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The Impact of Different Grades of Rheumatic Mitral Valve Stenosis on the Timing/Mode of Delivery and Neonatal Outcomes among Egyptian Females in Their Third Trimester-a Prospective Cohort Study

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Abstract: This study investigated the effect of rheumatic mitral valve stenosis on pregnancy and compares the impact of the different degrees of mitral stenosis on the timing/mode of delivery, antepartum/intrapartum fetal condition and neonatal outcome. Sixty pregnant females with a gestational age >28 weeks and with varying degrees of rheumatic mitral valve stenosis were included in this study.The cohort of enrolled women was divided into three groups according to the mitral valve area: Group A: Mitral valve area <4 cm^2 but more than 2 cm^2, Group B: Mitral valve area between 2 and 1.3 cm^2 and Group C: Mitral valve area less than 1.3 cm^2. The study showed that pregnant women with significant mitral stenosis are at a relatively high risk of experiencing maternal, fetal and neonatal complications. The degree of mitral valve stenosis was also strongly and significantly associated with the risk of maternal events. The results of this study indicated that the need for close maternal follow-up and fetal surveillance in pregnant patients with significant mitral valve stenosis. This study showed that these patients have higher incidence of adverse maternal and fetal outcome, thus they need close follow up in experienced maternal-fetal medical centers and interventional procedures to correct their cardiac lesions should be considered before or during pregnancy to improve the maternal and neonatal outcomes.

Key words: Rheumatic mitral valve stenosis · Mode of delivery · Fetal condition · Neonatal outcome

INTRODUCTION

Rheumatic heart disease is the main cause of valvular disease in young women and mitral stenosis is the most frequently encountered, which is particularly important because it is the most poorly tolerated valvular disease during pregnancy [1]. Rheumatic valvular disease dominates in non-western countries, comprising 56-89% of all cardiovascular diseases in pregnancy [2, 3]. Mitral stenosis (MS) remains the most common important pre-existing heart condition in pregnancy worldwide. Asymptomatic women with MS may deteriorate in pregnancy and a previously uneventful pregnancy course does not preclude deterioration in a subsequent pregnancy, because degeneration of the valve may lead to increased stenosis over time. Women may deteriorate secondary to tachycardia, arrhythmias or the increased cardiac output of pregnancy. Pulmonary oedema may also be precipitated by increased volume (for example, during the third stage of labour or following injudicious use of intravenous fluid therapy). The risks are increased in women with severe MS, with moderate or severe symptoms prior to pregnancy and with a diagnosis late in pregnancy [4, 5]. Pregnancy in a patient with severe mitral stenosis is nearly always associated with a marked deterioration of clinical status [6, 7]. Women with symptomatic mitral stenosis (New York Heart Association [NYHA] class II to IV symptoms) or severe pulmonary hypertension (defined as pulmonary artery pressure >75% of systemic pressure) should be referred for prophylactic percutaneous mitral balloon valvotomy (PMBV) or open commissurotomy before becoming pregnant according to the guidelines of the American College of Cardiology/ American Heart Association (ACC/AHA) in 2006 [8].

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Mitral balloon valvuloplasty is considered a safe and useful procedure during pregnancy, with no short or long term adverse effects on the mothers and children born of subsequent pregnancies exhibited normal physical and mental development [9]. Induction, management of delivery and post-partum surveillance require specific expertise and collaborative management by skilled cardiologists, obstetricians and anaesthesiologists, in experienced maternal–fetal medicine units [8, 10].

MATERIALS AND METHODS

This prospective observational study was conducted in Hospital of Kasr Al-Ainy, Obstetrics and Gynecology Department Faculty of Medicine, Cairo University, Egypt during the period between 2/2013 and 8/2014. It was approved by the Scientific and Ethical Committee of the Obstetrics and Gynecology department of Cairo University. It included a cohort of 60 women with singleton pregnancies with a gestational age >28 weeks and with varying degrees of rheumatic mitral valve stenosis as evidenced by echocardiography, who were recruited from the High Risk Pregnancy Clinic and the casualty unit of our department. Those who suffered from pulmonary hypertension or atrial fibrillation on top of mitral stenosis were also included.Women with concomitant valvular lesion apart from tricuspid regurge were excluded, as well as any other medical disorder or pregnancy-related medical complications, multiple pregnancy or congenital fetal anomalies. Patients were diagnosed and managed through the antenatal period and until time of delivery through a collaborative approach involving the Cardiology Department of Cairo University Hospital. Any patient showing a compromise or deterioration of her cardiac condition was admitted at the High Risk Pregnancy Unit to be kept under close maternal and fetal surveillance. Some patients were also recruited from the casualty unit of our department, who were coming in laboror scheduled for elective primary or repeat Cesarean section, where a recent echocardiographic report of their cardiac condition was a prerequisite.

An informed written consent was obtained from all women prior to enrollment. All patients were subjected to detailed history taking with special focus on maternal age, parity, gestational age, cardiac condition, any related medical or surgical intervention for mitral stenosis; mode of delivery in previous pregnancies-if any; antenatal/ intrapartum or postpartum complications due to existing cardiac condition. Complete physical examination and assessment of the cardiac condition was done using NYHA classification and echocardiography for diagnosis and grading of mitral stenosis. The cohort of enrolled women was divided into three groups according to the mitral valve area estimated by echocardiography performed by a single operator to avoid interobserver variability:

- Group A: Mitral valve area<4 cm^2 but more than 2 cm^2.
- Group B: Mitral valve area between 2 and 1.3 cm^2.
- Group C: Mitral valve area less than 1.3 cm^2.

The individual groups were further classified functionally based on the New York Heart Association functional classification into 4 classes as follows:

- Class I: Uncompromised (no limitation of physical activity).
- Class II: Slight limitation of physical activity.
- Class III: Marked limitation of physical activity.
- Class IV: Severely compromised (inability to perform any physical activity without discomfort).

Assessment of fetal well being was done using serial abdominal ultrasound for fetal biophysical profile together with Doppler velocimetry of the fetal umbilical artery for pulsatility index(PI) and resistance index (RI) as well as Non-stress test. Fetal biometry and estimation of fetal weight were performed using the Hadlock formula. Ultrasound examination was done within 24 hours prior to delivery. All obstetric ultrasound measurements were performed by using VOLUSON E6, MINDRAY DC3 and ACCUVIX X 8, ultrasound machine equipped with a 3.5-MHz convex transabdominal probe. The obstetric outcomes were recorded including the gestational age at delivery/termination, incidence of vaginal delivery, Cesarean section and instrumental delivery. All the patients received prophylactic antibiotics as a measure against peripartum infective endocarditis. Maternal complications such as postpartum hemorrhage, cervical and vaginal lacerations or deterioration of maternal general condition, the need for postoperative ICU admission were reported. The incidence of deliveries requiring intervention for fetal distress and admission into a neonatal intensive care unit (NICU) was also recorded. Following delivery, the neonatal outcome was recorded in terms of Apgar scoring at 5 min, neonatal birth weight and the need for NICU. Neonatal birth weight was measured using a spring-operated scale, with a sensitivity of ±50g. Perinatal outcomes such as fetal growth restriction (FGR; under the 10^{th} percentile), prematurity (before 37 weeks of gestation) and any birth defects were also recorded.

Statistical Analysis: Data were statistically described in terms of range, mean, standard deviation and median for quantitative variables or frequency and percentage for qualitative ones. Data was entered on the computer using "Microsoft Office Excel Software" program (2010) for windows, then transferred to the Statistical Package of Social Science Software program, version 21 (SPSS) to be statistically analyzed. Comparison between groups was performed using one way ANOVA test with post hoc Tukey's test for pairwise comparisons (if quantitative variables) and Chi square with Fisher's exact test (if qualitative ones). P values less than 0.05 were considered statistically significant and less than 0.01 were considered highly significant.

RESULTS

Sixty (60) pregnant women with rheumatic mitral stenosis confirmed by echocardiography consented to participate in our observational study. The enrolled women were divided into 3 groups according to the mitral valve area (MVA) and were comparable regarding the mean maternal age and the mean gestational age at termination as shown in Table 1. All the women studied delivered at a gestational age of ≥37 weeks with only one preterm delivery at 36 weeks in group C owing to her serious cardiac condition that necessitated an early termination. A greater proportion of women in group C belonged to NYHA functional classes III and IV (Table 2). Majority of the patients delivered via Cesarean section (49/60) accounting for 81.67% of the presenting women. 57.14% of Cesarean section cases (28/49) were primary Cesarean sections whether indicated as an emergency or scheduled. Vaginal delivery occurred only in 16.67% of cases (10/60), while we encountered only 1 case that required instrumental delivery in terms of a short outlet forceps in Group C to hasten delivery and shorten the second stage (Table 3). The highest incidence of cesarean delivery was among group C with the smallest MVA. However, this was not significant when compared to the milder groups due to the high incidence of repeat caesarean delivery among these two groups. The leading cause of C/section in Group C was a cardiac indication, where deterioration in maternal cardiac status necessitated immediate termination accounting for 61.1% (11/20) of Cesarean sections in this group. This was of statistical significance when compared to the indication due to cardiac cause in Group A and Group B (p=0.001 and 0.01, respectively).

Table 1: The clinical maternal and fetal characteristics of the 3 studied groups

Group ----------	Group A (n=20)	Group B (n=20)	Group C (n=20)
Age	27 (20- 42)	28 (23 -40)	28 (18 -36)
Parity			
• Multigravidas	17 (85%)	17 (85%)	15 (75%)
• Primigravidas	3 (15%)	3 (15%)	5 (25%)
Mean Mitral valve area (cm^2) (MVA)	2.4±0.3 (2.1-3.0)	1.6±0.2 (1.3 -2.0)	1.0±0.2 (0.6–1.2)
Pulmonary artery pressure (PAP)			
• Elevated (>25 mm Hg)	5 (25%)	6 (30%)	15 (75%)
• Non-elevated (≥ 25 mm Hg)	15 (75%)	14 (70%)	5 (25%)
Umbilical artery pulsatility index (PI)	0.95±0.11(0.8-1.1)	0.98±0.11 (0.8–1.2)	0.98±0.17 (0.87-1.2)
Resistance index (RI)	0.59±0.08 (0.50 - 0.71)	0.61±0.08 (0.53-0.76)	0.61±0.09 (0.54- 0.75)
Gestational age at termination(wks)	38.5±0.5(38.0 -39.0)	38.2±0.4 (38.0-39.0)	37.9±0.9(36.0 -39.0)
Neonatal birth weight (kg)	3.1±0.4 (2.6-4.5)	3.1±0.2 (2.9-3.6)	2.9±0.2(2.6-3.3)

Data expressed as mean± S.D (standard deviation), range, number of cases and percentages

Table 2: NYHA classes among different studied groups.

Groups ----------						
Variables	Group A (n=20)		Group B (n=20)		Group C (n=20)	
NYHA	N	%	N	%	N	%
I	17	85%	15	75%	0	0%
II	3	15%	2	10%	5	25%
III	0	0%	3	15%	6	45%
IV	0	0%	0	0%	9	30%

Data were presented as frequency and %.

Table 3: Maternal and neonatal outcomes among the studied groups

Groups	Group A		Group B		Group C		
Variables	N	%	N	%	N	%	*P* value
Mode of delivery							
• Vaginal delivery	4	20	5	25	1	5	0.39(NS)
• Cesarean section	16	80	15	75	18	90	
• Instrumental delivery	0	0	0	0	1	5	
Birth weight in grams							
• 2500 -3000	13	65	12	60	15	75	0.53 (NS)
• 3000 -4000	6	30	8	40	5	25	
• >4000	1	5	0	0	0	0	
Apgar score at 5 mins							
• < 7	1	5	0	0	3	15	0.46(NS)
• ≥ 7	19	95	20	100	17	85	
Indication for C/section							
• Cardiac	0	0	2	13.3	11	61.1	0.03(S)
• Previous C/section	11	68.8	7	46.7	3	16.7	
• Other obstetric indication	5	31.2	6	40	4	22.2	

S stands for significant difference;NS stands for non-significant

Only one fetus in Group A experienced intrapartum distress during a failed trial for vaginal delivery which was followed by an emergency Cesarean section and was born with an average weight of 3 kg; a low Apgar score at 5 mins and developed meconium aspiration syndrome that necessitated NICU admission for 1 week, after which discharged with no permanent disability. However in Group C, 3/20 (15%) neonates had very low Apgar scores at 1 min (<4), which slightly improved at 5 mins. These were born by Cesarean section with average weights of 3, 3.2 and 3.1 kg and were discharged within 5 days of NICU admission with no intervention.The mean Apgar score at 5 mins in Group B (MVA: 1.3-2cm^2) was 8.8±0.7 and in Group C (MVA<1.3cm^2) was 7.3±2.1 and this was statistically significant difference (p=0.002) which was not the case when comparing Group A with Group B (p=0.40) where the mean Apgar score in Group A was 8.4±1.2. Regarding the neonatal mean birth weight, a statistically non-significant difference was found when comparing the 3 groups (p=0.56). In group C with the most evident stenotic lesion, three women (15%) needed postoperative ICU due to pulmonary edema; one had mitral valve area 1 cm^2 with atrial fibrillation, another had mitral valve area 1 cm^2 with PAP 80 mmHg and the third had mitral valve area 0.6 cm^2. However, all of them improved within 1 week after admission in the critical care unit (CCU) with no maternal mortality. In the other two groups with milder lesions, no significant maternal complications were encountered.

DISCUSSION

Apart from obstetric indications, any clear symptoms or signs pointing towards a worsening in the cardiac status were accepted as a reason for admission at the High Risk Pregnancy Unit of our tertiary hospital centre. In case of stable cardiac condition, patients were admitted at 36 weeks of gestation to determine the mode and timing of delivery unless otherwise presenting in labor. The decision to deliver the patient and the route of delivery were discussed within our team of obstetricians and cardiologists and determined according to the obstetric indication and cardiac functional capacity. 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 or development of any obstetric complication were recorded.

A great proportion of our patients delivered through Cesarean section which accounted for 81.67% of the studied cases (49/60) compared to a much lower incidence of vaginal deliveries which only accounted for 16.67% of the total enrolled women and this could be possibly explained by the high percentage women (21/60; 35%) who were scheduled for a repeated Cesarean section. Added to this, the leading cause of Cesarean delivery of the cases in group C was due to a cardiac indication (11/20; 61.1%) where the studied mothers experienced

deterioration in the cardiac functional capacity with more elevation in the pulmonary pressure which was significantly reflected on their clinical status with more mothers with NYHA class 3 and 4. Based on the cardiologist's evaluation, such mothers were not candidates for vaginal delivery as they would not to tolerate the stress of prolonged induction or straining. This is in contrast to a retrospective case-control study by Hameed *et al.* [7] conducted on 66 pregnant women with varying degrees of mitral stenosis where vaginal delivery was the rule and Cesarean section almost exclusively performed for an obstetric indication.

In our study, 3 patients in group A (with MVA less than 4 cm^2 but more than 2 cm^2) and 2 patients in group B (with MVA 1.3-2 cm^2) had mitral valve repair prior to pregnancy, which led to better neonatal and maternal outcome in comparison to group C (with MVA less than 1.3 cm^2). Among the patients in our study, pregnancies associated with higher rates of adverse fetal effects were those with mitral valve area less than 1.3 cm^2 compared to the other two groups with less evident stenotic lesions. However, we did not witness any fetal or neonatal mortality. Regarding the mean neonatal birth weight, a statistically non-significant difference was found among the studied groups (p=0.56) which is possibly attributed to the mean gestational age at delivery where majority of cases delivered after 37 weeks. Only one neonate in Group B had an Arnold Chiari malformationwhich was diagnosed prenatally late in the third trimester. Demir *et al.* [11] showed the effect of mitral stenosis on maternal and fetal outcome in pregnancy. Forty-one patients with moderate and severe mitral stenosis were enrolled in the study. The greater part of the neonates had low birth weights (mean 2555.6 ± 617.2g). Twenty patients (48.8%) delivered through caesarean section demonstrating a higher incidence of low birth weight and lower neonatal Apgar scores compared to the vaginal delivery group. The incidence of Cesarean deliveries was higher in patients who had increases in the left atrial diameter; maximum mitral valve pressure gradients and higher pulmonary pressure which agrees with our study were the Cesarean section rate was higher in Group C with the most evident stenotic lesion.Their study showed a higher incidence of low birth weight and Apgar score of the neonates when compared to our study, may be due to the earlier timing of delivery at a mean gestational age of 33.2±3.2 weeks, which also led to a higher neonatal morbidity. Ten neonates (24.3%) required NICU admission compared to only 4 neonates (6.7 %) in our study. However, we demonstrated a much higher incidence of caesarean delivery of 81.7% (49/60) where 42.8% (21/49) patients were indicated for having a previous C.S and where VBAC is not much adopted at our institution. Demir *et al.* [11] concluded that it was hard to manage pregnancy period with mitral stenosis and that adverse maternal and neonatal outcome rates dramatically increase in high risk patients. They recommended repair of valvular stenosis in such patients prior to pregnancy whenever possible [11].

According to our data, pregnant women with mitral stenosis are still at a relatively high risk of experiencing maternal complications. The association of the NYHA functional class with the risk of maternal events draws the attention to the possibility of reducing these complications in pregnant women with mitral stenosis by means of early interventions aimed at improving their functional class. The mitral valve area was also strongly and significantly associated with the risk of maternal events. Based on this assumption and with the purpose of reducing the gestational risks, interventional treatment (balloon mitral valvulotomy or surgery) prior to conception is recommended to patients with severe mitral stenosis who wish to get pregnant. Similarly procedures such balloon valvotomy should be seriously considered for the treatment of pregnant women with mitral stenosis with a greatly reduced mitral valve area, independent of their functional NYHA class. This is greatly supported by the recommendations of Barbosa *et al.* [12] concerning the greater use of mitral balloon valvotomy in highly symptomatic patients with mitral stenosis and with major risk for maternal complications aiming to reduce the corresponding maternal and fetal adverse events. Also, this is in concordance to the study of Gulraze *et al.* [9], who recommended this procedure during pregnancy. An important limitation of the present study worthy to mention is that not all patients included were examined in the early antenatal period; some of them just presented in their third trimester which did not give us the chance to recognize the various hemodynamic changes and the gradual effect of pregnancy on their heart's functional capacity. Moreover, those patients with the severe lesions didn't get the chance to benefit from early intervention that could have decreased the expected hazards. However, we believe that these factors did not have a major impact on the statistical analysis of the study as the patients were thoroughly examined and evaluated through a collaborative obstetrical and cardiological approach as soon as they presented. In spite of the relatively small sample size of our study, we could reveal a statistically significant association between the mitral valve area and possible adverse maternal and neonatal events.

CONCLUSION

It can be concluded that the results of this study indicated the need for close maternal follow-up and fetal surveillance in pregnant patients with moderate or severe MS. Repair of valvular stenosis in such patients should be performed prior to pregnancy, if possible. In addition, correction of the severe lesions should be considered during pregnancy. The possible benefits of this procedure, however, should be carefully weighed against its potential risks during pregnancy. And because of the higher incidence of adverse maternal and neonatal events in patients with significant mitral valve stenosis as shown in our results, we recommend that these patients should not be allowed to get pregnant before interventional procedure to correct these lesions. The presented results can present a basis for the development of larger studies to evaluate the prognosis of pregnant women with mitral stenosis with special emphasis on antenatal surgical intervention and corresponding maternal and fetal outcomes.

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