The Effect of Mitral Stenosis on Maternal and Fetal Outcome in Pregnancy

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Abstract

Objectives: The aim of the study was to evaluate maternal and fetal outcomes of mitral stenosis at pregnant women.

Methods: Forty-one pregnant women with moderate and severe mitral stenosis were enrolled in the study. Predictive variables were the Apgar score, new born weight and delivery week. Progression of NYHA functional class, thromboembolism, death, new onset atrial fibrillation was accepted as maternal event. Abortion, fetal or neonatal death, prematurity or low birth weight were accepted as fetal events.

Results: In newborn babies, 10 were followed-up in intensive care. The mothers of these infants had higher LA diameters, their MVA’s were smaller and the pulmonary hypertension was higher. It was observed that the LA diameter and warfarin treatment were independent risk factors for the need for intensive care. The NYHA was primarily dependent from the LA diameter, followed by the MVA, mean difference in the pressure and the pulmonary artery pressure (PAP). The independent risk factors of the birth weight and the 1st min. and 5th min. Apgar scores, only the LA diameter was found as significant. Also, the independent risk factors of the gestational age at birth are the NYHA classification and the MVA. Warfarin treatment in the mother has also been observed as a risk factor for IUGR.

Conclusion: These results reveal that especially patients with mitral stenosis should be closely monitored throughout their pregnancy.

Introduction

Although a rarely observed heart condition, severe forms of rheumatic mitral stenosis (MS) may be life-threatening during pregnancy [1,2]. In developing countries, rheumatic heart disease is still predominant and continues to be a major cause of maternal morbidity and mortality [3,4]. MS has already been observed to be related with significantly higher incidences of congestive heart failure, arrhythmia, and initiation or increase of cardiac medications and hospitalizations [5,6]. Previous studies have demonstrated that MS influences the fetal outcome and may lead to higher risks of preterm delivery, intrauterine growth retardation and reduced birth weight [5]. Therefore, it may be wise to advise women with moderate or severe MS planning to get pregnant to undergo corrective treatment for the valvular disease before motherhood. On the other hand, if the stenosis is first diagnosed during the pregnancy, surgical repair and percutanetransluminalcommissurotomy of mitral stenosis is suggested in pregnancy when mitral stenosis is severe and medical therapy does not work [7,8]. Considering the risk profiles of the individual treatment modalities, the correct selection of the medication to be applied during pregnancy is of utmost importance both for the mother and the fetus. The aim of the present study is to assess the influence of MS on the maternal and fetal outcome of the pregnancy.

Method

Our study was designed to evaluate the outcome of the pregnancy in patients with rheumatoid MS in a retrospective manner. All the patients were followed-up during pregnancy, labor, and delivery at the Çukurova University Hospital, which is a tertiary-care facility with established ob-gyn and cardiology clinics for high-risk patients. Patients with prosthetic heart valves and performed mitral commissurotomy, patients with other serious valvular lesions and those who have undergone therapeutic abortion due to non-cardiac reasons were excluded from the study. The enrolled patients were classified into four groups according to the New York Heart Association (NYHA) functional classification [9]. During the initial antenatal visit at 8th week, baseline data such as maternal age, parity, NYHA functional class, any cardiac interventions performed prior to the pregnancy, cardiac medications and anticoagulant therapy - if any - were recorded. All the enrolled patients underwent electrocardiographic and echocardiographic examinations. A gynecologist-obsetrician and a cardiologist collaborated to monitor the patients throughout their pregnancies. The patients were evaluated by cardiology and obstetric clinics once in two months in the first two trimesters and in the last trimester once in a month or in case of a new complaint of pregnancy. In all cardiology consultation, ecocardiographic evaluation was also done during follow-up. In the first trimester heparin was...
used in patients having atrial fibrillation, later warfarin was added to treatment. Monthly INR follow-up was done in patients taking warfarin. The starting dose of Coumadine was arranged as 5 mg and INR level was tried to be kept at 2.3-2.3-2.3 weeks before acquisition birth date, patients on treatment with anticoagulant agents were switched to heparin; and heparin treatment was also suspended at the onset of labour to be resumed 6 hours following the delivery. Cesarean under epidural anaesthesia was applied to patients were on warfarin treatment and giving birth before acquisition date.

Apart from obstetric indications, any clear symptoms or signs pointing towards a worsening in the cardiac status were accepted as reason for admittance to the hospital. The decision to deliver the patient and the route of delivery were discussed within the team and determined according to the obstetric indication and cardiac functional capacity. All the patients received prophylactic antibiotic therapy as a measure against peripartum infective endocarditis. All neonates were examined by a paediatrician, and a paediatric cardiologist was consulted if necessary. Any changes in the cardiac status of the patient, onset or exacerbation of any cardiac complications, need for new cardiac treatment modalities or modifications in the doses of existing cardiac medications, cardiac interventions required during pregnancy, any obstetrical complications, gestational age at delivery, mode of delivery and postpartum complications were assessed. Perinatal outcomes such as fetal growth restriction (FGR; under the 10th percentile), prematurity (before 37 weeks of gestation), stillbirth (intrauterine death after 20 weeks of gestation) or neonatal death (death within the first 28 days of life), birth weight and birth defects were also investigated.

Appar test

The APGAR test, which is a practical method for the assessment of the neonate at the 1st and 5th minutes after birth, was carried out by a physician. The score at the first minute indicates how well the infant tolerated the delivery and the score at the 5th minute assesses the adaptation of the neonate to the new environment. Also, a healthcare professional examined the infant’s breathing effort, heart rate, muscle tone, reflexes and skin colour.

Echocardiography

The echocardiographies were carried out with the Acuson Sequoia C 256 device (Acuson Corporation, Mountain View, CA, USA) and a 2.5-3.5-MHz transducer. The obtained echocardiographic images were performed according to the criteria of the American Society of Echocardiography [10]. In the parasternal long axis position, the diameters of the aorta, left atrium, and the diastolic and end-systolic diameters of the left ventricle have been measured. The rheumatic involvement of the mitral valve was graded according to the Wilkins scoring system. The mitral, aortic and tricuspid valve insufficiencies were evaluated according to the standard method through Doppler echocardiography. The classification of the MS was based on the calculated mitral valve area (MVA) during the echocardiography. A valve area of ≥1.5 cm² was classified as mild, an area between 1.5 and 1.0 cm² as moderate and <1.0 cm² was classified as severe.

Statistical analysis

Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS), version 11.0, and all values were expressed as mean ± standard deviation. Student’s t-test and chi-square test were used to evaluate the comparing data. The correlation analysis was used for relation of clinical, laboratory and echocardiographic findings. A p value of <0.05 was considered significant. The linear logistic regression analysis was performed for the determination of the independent predictors for birth weight, apgar scores and gestational age at birth.

Results

Forty-one patients were enrolled in the study. The mean age of the patients was 27.6 ± 4.7 (between 20 and 35) years. The demographical and echocardiographic features of the patients are presented in Table 1. Also, 10 patients (24.4%) were observed to have other mild and moderate valvular diseases besides the mitral valve stenosis. During the follow-up of patients having additional valve problem, there was no sign of problem obtained associated with mother and child.

While 10 among our patients had atrial fibrillation (AF) at the beginning of the study, 5 more have developed paroxysmal AF in the course of the study. In these patients sinus rhythm was provided by electrical cardioversion. During the follow-up of fetal and mother, there was not any statistically significant difference obtained. During the follow-up, 9 patients were on coumadin treatment and all of these patients were under monitoring due to atrial fibrillation. Thrombosis occurred in 2 patients during the follow-up period (Table 2). These patients were on warfarin treatment and one of them died at the 26th week of gestation. This patient was classified as NYHA class 4 and had moderate tricuspid insufficiency.

The gestational week at delivery was mean: 33.2 ± 3.2 week. Also, the greater part of the neonates had low birth weights (mean 2555.6 ± 617.2 gr) and the 1st min. and 5th min. Apgar scores were 7.2 ± 1.8 and 8.9 ± 1.8, respectively (Table 3).

Twenty patients had caesarean sections (CS). Caesarean deliveries were observed to be more frequently applied in patients who had increases in the LA diameter and maximum mitral valve gradients. Also, the neonates delivered through CS had lower gestational ages and lower Apgar scores compared to those who had normal deliveries (Table 4).

In newborn babies, 10 were followed-up in intensive care. The gestational weeks, birth weights and the 1st min. and 5th min. Apgar scores of these infants were lower. Also, the mothers of these infants had moderate Atrial Fibrillation. The echocardiographic features of the patients are presented in Table 1.

<table>
<thead>
<tr>
<th>Age</th>
<th>n (%)</th>
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</thead>
<tbody>
<tr>
<td>27.6 ± 4.7</td>
<td>20 (48.8)</td>
</tr>
<tr>
<td>Concomitant valvular disease</td>
<td>10 (24.4)</td>
</tr>
<tr>
<td>Caesarean</td>
<td>10 (24.4)</td>
</tr>
<tr>
<td>AF</td>
<td>10 (24.4)</td>
</tr>
<tr>
<td>NYHA II</td>
<td>12 (29.2)</td>
</tr>
<tr>
<td>III</td>
<td>26 (63.4)</td>
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<tr>
<td>IV</td>
<td>3 (7.4)</td>
</tr>
<tr>
<td>New onset AF</td>
<td>5 (12.2)</td>
</tr>
<tr>
<td>Death of mother</td>
<td>1 (2.4)</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>2 (4.9)</td>
</tr>
<tr>
<td>Warfarin</td>
<td>9 (22)</td>
</tr>
<tr>
<td>NICU</td>
<td>10 (24.4)</td>
</tr>
<tr>
<td>LV EF</td>
<td>62.5 ± 3.9</td>
</tr>
<tr>
<td>LA diameter</td>
<td>53.2 ± 4.2</td>
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<tr>
<td>MVA</td>
<td>1.1 ± 0.2</td>
</tr>
<tr>
<td>PAP</td>
<td>52.5 ± 8.8</td>
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<tr>
<td>Max grad.</td>
<td>18.6 ± 4.9</td>
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<tr>
<td>Mean grad.</td>
<td>10.3 ± 3.0</td>
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Table 1: The demographical and echocardiographic features of the patients.
had higher LA diameters, their MVA’s were smaller and the pulmonary hypertension was higher. Besides, the greater part of those mothers had AF and they were on warfarin treatment (Table 5). When the infants admitted to intensive care were assessed using the logistic regression analysis, it was observed that the LA diameter and warfarin treatment were independent risk factors for the need for intensive care (p=0.004, r=-0.632, p=0.011, r=-0.621, respectively).

The correlation analysis revealed that the NYHA was primarily dependent from the LA diameter (p<0.001, r=0.583), followed by the birth weight (p<0.001, r=0.632) and the MVA (p=0.002, r=0.452).

### Discussion

The main symptom of our study was to show the finding of extremely high fetal and maternal risk in pregnant having moderate and extensive mitral stenosis. In mitral stenosis pregnancies in order to obtain the best result in maternal and fetus, the patients must be followed closely and their treatments must be optimized.

The optimum treatment modality in pregnant patients with MS should target a reduction in the heart rate and the LA pressure. The medications of choice are beta blockers. The LA pressure can be controlled by limiting the salt intake and the careful use of diuretics. It must be noted that the increased incidence of cardiac arrhythmias during pregnancy [11,12] may be associated with the changes brought about by the gestational hormones and a greater sensitivity to catecholamines [13]. All the patients who were taken to our study, were taking beta blocker and during controls diuretic was carefully started about by the gestational hormones and a greater sensitivity to catecholamines [13]. All the patients who were taken to our study, were taking beta blocker and during controls diuretic was carefully started.

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Nine patients were on warfarin treatment and all of these patients were already being monitored due to chronic AF. Warfarin is an anticoagulant that passes placenta and has teratogenic effect. During pregnancy warfarin usage causes spontaneous abortion, premature or dead birth, fetal bleeding and cerebral hemorrhages. If warfarin is used in the first trimester, it causes embroyopathy, nasal hypoplasia and in any other trimester of pregnancy it causes central nervous system malformations [14,15]. However, with current datas and strict INR control throughout pregnancy, it was mentioned that warfarin usage is the most secure method for the mother [14]. In a study, a group of patients used anticoagulant during pregnancy was compared to the other group who used anticoagulant after heparin in the first trimester, and the risk of embroyopathy between two groups were found the same so it was indicated that the embroyopathy due to warfarin usage was exaggerated and anticoagulant usage throughout pregnancy was offered [16]. In our study 9 patients were using warfarin as anticoagulant. A strict INR control was provided in those patients and the INR level progressed between 2.0-3.5. There was not any embroyopathy due to warfarin usage reported in our study but warfarin was found as an independent risk factor in intrauterine growth retardation. That was thought to be related with the finding of arrhythmia that causes IUGR in those patients. Despite of warfarin usage, one of the patients experienced transient ischemic attack and in the other one there was a development of trombus on left atrium. The patient having trombus on the left atrium was lost in the postpartum period, 6 days after a successful CS delivery performed in conjunction with a mitral valve replacement and thrombectomy.

The link between the conditions leading to this patient’s death and her pregnancy is unclear. In pregnant women with MS, the increased blood volume and heart rate bring about an increase in the mitral valve gradient. This condition further leads to an increase in the LA pressure and thus to pulmonary congestion [17,18]. The leading cause of death in pregnant women with MS has been reported as acute pulmonary edema [19]. Especially the fast increase in the venous return before and after the delivery is an important cause for cardiac decompensation. Mortality has been reported as 0.4% in NYHA class I-II patients and as 6.8% in class III-IV patients [2]. Among the patients enrolled in our study during labor and delivery, 12 were NYHA class II, 26 were NYHA class III and 3 patients were NYHA class IV. In our study the independent risk factors of the gestational week at delivery were found that the NYHA classification and the mitral valve area. The patient was died classified as NYHA class 4 at delivery. Apart from that, both our data and additional data from other reports [20,21] point out that mortality rates in pregnant women with MS can be reduced by a timely diagnosis and meticulous follow-up.

In pregnant patients with MS, before, during and after the birth when the venous return is increased due to the relief of the uterocaval obstruction, the pulmonary edema may become more severe. Therefore, patients must be hemodynamically monitored during the peripartum period (12-24 hours). Vaginal delivery is a well-tolerated preferred method in mitral stenosis pregnancies [22]. Vaginal delivery should be individualized by taking birth time, induction method, anesthesia technique and necessity of monitorization into consideration. The patients having vaginal deliver are suggested epidural anesthesia in order to prevent catecholamine induced tachycardia [23]. Also, hemodiamic control is easy with epidural anesthesia since anestesia is provided slowly [24]. When vaginal delivery is compared to cesarean delivery, there is less bleeding and infection risk however the risk of venous thrombosis and thromboembolism is higher. Although if there is not a complete consensus on the situations which vaginal delivery contraindicated, at the beginning of birth the cardiopulmonary reserve of mother should be evaluated carefully and cesarean delivery should be considered [25-29]. During the beginning of delivery in some situations such as acute decompensated cardiac insufficiency and oral usage of anticoagulant, cesarean delivery is preferred. In our study, 10 patients having acute cardiac insufficiency and were unstable as hemodynamic, were applied cesarean. Among these patients 7 of them were using warfarin. In conclusion, when CS and normal deliveries were compared, it was observed that CS was more frequently performed in patients with increased LA diameter and maximum gradient values. In addition, CS delivery patients were terminated at an earlier gestational period and have low apgar score.

Besides investigating the relationship between MS and maternal mortality, the present study also focussed on the relationship between MS, pregnant and the fetal outcome [14,15]. Among the patients in our study, gestation was associated with higher rates of IUGR, preterm deliveries, and lower birth weight; particularly among the patients with moderate or severe MS. The higher incidence of the intrauterine growth retardation among our patients with valvular heart disease may be explained by the hemodynamic compromise brought about by the valvular stenosis and the consequent decrease in uterine blood flow. Since maternal arrhythmias have also been demonstrated to cause fetal distress [30], they may be an additional factor leading to a compromise in the uterine blood flow and even to fetal outcomes. Although the effect of cardiovascular treatments on the fetus could not be evaluated, medications such as beta-adrenergic blockers, digitalis derivatives or diuretics have been associated with impaired uterine blood flow and increased incidence of IUGR/prematurity [31-33]. In our study, the LA diameter was found as an independent risk factor for the birth weight and the 1st and 5th minute Apgar scores. Ten of the neonates (24.4%) had to be monitored in the neonatal intensive care, and a significant relationship was observed between the need for neonatal intensive care and factors such as the presence of AF, thrombosis, LA diameter, ejection fraction, MVA and pulmonary arterial pressure. It was observed that the LA diameter was independent risk factors for IUGR. The higher incidence of IUGR found in our study underline the importance of anteptum fetal surveillance and periodic ultrasonographic examinations in order to monitor the fetal growth in patients with moderate or severe mitral valve stenosis. Also, in our study, it was observed that the LA diameter and warfarin treatment were independent risk factors for IUGR.

It is hard to manage pregnancy period of pregnant having mitral stenosis. Maternal and neonatal event rates, however, dramatically increase in high risk patients. In these patients the clinical risk should be identified and treatment should be individualized according to patient.

Repair of valvular stenosis in such patients should be performed prior to pregnancy, if possible. The summary of all these parameters suggests the conclusion that especially patients with risk factors should be closely monitored throughout their pregnancy. Limitations

In our study the results of mitral stenosis on pregnant and fetus were evaluated. Although monthly ultrasonographies and when necessary fetal non-stress tests were applied during their follow-up, this subject was not additionally given a place in our article. Also this study was limited by patients having chronic atrial fibrillation, paroxysmal atrial fibrillation and the ones provided sinus rhythm. However, for this group of patients there needed other studies in which arrythmias are separately evaluated or may be Holtermonitorization is used. Because the absence of warfarin effect and necessary number of patients, this
subject was not explained in details in the aim of our study. Also, since the postpartum follow-ups were not the main subject of this study, they were not evaluated particularly.

References


