



Comparison of maternal and fetal outcomes in mothers with non-congenital mitral valve stenosis and healthy control

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ABSTRACT

Background: Physiological changes during pregnancy cause complications in mothers with mitral stenosis and their infants. This study was designed to assess maternal and fetal pregnancy outcomes in women with rheumatic mitral valve stenosis and compare them with the control group.

Materials and methods: This study is a case-control study on 153 pregnant women, including 51 with mitral stenosis (MS) and 102 without MS as the control group, between 2007–2022. For each studied patient, two control participants were selected and matched in residence, age, and year of pregnancy. SPSS version 22 was used for data analysis.

Results: The mean age was 31.7 ± 4.6 years in cases and 31.6 ± 4.7 in the healthy controls. Demographic variables were not significantly different between the case and control groups. The rate of stillbirth (5.9% vs. 0.0%), NICU admission (13.7% vs. 2.0%), and IUGR (5.9% vs. 0.0%) were higher in the fetal case group compared with the control group. On the other hand, maternal outcomes, including pulmonary edema (13.7% vs. 0.0%), ICU admission (23.5% vs. 0.0%), limb edema (15.7% vs. 0.0%), dyspnea (37.3% vs. 0.0%), pulmonary hypertension (9.8% vs. 0.0%), palpitations (21.1% vs. 0.0%) and hospital admission during pregnancy (37.2% vs. 4.9%) were statistically more common in the case groups.

Conclusions: Pregnancy is associated with significant fetomaternal morbidities in women with mitral valve heart disease. So they need a multidisciplinary approach in preconception and antenatal care.

1. Introduction

Mitral valve stenosis occurs when the mitral valve opening is narrowed, leading to reduced blood flow and increased blood volume and pressure in the left atrium [1,2].

An autoimmune reaction to a group A streptococcus (GAS) bacterial infection in acute rheumatic fever can cause Rheumatic heart disease (RHD) [3]. In developing countries, permanent damage to the valves caused by RHD [4,5] persists as a major cause of cardiac morbidity and mortality, especially among young female adults [6,7]. Mitral stenosis (MS) is the most common valvular sequel [8]. Moreover, mitral valve disease, particularly Mitral Stenosis (MS), is the most common cardiac valvular disease observed among pregnant women [9,10].

The prevalence of RHD has declined in developed countries; for example, the prevalence of RHD is less than 5 per 100,000 persons in the

United States. However, higher prevalences of RHD are reported in developing countries leading to higher rates of MS. The prevalence of MS in developing countries exceeds 10 per 1000 [11], and the prevalence of mitral valve disease is reported to be 8 per 1000 in Iran [9].

The hemodynamic change during pregnancy can unmask previously asymptomatic heart disease. Cardiovascular changes during pregnancy increase the demand on the heart, thereby exacerbating manifestations such as dyspnea, palpitations, syncope, fatigability, and hemoptysis [8, 12–14]. Moreover, maternal mitral valve disease is associated with an increased rate of IUGR, preterm delivery, and lower birth weight [15].

Patients with mitral valve disease may develop atrial fibrillation (AF) and pulmonary edema during pregnancy and require hospital admission for cardiac reasons [16]. They may also experience changes in NYHA class, cardiac failure, and arrhythmias during pregnancy [15,16]. Cardiac decompensation and pulmonary edema often occur in the second or

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third trimester, along with the hemodynamic burden peak during pregnancy [17].

Persistent preventive and therapeutic measures can prevent the progression and complications of maternal heart disease, which would otherwise be associated with risk for both mother and fetus [18]. Also, it is important to identify pregnancy-related cardiac and neonatal complications. Identifying prior risk factors predicting the likelihood of adverse pregnancy outcomes is equally important [19]. Further, contemporary data on pregnancy outcomes in women with rheumatic mitral valve stenosis will be helpful in risk stratification, enabling the identification of high-risk women for appropriate consultation and management [20–22].

Most studies in this regard have only assessed the patients, and studies with a control group comparisons are very limited [23]. On the other hand, many studies have investigated valvular heart diseases without further discrimination; there are limited studies exclusively on pregnant women with MS [24–26]. Hence, such studies are required to provide evidence for guidelines on pregnancy management in pregnant women with MS. This study aims to assess maternal and fetal pregnancy outcomes in women with rheumatic mitral valve stenosis and compare them with the control group.

2. Methods

2.1. Study design and study population

The present study was designed as a case-control study of pregnancy outcomes in pregnant women with MS compared to healthy controls between 2007–2022 who gave birth at Vali-e-Asr Hospital in Birjand. All cases were followed during pregnancy and labor at Birjand University of Medical Sciences, Iran. The research ethics committee approved the study protocol (IR.BUMS.REC.1400.253). Mitral stenosis (MS) was classified according to calculated valve area established by either cardiac catheterization or echocardiography as mild ($>2 \text{ cm}^2$), moderate ($1.5 \text{ to } 1.0 \text{ cm}^2$), and severe ($<1.0 \text{ cm}^2$) [27]. The sample size was calculated using Gpower software (Ver. 3.1) considering Silver et al.'s study [12]. In the present study, 51 patients were enrolled in the case group and 102 in the control group, who were selected through convenient sampling. For each case, two healthy controls were selected individually from delivery records at the same medical center, matching the patient in age, residence, and year of pregnancy.

2.2. Exclusion criteria

Incomplete records, prosthetic heart valves, therapeutic abortion due to noncardiac causes, Body Mass Index (BMI) > 40 , immunodeficiency, malignancy, underlying diseases, such as asthma, respiratory, hepatic, and renal diseases, and multifetal pregnancy.

2.3. Data collection

The relevant data were extracted from the patient's medical records. The following items were considered for maternal outcome: 1) change in New York Heart Association (NYHA) functional class; 2) the level of mitral stenosis; 3) heart complications during pregnancy, delivery, and labor; 4) vital signs in labor; and 5) mode of delivery. On the other hand, the following items were considered for fetal outcome: 1) preterm labor; 2) stillbirth; 3) birth weight, head circumference, height, and one-minute and five-minute Apgar scores; and 4) intrauterine growth retardation (IUGR).

2.4. Data analysis

The data were analyzed to evaluate the maternal and fetal outcomes. Baseline characteristics and the mentioned items for maternal and fetal outcomes were compared between patients with MS and healthy

controls using the Fisher exact test and Chi-square. Kolmogorov-Smirnov and p-p plots were used to assess data normality. The independent t-test was used to compare quantitative variables. All values were presented as mean \pm SD. SPSS version 22 was used for data analysis. A P-value below 0.05 was considered statistically significant.

3. Results

The present study is a case-control study on the course of pregnancy and delivery of 153 pregnant women, including 51 pregnant women with MS and 102 without MS in the control group. The mean \pm SD age was 31.7 ± 4.6 years in pregnant women with MS and 31.6 ± 4.7 in the healthy controls (P-value = 0.865). Demographic variables were not significantly different between the case and control groups (Table 1).

3.1. Fetal outcomes

Pregnancy was associated with an increased rate of fetal outcomes and decreased prenatal indexes in the case group compared with the control group. The rate of stillbirth (5.9% vs. 0.0%), neonatal intensive care unit (NICU) admission (13.7% vs. 2.0%), and IUGR (5.9% vs. 0.0%) were higher in the case group compared with the control, representing a statistically significant difference (P-value < 0.05) (Table 2). Moreover, birth weight was significantly lower in the case group compared with the control group ($3013.6 \pm 535.3 \text{ g}$ vs. $2807.9 \pm 524.7 \text{ g}$; P-value = 0.041). Besides, head circumference and height were lower in neonates of mothers with MS, though the difference was not statistically significant (Table 2).

3.2. Maternal outcomes

Women with MS have a high rate of clinical complications and a marked increase in morbid events during pregnancy compared to controls. The rates of pulmonary edema (13.7% vs. 0.0%), ICU admission (23.5% vs. 0.0%), limb edema (15.7% vs. 0.0%), dyspnea (37.3% vs. 0.0%), reduced O₂ saturation (11.8% vs. 0.0%), pulmonary hypertension (9.8% vs. 0.0%), palpitations (21.1% vs. 0.0%), and hospital admission during pregnancy (37.2% vs. 4.9%) were significantly higher among the case group compared with the control group. Most hospital admissions during pregnancy occurred in the third trimester (Table 3). In the case group, 27.4% of the patients were informed of their disease during pregnancy and delivery (Table 4).

Twenty patients (39.2%) with MS were in the NYHA functional class I, 15 (29%) in class II, 10 (19.6%) in class III, and 6 (11.8%) in class IV. Functional class deterioration during pregnancy occurred in 41.2% of pregnancies, mainly in the third trimester (Table 4).

Table 1
Demographic data of patients and controls.

Variable	Case group Frequency (percentage)	Control group Frequency (percentage)	P-value
Newborn sex			0.633
Female	25(58.1)	50(53.8)	
Male	18(41.9)	43(46.2)	
Mother's job			0.321
Employed	7(13.7)	6(8.1)	
Housewife	44(86.3)	68(91.9)	
Mother's educational			0.396
Diploma and undergraduate	35(71.4)	54(78.3)	
University degree	14(28.6)	15(21.7)	
Residence State			1.000*
Urban	35(68.6)	70(68.6)	
Rural	16(31.4)	32(31.4)	

* Significant value is based on Fisher's exact test.

Table 2
Fetal Outcome and prenatal indexes in Patients and their Controls.

Variables	Case group Frequency (percentage)	Control group Frequency (percentage)	p-value
Stillbirth	3(5.9)	0(0.0)	0.036*
IUGR	3(5.6)	0(0.0)	0.036*
NICU admission	7(13.7)	2(2.0)	0.004
Immaturity	4(7.8)	2(2.0)	0.096*
Abortion	7(13.7)	7(6.9)	0.165
Cardiac arrhythmia	1(2.0)	0(0.0)	0.333*
Preterm birth	14(27.5)	23(22.5)	0.504
Gestational Age (Weeks)	33.8 ± 8.9	36.0 ± 7.8	0.121
Head circumference (cm)	33.9 ± 1.7	34.6 ± 2.4	0.117
Height (cm)	49.0 ± 2.9	49.6 ± 3.81	0.327
Weight (g)	2807.9 ± 524.7	3013.6 ± 535.3	0.041
One-minute APGAR Score	8.6 ± 1.1	8.8 ± 0.7	0.256
Five-minute APGAR Score	9.4 ± 0.7	9.6 ± 0.5	0.027

* Significant value is based on Fisher's exact test.

Atrial fibrillation, cardiopulmonary resuscitation, pulmonary hypertension, respiratory distress, and limb edema were more frequently observed in severe cases of mitral stenosis. The rate of cesarean section (mild MS 38.9%, moderate MS 46.2%, severe MS 65.0%) and incidence of pulmonary hypertension (mild MS 0.0%, moderate MS 0.0%, severe MS 20.7%) have been related to the severity of MS. However, there is no significant relationship between MS severity and other maternal and fetal outcomes and drug usage (Table 5).

3.3. Delivery

The mean ± SD gestational age was 33.8 ± 8.9 weeks in the case group and 36.0 ± 7.8 weeks in the control group. The cesarean section comprised 51.0% of the deliveries in the case group and 50% of deliveries in the control group (Table 2).

4. Discussion

4.1. Main result

Previous Similar studies have mostly been done with case series design, and a few case-control studies were conducted. The present study was designed to assess the maternal, fetal, and delivery outcomes in the case group compared with the control group. The results of the present study were reported separately in terms of maternal, fetal, and delivery outcomes. Generally, the results showed that MS significantly affects both maternal and fetal outcomes.

4.2. Maternal outcome

Although subgroup analysis, based on the severity of MS, of our findings may be limited owing to the relatively small number of pregnant women in each subgroup, a clear relationship can be found between the severity of MS and maternal and fetal outcomes. However, women with MS generally had a high rate of clinical problems and a marked increase in morbid events during pregnancy, including pulmonary edema, limb edema, dyspnea, pulmonary hypertension, and hospital admission [16,23]. Additionally, 27.4% of patients were informed of their disease during pregnancy and delivery. The marked hemodynamic changes normally occurring during gestation increased incidence of maternal outcomes in patients with MS is not surprising [28].

Table 3
Comparison of the maternal outcome, mode of delivery, and labor indexes in the case and control groups.

Variable	Case group Frequency (percentage)	Control group Frequency (percentage)	P-value
Pulmonary edema	7(13.7)	0(0.0)	p < 0.001*
ICU admission	12(23.5)	0(0.0)	p < 0.001
Respiratory distress	3(5.9)	0(0.0)	0.036*
Limb edema	8(15.7)	0(0.0)	p < 0.001
Reduced O ₂ saturation	6(11.8)	0(0.0)	0.001*
Dyspnea	19(37.3)	0(0.0)	p < 0.001
Pulmonary hypertension	5(9.8)	0(0.0)	0.004*
Palpitation	11(21.6)	0(0.0)	p < 0.001
AF	1(2.0)	0(0.0)	0.333*
Hemoptysis	1(2.0)	0(0.0)	0.333*
CPR	1(2.0)	0(0.0)	0.333*
Bradycardia	1(2.0)	0(0.0)	0.333*
Preterm labor	9(17.6)	20(19.6)	0.771
Fever	2(3.9)	0(0.0)	0.110*
Preeclampsia	2(3.9)	7(6.9)	0.531
Hydronephrosis	1(2.0)	0(0.0)	0.333*
Hospital admission	19(37.2)	5(4.9)	p < 0.001
Cause of Hospitalization			p < 0.001
Cardiac	9(17.6)	0(0.0)	
Non-cardiac	10(19.6)	5(4.6)	0.875
Hospitalization trimester			
First trimester	2(11.8)	1(20.0)	
Second trimester	3(17.6)	1(20.0)	
Third trimester	12(70.6)	3(60.0)	
Mode of delivery			0.596
Cesarean section	26(51.0)	51(50.0)	
Vaginal delivery	21(41.6)	47(46.1)	
Curettage	7(7.8)	4(3.9)	
Temperature (°C)	37.0 ± 0.25	36.5 ± 3.6	0.389
Respiratory rate	19.0 ± 3.3	18.7 ± 2.1	0.751
Systolic blood pressure (mmHg)	117.0 ± 20.0	113.7 ± 14.2	0.242
diastolic blood pressure (mmHg)	69.3 ± 14.7	70.7 ± 11.1	0.532
Heart rate	88.1 ± 12.3	81.6 ± 8.1	p < 0.001

* Significant value is based on Fisher's exact test.

Table 4
Pregnancy NYHA class and informed of disease in the patients.

Variable	Number	percent
Time of inform		
In pregnancy	10	19.6%
On delivery	4	7.8%
Before pregnancy	37	72.5%
NYHA		
I	20	39.2%
II	15	29.4%
III	10	19.6%
IV	6	11.8%

Increased hemodynamic burden during gestation is also a possible mechanism for the new onset or clinical deterioration of MS in this study [29,30].

NYHA class is one of the important features in predicting the mortality risk of pregnant women with MS. The rate of NYHA class change in the current study was 41.2%, and the highest rate was observed in the

Table 5

Maternal and fetal outcomes and mode of delivery and NYHA class based on the severity of MS.

Variable	Mild MS (n = 18) Frequency (percentage)	Moderate MS (n = 13) Frequency (percentage)	Severe MS (n = 20) Frequency (percentage)	P-value
AF	0(0.0)	0(0.0)	1(2.0)	0.454
Pulmonary edema	2(11.1)	2(15.4)	3(15.0)	0.306
CPR	0(0.0)	0(0.0)	1(2.0)	0.454
ICU admission	3(16.7)	4(30.8)	5(25.0)	0.485
Pulmonary hypertension	0(0.0)	0(0.0)	4(20.7)	0.072
Respiratory distress	1(5.6)	0(0.0)	2(10.0)	0.676
Bradycardia	0(0.0)	0(0.0)	1(2.0)	0.265
Reduced O ₂ saturation	1(5.6)	2(15.4)	3(15.0)	0.596
Dyspnea	6(33.3)	6(46.1)	7(35)	.0347
Fever	0(0.0)	1(7.7)	1(5.0)	0.525
Palpitation	5(27.7)	4(30.7)	2(11.1)	.0340
Limb edema	2(11.2)	1(7.7)	5(25.0)	0.262
Hydronephrosis	0(0.0)	1(7.7)	0(0.0)	0.225
Hypertension in NICU	4(22.2)	1(7.7)	2(10.0)	0.421
Preterm birth	3(16.7)	0(0.0)	1(5.0)	.0195
Abortion	3(16.7)	1(7.7)	3(15.0)	0.756
Newborn Heart arrhythmia	1(5.6)	0(0.0)	0(0.0)	0.393
IUGR	2(11.1)	1(7.7)	0(0.0)	0.330
Preeclampsia	2(11.1)	0(0.0)	0(0.0)	0.148
Stillbirth	0(0.0)	2(15.2)	1(5.0)	0.195
Mode of delivery				0.712
Cesarean section	7(38.9)	6(46.2)	13(65.0)	
Vaginal delivery	8(44.4)	6(46.2)	5(25.0)	
Hard delivery	2(11.1)	1(7.7)	1(5.0)	
Curettage	1(5.6)	0(0.0)	1(5.0)	
NYHA				p < 0.001
I	6(33.3)	6(46.4)	8(40.0)	
II	7(38.8)	2(15.3)	6(30.0)	
III	5(27.7)	2(15.3)	3(15.0)	
IV	0(0.0)	3(23.0)	3(15.0)	

third trimester. Similarly, Barboza et al. [31] reported a change in NYHA class in 48.8% of patients. On the Other hand, Samii et al. [32] found that the NYHA class changed during pregnancy in 26.3% of patients, mostly in the third trimester. ICU admission was 23.5% in the present study compared with 6.3% in Pilo et al.'s study [33], which can be related to the proportion of patients with severe MS. In our study, pulmonary hypertension was seen in 9.8% of pregnant women with MS, which was similar to that of J. Relmasira et al. [34] (8.3%) and Pilo et al. [25] (10.5%). The rate of pulmonary hypertension was higher in Pandy et al.'s study [35] (29%), possibly due to their prospective study design and higher sample size.

The rate of pulmonary edema in our study was 13.7% which was similar to that of P. A. Poli et al. [33] (16.7%) and J. Relmasira et al. [34] (11.1%). However, significantly higher rates of pulmonary edema were reported by Silverside et al. [36] (31.25%) and Desia et al. [37] (35%). This inconsistency can be attributed to the difference in sample size, the number of patients in the studied groups, and the study design (retrospective/prospective nature). Consistent with other reports, palpitations were observed in 21.1% of the patients in the present study [36,38].

The hemodynamic and cardiovascular changes during pregnancy increase the cardiac demand. In patients with MS, the heart cannot compensate for the higher demand; thus, the left atrium dilates, and the left atrial pressure increases. The retrograde pressure applied to the pulmonary veins leads to pulmonary venous congestion and, in severe cases, pulmonary edema. Besides, pulmonary venous congestion leads to pulmonary hypertension. The increased volume load and tachycardia together lead to patient deterioration and NYHA class elevation. Due to

cardiac decompensation, silent MS may become symptomatic, particularly during pregnancy's second or third trimester [16,39,40].

4.3. Fetal outcome

The present study showed that MS affects the fetal outcome as well as the maternal outcomes. In the current study, pregnancy was associated with a statistically elevated rate of stillbirth, NICU admission, and IUGR. Valvular stenosis leads to hemodynamic alterations, which reduce the uterine blood flow, which explains the high rate of impaired intrauterine fetal growth in MS patients in this study [41–43]. The rate of IUGR (5.6%) in the present study was similar to Roos-Hesselink [44] (4.4%), though considerably lower compared with other studies, including Afshan Hamid (21.3%) and Rajesh Vijayvergiya (62.5%) [23,45]. In our study, the rate of stillbirth was 5.9% in MS patients, which was similar to the previous studies reporting stillbirth rate in the 4–9% range [23,31,46]. The increased incidence of fetal outcomes observed in the present study suggests the need for serial ultrasound determinations of fetal growth in pregnant women with MS and antepartum fetal surveillance [47]. These outcomes show that women suspected of valvular disease should undergo clinical evaluation before pregnancy, and exercise testing is useful before pregnancy for risk assessment [48,49].

4.4. Delivery

This study was done as a retrospective study so the rate of induced delivery was not clear but the total rate of vaginal delivery was 41.6%, and cesarean section accounted for 51% of deliveries although vaginal delivery was more common in the control group. The rate of cesarean section in the present study was similar to that of Hagen et al.'s study (52.2%) [16], Rania Hammami's study (68%) [25], and J. Roos-Hesselink's study (48%) [44]. However, in the most other previous study the cesarean section rate was between 8% to 36% [15,23,34–37]. The study population, the inequality in MS severity, and the type of study could have caused this wide difference. Cesarean section is often performed as a delivery method in patients with heart diseases. Still, it should be reserved for patients with obstetrical indications or cardiac instability.

4.5. Strengths and limitations

One of the strengths points of this study was the consideration of the control group. To increase the power of the study, two controls were considered for each case. In addition, several outcomes were assessed in this study, including maternal, fetal, and delivery outcomes. Considering that this study was conducted over a long period, patients in the control group were matched with patients in the case group in terms of year of pregnancy as well as age and place of residence to eliminate the effect of the quality of medical services.

The limitations of the present study include retrospective study design and defect in patient information, unclarity about the cause of cesarean sections and frequency number of inductions, and the small sample size for the rare outcome.

5. Conclusion

Pregnancy is associated with significant maternal and neonatal morbidities in women with mitral valve heart disease. The findings of the current study highlight the need for a multidisciplinary approach in preconception and antenatal care of women with mitral valve heart disease involving obstetricians, neonatologists, and cardiologists.

Ethical approval

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Declaration of Competing Interest

None of the authors has any relevant or significant industrial interests and benefit related to the research described in this article.

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