrent syncope was documented in two patients with Eisenmenger’s syndrome and one with aortic valve stenosis.

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

In 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 cases, who presented paroxysmal atrial tachycardia intermittent. (Table II).

In the cardiomyopathy group, there was a high complication rate (41.8%), involving 18 patients (Table II): five out of seven patients with congestive heart failure had hypertrophic cardiomyopathy; four cases of cardiac arrhythmias included three acute atrial fibrillation and five cases of angina also in patients with hypertrophic cardiomyopathy. Both patients who presented thromboembolic complications had dilated cardiomyopathy. Recurrent syncope was recorded in one woman with dilated cardiomyopathy. No patients developed the disease
during gestation; peripartum cardiomyopathy cases was diagnosed in previous pregnancy. All maternal deaths occurred in dilated form of disease, although the small number does not permit comparison, complications or mortality in patients with peripartum cardiomyopathy, were not observed.

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

Only seven (53.8%) of the 13 patients in the pulmonary vascular disease had an uneventful pregnancy; the remaining experienced various events including two maternal bleeding after delivery and one case of hemorrhage owing to ruptured esophageal varices.

Conversely, 13 (92.8%) women with coronary arterial disease achieved full-term gestation, including seven (50%) who were free of cardiovascular events. Four patients, however developed unstable angina, two requiring coronary angioplasty and one needed surgical revascularization. It did not observed coronary artery dissection 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 reoperation in eight patients; surgical repair of congenital cardiac defects in five cases. Heart surgical procedures resulted in 1/25(4.0%) maternal death and four (16.0%)
stillbirths. Other cardiac intervention procedures applied in 18 patients (Table III) included percutaneous balloon mitral valvuloplasty (10 cases), coronary angioplasty (2 cases) and pacemaker implantation (6 cases).

The overall maternal mortality, underlying disease and complications are presented in table III. The main clinical situations associated to 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’s 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, most of them for obstetrical indications. The main obstetrical reasons were fetal growth retardation, fetal distress and labor induction failure. In less than 5% of the cases, cesarean section was indicated by heart disease, such as diseases of aorta and severe impairment of maternal hemodynamic, 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 2926 ± 654g. Twins occurred in five cases. Out of 29 (2.9%) stillbirths, five were immediately after the onset of acute atrial fibrillation. Among 22 (2.2%) cases of fetal pathology correlated to maternal cardiac disease there were four cases of congenital Chagas’ disease, an infant with neurological disease, whose mother underwent aortic valve replacement during the 2nd trimester of gestation and the remaining with cardiac disease.

DISCUSSION

This observational study, one of the most extensive ever reported on follow-up of
gestation in women with heart disease in the same Institution, documented a 23.5 incidence of cardiovascular complications, a 2.7% overall mortality rate and 7.7% of spontaneous abortion and stillbirth, in 1000 cases studied. The adherence to 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 prognosis and characteristics of the underlying diseases, each situation will be address individually.

*Rheumatic heart disease* which was present in more than half of patients (Table I), remains the most frequent valve disease cause. 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 functional class I/II (NYHA) at the beginning of pregnancy. In fact, according our previous report, functional class I/II at the start does not assure an uneventful pregnancy in mitral stenosis[^8^]. In these cases use of furosemide and propranolol allowed the clinical control in most of them until delivery, fact that favor a medical therapy as 1st 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, propranolol,[9] are related to doses and have not been observed at doses up to 80 mg/day.

In cases of paroxysmal atrial fibrillation, also an usual complication, electrical cardioversion should be considered as first alternative for reversing to sinus rhythm because it is effective, shortens the period of low cardiac output and avoids the potential danger to fetus of use of high doses of antiarrhythmic drugs. Atrial fibrillation apparently increased the risk of thromboembolism, since it that 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] Nevertheless, this is a controversial issue, we tend to avoid preventive intervention, because this procedure is associated with 0.5% of mortality, 1% of cerebral embolic events, 1% of cardiac perforation, 2% of mitral regurgitation requiring valve replacement and 15 % of 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 prosthesis, four (15.4%) cases had thromboembolic episodes, three of them occurred 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 the 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 bioprosthesis implies a worse clinical and
hemodynamic prognosis during gestation. Nevertheless, these data do not support the hypothesis that pregnancy accelerates the degeneration of bioprosthesis\textsuperscript{[15-16]}, because in the majority of these cases some dysfunction was recognized before gestation. Indeed, the results of a contemporary prospective and comparative five-year study did not indicate that pregnancy contributes to bioprosthesis deterioration\textsuperscript{[17]}, consistent with findings in other studies\textsuperscript{[18,19,20]}. 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 bioprosthesis without disfunction, low rate of fetal demise and dispensable anticoagulation prompt us to recommend bioprosthesis rather than mechanical prosthesis in women with childbearing.

\textit{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 to pulmonary hypertension, chiefly in Eisenmenger's syndrome, are dangerous owing to increased thromboembolism risk and right heart failure\textsuperscript{[21]}. In addition, long-term prevention with use of anticoagulants, frequently leads to hemorrhagic complications\textsuperscript{[22]}. Although controversial, the use of heparin in this set 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 to congestive heart failure, sudden death, thromboembolism and infection emphasize the obstetrical and fetal risks of pregnancy in this group of patients. Indeed, out of 21 pregnancies with Eisenmenger’s syndrome only seven were discharged with both, mother and infant alive. This result supports\textsuperscript{[23,24]} the notion that patients with Eisenmenger’s syndrome should avoid pregnancy, and if pregnant should be advised them to have an elective abortion without delay.

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

These data confirm the adverse prognosis of pregnancy in women with significant symptomatic aortic stenosis specifically with an aortic gradient above 70 mm Hg.\textsuperscript{[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 commonest cyanotic malformation; most of them had been surgically corrected in early childhood allowing a favorable maternal and fetal outcomes. Ebstein’s anomaly, the most frequent uncorrected type of cyanotic (Table I), presented wide variation in the severity of lesion which determinated its clinical manifestation however a paroxysmal tachycardia caused cyanosis in two patients, probably due to increase the right-to-left shunting.

\textit{Chagas’ disease}: In Brazil the prevalence of pregnant women infected by
Trypanosoma cruzi ranges from 2.0 to 16.4%, two thirds of them without heart injury, however in this 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 indeterminate form, defined as the absence of apparent cardiac damage, but with serum positive tests, experienced uneventful courses during gestation. Conversely, patients with conduction disorders associated or not to myocardial dysfunction there were 76.2% of cardiac arrhythmias and 19.0% of congestive heart failure (Table II). In addition, some complications were refractory to medical treatment, including four 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 em four cases add reasons to restrict pregnancy in this group of patients.

Cardiomyopathy had a complication and mortality rates of 30% and 10%, respectively: this underscore the harmful maternal prognosis specifically associated to left ventricular dysfunction. The small number does not be permit to compare the pregnancy outcome between peripartum and idiopathic cardiomyopathy: even more, 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, for 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 which indicated a poor maternal outcome in obstructive forms of them or when there are symptoms or atrial fibrillation before gestation. 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 fetus. The high complication rate and relative lack of effective therapeutic measures prompt us to advise women with symptomatic hypertrophic to avoid pregnancy.

Cardiac arrhythmias without structural lesions usually present a favorable maternal and fetal outcomes and generally requiring no antiarrhythmic drugs; however this study was limited to patients with significant and symptomatic cardiac arrhythmias which required treatment with antiarrhythmic drugs during pregnancy guided by a careful clinical and Holter monitoring for 24 hours. 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 indicates it is associated to neonatal bradycardia, prolonged QT interval, small for gestacional age, prematurity and prenatal hypothyroidism. 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 which outcome depended on the degree of mitral regurgitation and/or the presence and type of cardiac arrhythmias. Our results were similar to previous report documenting an uneventful course of pregnancy in women with mitral valve prolapse,\(^{31}\) except 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 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\% who required intensive medical therapy and eventually intervention procedures (percutaneous coronary angioplasty in two cases; surgical myocardial revascularization in one) to obtain a successful maternal outcome.

Pulmonary vascular disease was associated to complication and mortality rates of 86\% and 38\%, respectively, data which 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 owing to ruptured esophageal varices, in another two. These observations are similar to the Weiss' study,\(^{33}\) that showed a maternal mortality of 56\% for secondary pulmonary hypertension compared to 36\% for primary pulmonary hypertension, these differences were attributable to additional adverse factors such as hepatitis, systemic connective tissue or vascular inflammatory disease. Despite of strict current management protocol, pulmonary vascular disease is
associated with an ominous maternal prognosis, independent of the underlying cause\cite{34} and pregnancy is absolutely contraindicated in women with pulmonary vascular disease.

**Obstetrical and fetal considerations**

In the majority of patients, delivery method was determined by obstetric reasons or fetal demands. The high rate of 37.5% of cesarean section was related to peculiarity inherent of pregnancy in patients with severe heart disease, associated to 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 gestacional 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 a healthy babies, comparable to that in general population, which was rewarding considering the high incidence of severe cardiac disease in this cohort. The occurrence of 4.8% of spontaneous abortion is under the real rate of abortion in women with cardiac disease because since most of patients were referred from the first trimester of gestation.

Furthermore, high incidence of fetal pathologies in congenital heart disease, hypertrophic cardiomyopathy and Chagas’ disease groups (Table V) very strongly associated with of genetic or infectious nature and it is consistent with other reports.\cite{35,36} Thus, during prenatal care a detailed cardiac examination should be performed, including serial fetal ultrasound studies and eventually fetal echocardiography.

**STUDY LIMITATIONS**

This study has no control group, because the number of clinical situations is so large, that controls are virtually impossible. We do acknowledge that this fact limits interpretation and
extrapolation of the data. Besides the study covers a long observational period where therapeutic advances that occurred in the field, were incorporated gradually to 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 this broad clinical problems.

CONCLUSIONS

Our data support the prognosis of pregnant women with heart disease have improved, leading frequently to successful outcomes. However pregnancy should be 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 the maternal prognosis prior to the conception and adequate clinical follow-up during pregnancy are both fundamental measures to obtain a satisfactory outcome in these patients.

REFERENCES


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Table 1. Underlying diseases - 1000 cases

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

Table II. Complications relative to underlying disease

<table>
<thead>
<tr>
<th>Cardiac Diseases</th>
<th>Total N°/%</th>
<th>CHF/PC</th>
<th>Arrhy</th>
<th>Thromb</th>
<th>Angor</th>
<th>Hyp</th>
<th>IE</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatic Valvular- 557</td>
<td>119/21.4</td>
<td>85*/71.4</td>
<td>20/16.8</td>
<td>12/10.1</td>
<td>0</td>
<td>0</td>
<td>2/1.7</td>
<td>0</td>
</tr>
<tr>
<td>Congenital - 191</td>
<td>44/23.0</td>
<td>22/50.0</td>
<td>4/9.1</td>
<td>1/2.8</td>
<td>5/11.4</td>
<td>7/15.9</td>
<td>1/2.8</td>
<td>4/2.0</td>
</tr>
<tr>
<td>Chagas's disease - 85</td>
<td>21/24.7</td>
<td>4/19.0</td>
<td>16/76.2</td>
<td>1/4.8</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Arrhythmias - 51</td>
<td>11/21.5</td>
<td>2/18.2</td>
<td>9/818</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cardiomyopathy - 43</td>
<td>18/41.8</td>
<td>7/38.9</td>
<td>4/22.2</td>
<td>2/11.1</td>
<td>5/27.7</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Others - 73</td>
<td>22/30.1</td>
<td>3/13.6</td>
<td>7/31.8</td>
<td>3/13.6</td>
<td>4/18.2</td>
<td>0</td>
<td>2/9.1</td>
<td>3/13.6</td>
</tr>
<tr>
<td>Total - 1000</td>
<td>235/23.5</td>
<td>123/12.3</td>
<td>60/6.0</td>
<td>19/1.9</td>
<td>14/1.4</td>
<td>7/0.7</td>
<td>5/0.5</td>
<td>7/0.7</td>
</tr>
</tbody>
</table>
Angor - angina; Arrhy-cardiac arrhythmias; CHF/PC – congestive heart failure/pulmonary congestion; Hyp- hypoxemia; IE-infective endocarditis; Throm-thromboembolism.
### Table III. Maternal outcome - Overview of 1000 cases

<table>
<thead>
<tr>
<th>Cardiac Diseases</th>
<th>Total N.°/ %</th>
<th>RHD /%</th>
<th>CHD /%</th>
<th>Chagas /%</th>
<th>Arrhy /%</th>
<th>CM /%</th>
<th>Others /%</th>
</tr>
</thead>
<tbody>
<tr>
<td>N.°(%)cases</td>
<td>1000</td>
<td>557</td>
<td>191</td>
<td>85</td>
<td>51</td>
<td>43</td>
<td>73</td>
</tr>
<tr>
<td>No complications</td>
<td>765/76.5</td>
<td>438/78.6</td>
<td>147/76.9</td>
<td>64/75.3</td>
<td>40/78.5</td>
<td>25/58.2</td>
<td>51/69.9</td>
</tr>
<tr>
<td>Complication</td>
<td>235/23.5</td>
<td>119/21.4</td>
<td>44/23.1</td>
<td>21/24.7</td>
<td>11/21.5</td>
<td>18/41.8</td>
<td>22/30.1</td>
</tr>
<tr>
<td>Medical treatment*</td>
<td>161/68.8</td>
<td>82/68.9</td>
<td>29/65.5</td>
<td>14/66.7</td>
<td>10/90.9</td>
<td>15/83.3</td>
<td>11/50.0</td>
</tr>
<tr>
<td>Intervention†</td>
<td>47/20.0</td>
<td>28/23.5</td>
<td>8/18.2</td>
<td>4/16.7</td>
<td>1/9.1</td>
<td>0</td>
<td>6/27.2</td>
</tr>
<tr>
<td>Mortality</td>
<td>27/2.7</td>
<td>9/1.6</td>
<td>7/3.6‡</td>
<td>3/3.7</td>
<td>0</td>
<td>3/6.9</td>
<td>5/6.8</td>
</tr>
</tbody>
</table>

RHD - rheumatic valve disease; CHD – congenital heart disease; Chagas - Chagas’ disease Arrhy - arrhythmia; CM - cardiomyopathy; Others- miscellaneous conditions

* Successful medical treatment; † Interventional procedures during gestation
‡ Six of them with Eisenmenger’s syndrome
Table IV. Fetal outcome - overview of 1000 pregnancies

<table>
<thead>
<tr>
<th>Cardiac Diseases</th>
<th>Total N.° / %</th>
<th>RHD</th>
<th>CHD</th>
<th>Chagas</th>
<th>Arrhy</th>
<th>CM</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>N.° (%) cases</td>
<td>1000</td>
<td>557</td>
<td>191</td>
<td>85</td>
<td>51</td>
<td>43</td>
<td>73</td>
</tr>
<tr>
<td>Infants discharged</td>
<td>915/91.5</td>
<td>528/94.8</td>
<td>159/83.2</td>
<td>78/91.7</td>
<td>50/98.0</td>
<td>36/83.7</td>
<td>64/87.6</td>
</tr>
<tr>
<td>Abortions*</td>
<td>56/5.6</td>
<td>23/ 4.1</td>
<td>22/11.5</td>
<td>3/3.5</td>
<td>0</td>
<td>3/6.9</td>
<td>5/6.8</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>29/2.9</td>
<td>6/ 1.1</td>
<td>10/5.2</td>
<td>4/4.7</td>
<td>1/1.9</td>
<td>4/4.3</td>
<td>4/5.5</td>
</tr>
<tr>
<td>Prematurity</td>
<td>119/11.9</td>
<td>57/10.2</td>
<td>31/16.2</td>
<td>13/15.3</td>
<td>-</td>
<td>5/11.6</td>
<td>13/17.8</td>
</tr>
<tr>
<td>CHD</td>
<td>22/ 2.2</td>
<td>2/ 0.3</td>
<td>11/5.8</td>
<td>4/4.7</td>
<td>-</td>
<td>3/6.9</td>
<td>2/2.7</td>
</tr>
</tbody>
</table>

RHD Rheumatic valve disease; CHD – congenital heart disease; Chagas - Chagas' disease Arrhy - arrhythmia; CM - cardiomyopathy; Others- miscellaneous conditions; * Therapeutic abortion in 8(0.8%) cases.