Non-Operated Mild and Severe Rheumatic Mitral Valve Disease During Pregnancy

Opere Edilmemiş Hafif ve Ağır Romatizmal Mitral Kapak Hastalığı Olan Gebelerin Karşılaştırılması

Ahmet Cem İYİBOZKURT, MD,[a]
Süleyman Engin AKHAN, MD,[a]
Samet TOPUZ, MD,[a]
İbrahim KALELİOĞLU, MD,[a]
Tülay ÖZKAN, MD,[b]
Recep HAS, MD,[a]
Lem'i İBRAHİMOĞLU, MD[a]

Departments of
[a]Obstetrics and Gynecology,
[b]Anesthesiology and Reanimation,
İstanbul University
İstanbul Faculty of Medical, İSTANBUL

Geliş Tarihi/*Received:* 13.03.2008
Kabul Tarihi/*Accepted:* 29.08.2008

This article was presented as a poster at the FIGO Chili World in 2003.

Yazışma Adresi/*Correspondence:*
Ahmet Cem İYİBOZKURT, MD
İstanbul University
İstanbul Faculty of Medicine,
Department of Obstetrics and
Gynecology, İSTANBUL, TURKEY
cemiyi@yahoo.com

ABSTRACT Objective: Comparison of maternal and fetal outcomes in a large group of pregnant women with mild and severe rheumatic mitral valve disease that were delivered in our clinic. **Material and Methods:** Among 18553 deliveries of seven consecutive years, 209 women with nonoperated rheumatic mitral valve disease were retrospectively analyzed: 189 New York Heart Association criteria class I-II and 20 class III-IV patients were compared. All patients had their cardiac lesions confirmed by an echocardiogram during the third trimester. Peripartum measures like method of delivery, gestational week at delivery, birth weight, Apgar scores were recorded. Fetal and maternal outcome measures included maternal and fetal mortality, complications in the peripartum and postpartum period, the duration of hospitalization and requirement of intensive care in the postpartum period. All parameters were compared by either using Fischer's exact, chi-squared and student-t tests. **Results:** There was no significant difference between two groups in terms of age, parity, type of delivery, birth weights, and presence of intrauterine growth retardation. Maternal and fetal mortality was significantly increased in class III-IV patients (p=0.003, p=0.018 respectively). Intensive care requirement, presence of pulmonary hypertension, and development of any maternal complication were also more common in these patients. **Conclusion:** Maternal and fetal mortality is significantly increased in pregnant women with New York Heart Association class III and IV rheumatic mitral valve disease. To identify these pregnant women and provide their antenatal follow-up after proper work-up in specialized centers is important, since most are lacking proper antenatal care.

Key Words: Maternal mortality, mitral valve, perinatal mortality, pregnancy, rheumatic fever

ÖZET Amaç: Kliniğimizde doğum yaptırılan hafif ve ağır romatizmal mitral kapak hastalığı olan ve büyük bir grup oluşturan gebelerde maternal ve fetal sonuçların karşılaştırılması. **Gereç ve Yöntemler:** Yedi yıl içinde kliniğimizde yaptırılan 18 553 doğum içinde romatizmal mitral kapak hastalığı olan ve opere edilmemiş 209 gebe retrospektif olarak değerlendirildi: "New York Heart Association" (NYHA) kriterlerine göre 189 I-II. sınıf ve 20 III-IV. sınıf hasta çalışmada karşılaştırıldı. Bütün olgularda mitral kapak hastalığı varlığı üçüncü trimesterde yapılan ekokardiyografi ile doğrulandı. Tüm kadınlarda doğum şekli, doğumda gestasyonel hafta, doğum ağırlığı ve Apgar skorları ile maternal ve fetal mortalite, peripartum ve postpartum dönemde komplikasyon gelişimi, hastanede yatış süresi ile postpartum dönemde yoğun bakım ihtiyacı gibi fetomaternal parametreler çalışmada değerlendirildi. Bu parametreler Fischer exact, ki-kare ve Student-t test kullanılarak analiz edildi. **Bulgular:** Gruplar arasında yaş, parite, doğum şekli, doğum ağırlığı ve gelişme geriliği açısından anlamlı bir fark bulunamadı. Ancak maternal ve fetal mortalitenin NYHA III-IV sınıfındaki hastalarda anlamlı olarak arttığı saptandı (sırasıyla p=0.003 ve p=0.018). Yoğun bakım ihtiyacı ve pulmoner hipertansiyon varlığının da bu gebelerde daha sık olduğu görüldü. **Sonuç:** NYHA III ve IV sınıfındaki romatizmal mitral kapak hastalığı olup çoğunluğu takipsiz olan bu gebelerde maternal ve fetal mortalite anlamlı olarak artmıştır. Bu hastaların önceden saptanarak takip ve doğumlarını gereğinde kardiyak açıdan destek verebilecek yoğun bakım imkanı olan hastanelerde yapmaları uygun olacaktır.

Anahtar Kelimeler: Maternal mortalite, mitral kapak, perinatal mortalite, gebelik, romatizmal ateş

Turkiye Klinikleri J Gynecol Obst 2008;18(5):306-11

In the developing world, rheumatic heart disease (RHD) is still the most common cause of valvular heart disease in pregnant women. Arising secondary to rheumatic fever, group A β-hemolytic streptococci are involved in the process, but the pathogenic mechanism remains obscure.

Acute rheumatic fever most often occurs in children; the peak age-related incidence is between 5 and 15 years. Approximately 3% of individuals with untreated group A streptococcal pharyngitis develop rheumatic fever. Forty to sixty percent of patients with acute rheumatic fever have carditis and a significant number develop RHD. The most common lesion associated with RHD is mitral stenosis, occurring in 75% of the cases. Mitral stenosis combined with regurgitation is also relatively common, making up around 30% of the patients with carditis.

In our institution, rheumatic mitral valve disease is responsible for the majority of cardiac disease in pregnant women. Frequently, these women have a complication-free pregnancy and puerperium. However, in New York Heart Association (NYHA, 1964) functional status Class III-IV women, pregnancy poses a great threat to well-being of both mother and the fetus. Although complications including pulmonary edema and death may occur during pregnancy, many of these young women are asymptomatic, and are diagnosed to have RHD during pregnancy. The present study was designed to evaluate the effects of severity of non-operated rheumatic mitral valve disease (RMVD) on maternal and fetal outcome in a relatively large group of patients cared in a university-clinic setting.

MATERIAL AND METHODS

The patient population consisted of retrospectively analyzed 209 pregnant women with non-operated rheumatic mitral valve disease who delivered in our labor unit in 7 consecutive years starting from 1996. Among the 18.553 deliveries, 431 pregnant women had cardiac disease (2.3%); and 299 of them (69.3%) had valvular heart disease. The most frequently affected valve was the mitral valve (277 women). After excluding 47 patients diagnosed to have mitral valve prolapse, and 22 patients with prosthetic mitral valves, maternal and perinatal outcome of 209 patients were studied.

Age, parity, preliminary diagnosis at admittance, frequency and place of antenatal visits of all women were recorded. Then, women were assigned to a grade according to the assessment of functional status of the cardiac disease by NYHA criteria and had their cardiac lesions confirmed by an echocardiogram during the third trimester. The type of mitral valve disease, diagnostic method used, presence of pulmonary hypertension, and currently prescribed drugs were also noted.

Information about peripartum events like the method of delivery, gestational week at delivery, the birth weight of the newborn, 1-minute and 5-minute Apgar scores were recorded. All women received endocarditic prophylaxis during delivery.

Maternal and fetal outcome measures included maternal and fetal mortality, complications in the peri- and postpartum period (presence of pulmonary edema, cardiac failure, etc.), presence of congenital malformations, the duration of hospitalization and requirement of intensive care in the postpartum period.

The data obtained from patients' files was registered in a database formed by using Microsoft Access. Class I-II (mild) and Class III-IV (severe) patients were separated into two groups and the data was compared according to this classification. There were 189 mild and 20 severe women with RMVD. Quantitative and qualitative data were compared by SPSS 12.0 using independent-two variable t-test, Fishers' exact test and chi-square test, respectively. Statistical significance was accepted at $p< 0.05$.

RESULTS

Mean maternal age of severe RMVD patients were slightly higher than mild RMVD group (30.3 ± 5.1 vs. 28.4 ± 5.2), but the difference was not significant ($p=0.128$). Only 37.8% of the patients received prenatal care in our university clinic. Data

TABLE 1: Comparison of age, parity and frequency of perinatal care between the two groups. Values were expressed as mean ± SD and n (%) when applicable.

Parameters	Class I-II (n= 189)	Class III-IV (n= 20)	p
Age (years)	28.4 ± 5.2	30.3 ± 5.1	0.128
Number of nulliparous patients	117 (61.9%)	8 (40%)	0.091
Patients without prenatal care	104 (55%)	14 (70%)	0.24

about age, parity and frequency of perinatal care were detailed in Table 1.

The two most common mitral valve diseases in the mild RMVD group were isolated mitral regurgitation (51 patients, 26.9%) and isolated mitral stenosis (48 patients, 25.3%). However, the most common mitral valve disease in the severe RMVD group was combined mitral valve disease (stenosis and regurgitation) (35%). Distribution of valvular pathologies was detailed in Table 2.

Mean gestational age at the time of delivery was not different between the two groups (37.2 ± 4.3 and 37.0 ± 3.4 weeks in mild and severe RMVD groups, respectively). The rates of cesarean section were also similar (Table 3). The most common indication for cesarean delivery was 'elective' cesarean in both groups (Table 4). In the severe RMVD group, second most common indication was fetal distress (30%).

Maternal complications were more common in the severe RMVD group [11% mild vs. 65% severe, (p=0.0001)] (Table 5). Number of women having pre- or postpartum cardiac failure was also significantly more common in the severe RMVD group (p=0.0023). Presence of pulmonary hypertension was much more frequent (p=0.0001) in Class III-IV women when compared to class I-II women [(5.8% class I-II vs. 55% class III-IV, (p=0.0001)]. Women in the severe RMVD group required intensive care significantly more than the other group (p=0.0002) and had significantly longer hospital stay (p=0.0012).

Maternal mortality occurred in 3/20 (15%) of severe RMVD cases and in 1/189 (0.5%) of the mild RMVD cases (Table 5). The maternal mortality rate in the severe RMVD group was significantly increased (p=0.0029).

In terms of fetal outcome parameters, birth weight was estimated to be lower in the severe RMVD group (2918 ± 727 vs. 2742 ± 753 g), but it did not reach statistical significance (p=0.31) (Table 6). The mean Apgar scores were 7.96 ± 1.53 and 7.55 ± 1.87 at 1 minute, and 9.38 ± 0.99 and 8.95±1.76 at 5 mi-

TABLE 2: Distribution of valvular pathologies (a CM: Combined mitral valve disease [CM: Mitral stenosis + Mitral regurgitation]). Data are expressed as n(%).

	Class I-II (n= 189)	Class III-IV (n= 20)
Mitral stenosis	48 (25.3)	5 (25)
Mitral stenosis +Aortic regurgitation	12 (6.3)	2 (10)
Mitral stenosis + Aortic regurgitation + Aortic stenosis	4 (2.4)	
Mitral stenosis + Aortic regurgitation +Tricuspid regurgitation	1 (0.5)	
Mitral regurgitation	51 (26.9)	3 (15)
Mitral regurgitation + Aortic regurgitation	14 (7.4)	2 (10)
Mitral regurgitation + Aortic regurgitation + Tricuspid regurgitation	4 (2.4)	
Mitral regurgitation + Tricuspid regurgitation	2 (1)	
Mitral regurgitation + Aortic stenosis + Tricuspid regurgitation	1 (0.5)	
Mitral regurgitation + Pulmonary regurgitation	1 (0.5)	
CMa	41 (21.6)	7 (35)
CM+ Aortic regurgitation	9 (4.7)	1 (5)
CM + Tricuspid regurgitation	1 (0.5)	
Total	189	20

TABLE 3: Comparison of gestational week at delivery and type of delivery between the two groups. Values were expressed as mean ± SD and n (%) when applicable.

Parameters	Class I-II (n= 189)	Class III-IV (n= 20)	P
Gestational age (week)	37.2 ± 4.3	37.0 ± 3.4	0.768
Type of Delivery			
1. Vaginal	101 (53.4)	7 (35)	0.157
2. Vacuum extraction	14 (7.4)	3 (15)	0.212
3. Cesarean section	74 (39.2)	10 (50)	0.35

TABLE 4: Indications of cesarean section.

Indications of Cesarean Section (C/S)	Class I-II (n= 74)	Class III-IV (n= 10)
Electivea	27 (36.4)	5 (50)
Prior C/S	16 (21.6)	1 (10)
Fetal distress	7 (9.5)	3 (30)
Failed Induction	5 (6.7)	1 (10)
Breech presentation	8 (10.8)	---
Breech + Nulliparous	2 (2.7)	---
Arrest of labor	7 (9.5)	---
Cephalopelvic Disproportion	1 (1.4)	---
IUGRb + Oligohydramnios	1 (1.4)	---

(a: Elective includes cases in which C/S indication is favored by cardiologists and anesthesiologists. C/S is recommended by cardiologists and anesthesiologists in 17 patients in Class I-II, and all patients in Class III-IV and hence performed. b: Intrauterine growth retardation). Data are expressed as n(%).

nutes in the mild and in the severe RMVD patients, respectively (in both p=NS). There was no statistically significant difference between the two groups in the incidence of intrauterine growth retardation (IUGR). However, there was a significant difference in the perinatal mortality rate between the two groups [2.1% (4/189) class I-II vs. 20% (4/20) class III-IV ($p<0.01$)]. In the mild RMVD group, two fetuses of preeclamptic mothers at 29th week of gestation had no fetal cardiac activity on admission. Other perinatal deaths in this group were due to complications of premature deliveries: one intraventricular bleeding and one respiratory distress syndrome due to meconium aspiration. There were 4 perinatal deaths in the severe RMVD group. These died due to complications of prematurity in this group of patients. There were two maternal deaths in this group of patients.

Six fetuses in the mild and one fetus in the severe RMVD group had congenital malformations. These malformations were isolated hydrocephaly (two patients in the mild and the only patient with malformation in the severe RMVD group), hydronephrosis (2 cases), and mesenteric cyst (1 case). One fetus with multiple congenital malformations (gastrointestinal system obstruction, ambiguous genitalia, cleft lip and palate) was medically aborted at 22 weeks of gestation.

TABLE 5: Maternal outcome parameters in both groups. Values were expressed n (%).

Maternal Outcome Parameters	Class I-II (n= 189)	Class III-IV (n= 20)	p
Patients who develop maternal complications	21 (11)	13 (65)	0.0001
Maternal death	1 (0.5)	3 (15)	0.0029
Number of patients having pre- or postpartum cardiac failure	11 (5.8)	6 (30)	0.0023
Pulmonary Hypertension	11 (5.8)	11 (55)	0.0001
Patients in need of intensive care	9 (4.7)	7 (35)	0.0002
Duration of hospital stay (days)	3.5±3.4	6.5±7.1	0.0012

TABLE 6: Fetal outcome parameters in both groups. Values were expressed as mean ± SD and n (%) when applicable.

Fetal Outcome Parameters	Class I-II (n= 189)	Class III-IV (n= 20)	p
Birth weight (g)	2917.84 ± 727.04	2741.5 ± 753.47	0.305
1. minute APGAR	7.96 ± 1.53	7.55 ± 1.87	0.259
5. minute APGAR	9.38 ± 0.99	8.95 ± 1.76	0.093
IUGR	13 (6.8)	3 (1.5)	0.186
Perinatal death	4 (2.1)	4 (20)	0.001

DISCUSSION

There are a few publications on pregnant patients with RHD in the last decade. In 1998, Tan and de Swiet have examined 73 pregnant women with cardiac disease in West London and only 12% of these women had rheumatic valve disease.[1] In most of the developed countries, the increasingly important and most common cardiac problem in young pregnant women is congenital heart disease.[2] On the contrary, rheumatic valve disease is still the most common cause of cardiac disease encountered in pregnant women in our clinic. Mitral valve is the most frequently affected valve. It is of note that most of these women (around 85%) are living in rural areas.

Despite limitation by small number of patients in each subgroup of type of valvular pathology, the presence of combined mitral valve disease was associated with a higher NYHA class. The frequency of isolated mitral stenosis was comparable in both groups. Our finding of the relatively increased frequency of mitral regurgitation in the mild RMVD group was not surprising because mitral regurgitation is well tolerated in pregnancy, probably due to decreased systemic vascular resistance; and hence associated with a lower NYHA class.[3]

It is well known that women with severe RMVD have a significantly higher rate of complications including pre- and postpartum cardiac failure. In the series of Desai et al from South Africa, 51% of the 128 patients with mitral stenosis had complications and most were related to pulmonary edema.[4] In our series, the overall complication rate was 11% in the mild and %65 in the severe RMVD group. Siu et al published a series of 221 pregnant women with cardiac disease and the ratio of patients who developed heart failure was 18%.[5] Incidence of heart failure in our study was 5.8% and 30% in the mild and the severe RMVD patients respectively.

Our study also supports the view that pulmonary hypertension is an important operating factor affecting prognosis in patients with valvular heart disease, despite recent data shows that the maternal mortality due to pulmonary hypertension is decreasing.[6,7] Mortality rate in patients with pulmonary hypertension in our series was around 18% (4/22) and supports the recent literature. However, pulmonary hypertension was present in all of the four maternal deaths in our study. All of these patients were referred to our clinic due to unstable maternal status, and none had received a proper antenatal care. The only patient lost in the mild RMVD group had combined mitral valve disease, pulmonary hypertension and atrial fibrillation. She died postpartum due to cardiac failure and shock. Likewise, in the severe RMVD group all three patients died due to cardiogenic shock. One of these patients had combined mitral valve disease and pulmonary stenosis, and died after two hours of admittance due to cardiogenic shock. The other two patients had severe mitral stenosis and pulmonary hypertension. One of them developed cardiac failure after vaginal delivery, and died due to pulmonary embolism on the seventh postpartum day. The last patient was admitted in cardiogenic shock. She was delivered immediately by cesarean section due to fetal distress, but died on the second postpartum day.

In addition, our data shows that in class III-IV patients with RMVD, the need of intensive care and the duration of hospital stay are significantly increased, which would lead to a marked increase in health care costs of these patients. These results suggest a rationale for close hemodynamic monitoring in patients with severe RMVD.

The high rate of cesarean section in the present study reflects the decisions of a multidisciplinary team including a cardiologist, a neonatologist, an anesthetist, and an obstetrician. Although obstetricians in our institution are in favor of vaginal delivery, doctors from other specialties are recommending section in these high risk women.

The present study demonstrates an adverse effect on fetal mortality. Although birth weight, presence of intrauterine growth restriction, incidence of premature delivery and Apgar scores were not affected by the severity of the functional status of RMVD, perinatal mortality was increased in cases with class III-IV mitral valve disease. These results are not in accordance with some other published data. In the study of Shawney et al. preterm birth

and small for gestational age newborns were found to be increased in NYHA functional class III-IV patients.[8] Hameed and colleagues reported an increased incidence of preterm delivery, intrauterine growth restriction and reduced birth weight in patients with valvular heart disease when matched with controls.[9] Due to the relatively small number of patients with functional class III-IV in our present study, the results can not be conclusive.

An important limitation of our study is that, all of our results are valid for our tertiary care center and they should not be extrapolated to other pregnant women with mitral valve disease.

Overall, the present study demonstrates an important effect of severity of RMVD on fetal and maternal outcome of pregnancy, especially if it is neglected. Our data supports the current literature that maternal mortality is rare in non-operated patients with mitral valve disease at NYHA functional class I and II.[10] However, increased maternal complications and fetal mortality in non-operated pregnant women with mitral valve disease at NYHA class III-IV mandate close maternal and fetal follow-up in these patients with special emphasis on the presence of pulmonary hypertension. Closed mitral commissurotomy in case of severe stenosis during pregnancy is reported to be safe to perform especially in patients who are not responding to medical therapy if appropriate.[11] Women especially with severe mitral valve disease should be identified before pregnancy and should be followed by specialized centers in order to improve fetal and maternal outcome.

REFERENCES

1. Tan J, de Swiet M. Prevalence of heart disease diagnosed de novo in pregnancy in a West London population. Br J Obstet Gynaecol 1998;105:1185-8.
2. Lupton M, Oteng-Ntim E, Ayida G, Steer PJ. Cardiac disease in pregnancy. Curr Opin Obstet Gynecol 2002;14:137-43.
3. Cunningham EG, Gant NF, Leveno KJ, III.Gillstrap LC, Hauth JC, Wenstrom KD. Cardiovascular diseases. In: Cunningham EF, ed. Williams Obstetrics. 21st eds. New York, USA: McGraw-Hill; 2001. p.181-1207.
4. Desai DK, Adanlawo M, Naidoo DP, Moodley J, Kleinschmidt I. Mitral stenosis in pregnancy: a four-year experience at King Edward VIII Hospital, Durban, South Africa. BJOG 2000; 107:953-8.
5. Siu SC, Sermer M, Harrison DA, Grigoriadis E, Liu G, Sorensen S,et al. Risk and predictors for pregnancy-related complications in women with heart disease. Circulation 1997; 96:2789-94.
6. Almange C. Pregnancy and congenital heart disease. Arch Mal Coeur Vaiss 2002;95: 1040-4.
7. Valdés G, Matthei R, Fernández MS, Schacht C, Corthorn J, Germaín AM. Pulmonary hypertension and pregnancy. Rev Med Chil 2002;130:201-8.
8. Sawhney H, Aggarwal N, Suri V, Vasishta K, Sharma Y, Grover A. Maternal and perinatal outcome in rheumatic heart disease. Int J Gynaecol Obstet 2003;80:9-14.
9. Hameed A, Karaalp IS, Tummala PP, Wani OR, Canetti M, Akhter MW, et al J Am Coll Cardiol 2001;37:893-9.
10. Brady K, Duff P. Rheumatic heart disease in pregnancy. Clin Obstet Gynecol 1989;32:21-40.
11. Yavaş S, İşcan HZ, Mavioğlu L, Ünal U, Akgül A, Birincioğlu CL. Closed Mitral Commissurotomy In Mitral Stenosis And Pregnancy: Long Term Results . Turkiye Klinikleri J Cardiovasc Sci 2007;19:105-10.