



## Maternal and fetal outcomes in pregnant females with rheumatic heart disease

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### ABSTRACT

**Background:** Cardiac diseases are seen in 1–3% of pregnancies. In developing countries rheumatic heart disease (RHD) contributes a major cause of cardiac disorders.

**Objective:** To study the maternal and fetal outcome in women with valvular heart disease or prosthetic heart valve replacement secondary to RHD in a tertiary care center.

**Method:** The consecutive pregnant women with RHD attending our institute from May 2018 to August 2019 were included. A maternal adverse outcome was defined as cardiac death, new onset arrhythmia, heart failure, thromboembolic event, hospitalization for other cardiac reasons or cardiac intervention, aortic dissection, infective endocarditis and acute coronary syndrome. Fetal adverse outcome defined as fetal death, preterm birth, and low birth weight.

**Result:** Total 80 patients were included in this study, native RHD in 60(75%) and 20(25%) had mechanical prosthetic valve replacement. Maternal adverse event occurred in 34(42.5%), comprising of death in 1(1.2%), new onset AF 2(2.5%), 20(25%) underwent balloon mitral valvotomy, 3(3.7%) underwent mitral valve replacement, heart failure hospitalization in 7(8.7%). 1(1.2%) patient developed mitral valve infective endocarditis. Preterm delivery occurred in 19(23.7%), 7(8.7%) abortions and 1(1.2%) intrauterine death. Fetuses with low birth weight were 43(53.7%). Pregnancy with live birth occurred in 57(95%) women with valvular heart disease but no prosthesis and 16(80%) women with prosthetic valve disease.

**Conclusion:** Women with rheumatic heart disease carry a high risk both for mother and fetus. Early diagnosis, close follow-up during pregnancy, early recognition of deterioration in symptoms and timely cardiac intervention can lead to good maternal or fetal outcome.

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## 1. Introduction

1–3% of pregnancies have underlying cardiac diseases.<sup>1,2</sup> In developing countries rheumatic heart disease (RHD) continues to be a major cause of cardiac illness.<sup>3,4</sup> In India, RHD contributes to approximately 69% of cardiac disorders seen in pregnancy.<sup>5,6</sup> Since pregnancy is the first contact of the woman with a health care facility in many cases, the heart disease is diagnosed only at the time of pregnancy. The maternal mortality rate in women with cardiac disease is as high as 7% and morbidity rate higher than 30% during

pregnancy.<sup>7</sup> There has been decline in maternal mortality in the past decade, but there has been no change in cardiac maternal death.<sup>8</sup> Large prospective studies in Indian pregnant women with rheumatic heart disease are few.<sup>9</sup> Studies on the outcomes of pregnancy in women with RHD will help to stratify risk, identifying high-risk women and their appropriate counselling and management. Aim of the study was to prospectively assess the maternal and fetal outcome in patients with valvular heart disease or prosthetic heart valve replacement secondary to RHD in a tertiary care centre.

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## 2. Method

This is a prospective study which included consecutive pregnant women with valvular heart disease or prosthetic heart valve replacement secondary to rheumatic heart disease referred to our hospital from May 2018 to August 2019. Detailed clinical history, symptomatic class, treatment history, 12 lead electrocardiogram (ECG), 2D echocardiography were done in all the patients. Obstetric ultrasound was done at the time of first antenatal visit and then at 12 weeks, 18–20 weeks and 24 weeks. Subsequent growth scans were done at interval of 4–6 weeks or earlier as per the clinical and obstetrical examination findings. Echocardiography was done on GE Vivid 7 ECHO machine (GE healthcare, Waukesha, WI, USA) with 3.5 Hz probe. Assessment of valvular lesions were done according to the European Association of Echocardiography and American Society of Echocardiography recommendations.<sup>10–13</sup> Heart failure was defined according to American College of Cardiology/American Heart Association guidelines.<sup>14</sup> New York Heart Association (NYHA) classification was used to define whether patients were asymptomatic (NYHA class I) or symptomatic (NYHA class  $\geq$  II).<sup>15</sup> The patients were risk stratified according to modified World Health Organisation (WHO) score and Cardiac Disease in Pregnancy (CARPREG) I score.<sup>16,17</sup>

Patient was advised to follow up every 3 months or early if there was any change in symptomatic class till 36 weeks. Post-partum follow-up was done for 1 week after delivery, by visit to our hospital or telephonically. Depending on clinical status and NYHA class cardiac medications were modified and if needed patient was advised hospitalization. BMV was performed in pregnant patients with symptoms, MVA  $\leq$  1 cm<sup>2</sup> or systolic pulmonary artery pressure  $\geq$  50 mmHg despite medical therapy. Patients on warfarin, were changed to unfractionated heparin (UFH) from 6 to 12 weeks of gestation after detailed counselling regarding risks and benefit of continuing warfarin versus switching over to UFH and taking written informed consent. Warfarin was restarted after 12 weeks with switchover to UFH 36 weeks of gestation or earlier in patients with threatened preterm labour or any other complication requiring early delivery.<sup>18</sup>

### 2.1. Outcome

A maternal adverse outcome was defined as cardiac death, new onset arrhythmia, heart failure, thrombo-embolic event, hospitalization for other cardiac reasons or cardiac intervention, aortic dissection, infective endocarditis and acute coronary syndrome. Fetal adverse outcome was defined as fetal death, preterm birth, and low birth weight.

## 3. Statistical analysis

Demographic data were described as mean (standard deviation) for continuous variables and number (%) for categorical variables. Univariate and multivariate logistic regression analysis were performed to assess the predictors of adverse maternal and fetal outcomes.

Pregnancy outcomes were also compared between symptomatic (NYHA I) and asymptomatic patients (NYHA  $>$  II). Odds ratios and 95% confidence intervals were calculated. Statistical tests were considered significant if a P value was  $<$  0.05 (2-sided). All statistical analyses were performed using IBM SPSS Statistics 20.

## 4. Result

Between May 2018 to August 2019, 80 pregnant women with rheumatic heart disease or prosthetic heart valve visited the

hospital. Baseline demographic and clinical characteristics are provided in Table 1. Majority of patients presented during first (41%) and second trimester (40%) and only 19% presented during third trimester. 33(41.2%) were primigravida, 25(31.3%) were second pregnancy. Higher order pregnancy ( $>$ G3) were seen in 22(27.5%) of women. The meantime of prior intervention was  $57.4 \pm 39.1$  months in BMV group and  $42.7 \pm 39.2$  months in prosthetic valve replacement group. Nearly all patients had bileaflet mechanical prosthetic valve except 2 patients who had tilting disc at mitral position.

**Table 1**  
Baseline demographic, clinical and echocardiographic characteristics.

Parameters	N = 80(%)
Mean age (years) <sup>a</sup>	28.5 $\pm$ 4.6
Primigravida	33(41.2%)
Mean gestational age at presentation (weeks) <sup>a</sup>	17.1 $\pm$ 8.7
NYHA class	
I	15 (18.7%)
II	39 (48.7%)
III	23 (28.7%)
IV	3 (3.7%)
Prior cardiac intervention	51 (63.7%)
BMV	31 (39%)
Prosthetic valve	20 (25%)
Hypertension	2(2.5%)
Diabetes Mellitus	4 (5%)
Hypothyroid	11 (13.7%)
Preeclampsia	2(2.5%)
Atrial fibrillation	5 (6.2%)
Known case of RHD	65 (81.2%)
Mean dose of drugs <sup>a</sup>	
Warfarin (mg)	3.2 $\pm$ 1.3
Metoprolol (mg)	37.3 $\pm$ 13.6
Atenolol (mg)	34.1 $\pm$ 12.6
Furosemide (mg)	16.2 $\pm$ 8.9
Verapamil (mg)	126 $\pm$ 56.2
Thyroxine ( $\mu$ gm)	51.4 $\pm$ 15.8
Predominant Mitral stenosis	40 (50%)
Mild	1 (1.2%)
Moderate	14 (17.5%)
Severe	25(31.2%)
Predominant Mitral regurgitation	6 (7.5%)
Mild	1 (1.2%)
Moderate	2 (2.5%)
Severe	3 (3.7%)
Combined MS and MR	9 (11.2%)
Predominant aortic valve disease	0
Combined aortic and mitral valve disease	5 (6.2%)
Mean RVSP (mmHg) <sup>a</sup>	46 $\pm$ 20
Mean EF (%) <sup>a</sup>	55 $\pm$ 1.4
Prosthetic valve	
MVR	16 (20%)
AVR	1(1.2%)
DVR	3(3.7%)
Modified WHO risk score	
I	1 (1.2%)
II	1 (1.2%)
II-III	28 (35%)
III	21 (26.2%)
IV	29 (36.2%)
CARPREG score	
0	3 (3.7%)
1	28 (35%)
2	43 (53.7%)
3	6 (7.5%)

Abbreviations:- NYHA – New York Heart Association; BMV – balloon mitral valvotomy; RHD – rheumatic heart disease, MS – mitral stenosis, MR – mitral regurgitation, MVR – mitral valve replacement, AVR – aortic valve replacement, DVR – double valve replacement; a - data as mean + Standard deviation.

### 4.1. Cardiac medications

Dosing of cardiac medications is summarised in Table 1. 38(95%) of mitral stenosis patients were treated with beta blockers or CCB for rate control. Loop diuretics was prescribed in 62(77.5%) cases. Warfarin was prescribed in 24(30%) patients with mean dose of 3.2 ± 1.3 mg (maximum dose of 7 mg). Out of 24 cases, warfarin was switched to UFH in 7 cases between 6 and 12 weeks. In remaining 17 cases switching of warfarin to UFH during first trimester was not possible either due to late presentation of the case or inability to maintain adequate APTT. No patient was switched to low molecular weight heparin (LMWH).

### 4.2. Maternal outcome

Maternal outcome are summarised in Table 2. Majority of balloon mitral valvotomy was done during 2nd trimester (13 cases during 2nd trimester and 7 cases during 3rd trimester) at mean gestational age of 24.7 ± 6.3 weeks. Pregnancy with predominant mitral regurgitation and mild to moderate mitral stenosis were tolerated well with no maternal or fetal event. 3 patients of combined severe MS and MR were in NYHA IV, all underwent MVR during delivery. All 3 mitral valve replacement surgeries were done concomitant with lower segment caesarean section (LSCS) at the time of delivery. Since these patients were at high risk of mortality during labor and in the postpartum period, decision for combined surgery (simultaneous lower segment LSCS) followed by mitral valve replacement [MVR] was taken. Pregnancy with a live birth was 16(80%) in women with mechanical valve and 57(95%) in women with valvular heart disease but no valve prosthesis. The maternal adverse event rate was 0%, 0%, 14.2%, 9.5% and 79.3% in patients with modified WHO score risk stratification of I, II, II-III, III and IV respectively. The adverse event occurred in 0%, 17.8%, 48.9% in patients with CARPREG score of 0, 1 and ≥ 2 respectively.

### 4.3. Fetal outcome

Fetal outcome are summarised in Table 3. Abortion was induced in 3 cases due to fetal malformations and 3 due to underlying maternal cardiac disease (2 cases were of combined lesion of mitral stenosis with mitral regurgitation and severe pulmonary arterial hypertension and 1 case of DVR). Delivery was conducted in 41(51.3%) cases in our institute and 31(38.7%) cases had their delivery at their local hospital, none at home.

### 4.4. NYHA class and valvular lesion

Women who underwent surgical correction of the cardiac lesion prior to pregnancy majority were in NYHA functional class I or II. 7

**Table 2**  
Maternal outcomes.

Maternal Event	N = 80(%)
Maternal mortality	1 (1.2%)
Cardiac intervention	23 (28.7%)
BMV	20 (25%)
MVR	3 (3.7%)
New onset AF	2 (2.5%)
Heart failure hospitalization	7 (8.7%)
Infective endocarditis	1 (1.2%)
Mean gestational age of delivery (weeks) <sup>a</sup>	36.1 ± 1.6
Thromboembolic event	0

Abbreviations:- BMV- balloon mitral valvotomy; MVR – mitral valve replacement; AF – atrial fibrillation; a - data as mean ± Standard deviation.

**Table 3**  
Fetal outcomes.

Fetal outcome	N = 80 (%)
Abortion	7 (8.7%)
Spontaneous	1 (1.2%)
Induced	6 (7.5%)
Intra-uterine fetal death	1 (1.2%)
IUGR	4 (5%)
Oligohydramnios	11 (13.7%)
Live birth	72 (90%)
Preterm	19 (23.7%)
Term	53 (66.2%)
Mode of delivery	
Vaginal	24 (30%)
LSCS	48 (60%)
Emergency LSCS for cardiac reason	9 (11.2%)
Mean Birth weight (kg) <sup>a</sup>	2.32 ± 0.45
Low birth weight (<2.5 kg)	40 (50%)
Very low birth weight (<1.5 kg)	3 (3.7%)
Warfarin embryopathy	2

Abbreviations:- IUGR – intrauterine growth retardation; LSCS – lower segment caesarean section; a - data as mean ± Standard deviation.

patients of previous BMV were in NYHA III and underwent redo BMV. All patients with prosthetic valve replacement were in NYHA class I or II. There was worsening in NYHA status in 3 patients during third trimester; 1 was a case of severe mitral stenosis and 2 were combined mitral stenosis and mitral regurgitation.

### 4.5. Predictors of adverse outcome

Univariate logistic regression analysis is summarized in Table 4. On multivariate logistic regression NYHA class>1 was independent predictor for adverse maternal event.

## 5. Discussion

This prospective study evaluated outcome of pregnancy in women with rheumatic heart disease or prosthetic heart valve disease in a tertiary care hospital. The mitral valve was the most involved lesion with 50% had predominant mitral stenosis which is similar to previous studies.<sup>19,20</sup> Left sided stenotic lesions were more symptomatic as compared to regurgitant lesions. During pregnancy there is expansion of the plasma volume, which is poorly tolerated in the presence of severe left-sided stenosis.<sup>21,22</sup> In our study 95% of women with MS were treated with beta blockers or non-dihydropyridine CCB as compared to in ROPAC study only 40% of women with MS and heart failure were treated with β-blockers, despite the fact that β-blockers are well recognized to be an important component of the management of heart failure in the presence of MS.<sup>23</sup> This finding emphasizes the need of close monitoring and timely intervention which can improve the

**Table 4**  
Univariate logistic regression analysis for predictors of adverse maternal outcome.

Predictor	Maternal event		
	Odds ratio	Confidence interval	P value
RVSP >30 mmHg	5.56	1.69–18.26	0.005
MVA <1.5 cm <sup>2</sup>	5.05	1.76–14.52	0.003
NYHA >1	10.59	1.31–85.42	0.027
No prior cardiac intervention	8.87	3.12–25.36	<0.001
Anticoagulation	0.11	0.2–0.53	0.006
Late presentation	4.31	1.5–12.36	0.007

Abbreviations:- RVSP – right ventricular systolic pressure, MVA – mitral valve area, NYHA – New York Heart Association.

maternal outcome in pregnant women with valvular heart disease. Maternal adverse event rate excluding invasive cardiac intervention was 13.8% in our study which is similar to study by Baghel et al showing adverse cardiac event in 14.9% cases.<sup>9</sup>

This study showed that cardiac intervention in severe valvular disease helped women to tolerate pregnancy well with good fetal outcome. BMV being a less invasive procedure is effective and relatively safe during pregnancy and is preferred over a surgical procedure.<sup>24,25</sup> Post-surgical procedure there is increase maternal and fetal events having a risk of fetal death up to 20%.<sup>26</sup> The best timing for BMV has been suggested to be after the fourth month.<sup>27</sup> In our study the mean timing of BMV was  $24.7 \pm 6.3$  weeks. There have been few case reports of combined surgery (simultaneous LSCS and MVR) described in literature.<sup>28,29</sup> This strategy of simultaneous caesarean and open-heart surgery seems reasonable and can be successfully employed and lifesaving for severely symptomatic women who are unfit for percutaneous intervention and are unable to bear the stress of labor and delivery.

In our study, 63.7% of patients underwent palliative or valve replacement surgery prior to pregnancy. Majority of them tolerated pregnancy well. The European task force on the Management of Cardiovascular Diseases in Pregnancy also recommends correction of the valve defect prior to pregnancy.<sup>18</sup>

Pregnancy after mechanical heart valve replacement is considered high risk for both mother and child.<sup>30</sup> Two systematic reviews by Hassouna A et al and Xu Z et al, concluded that the risk of fetal loss to be dose-related (fetal loss rate with low-dose VKA was 13.4–19.2%, total fetal loss rate with VKA is 32.5%),<sup>31,32</sup> fetal loss rates with a combined UFH/VKA regimen were 22.7% and with LMWH throughout pregnancy was 12.2%. VKA use in the first trimester also results in embryopathy (limb defects, nasal hypoplasia) in 0.6–10% of cases. The risk of valve thrombosis relatively low with VKAs throughout pregnancy (0–4%); UFH and LMWH in the first trimester or throughout pregnancy indicates a high-risk of valve thrombosis (9–33%). Current evidence (lacking adequate randomized studies) indicates that the use of VKAs throughout pregnancy, under strict INR control, is the safest regimen to prevent valve thrombosis but at the cost of increase fetal loss and embryopathy. In our study out of 80 patients 24 were on warfarin. Out of 24 cases of warfarin intake there was fetal loss in 6 cases (25%) and warfarin embryopathy seen in 2 cases which is similar to world-wide data.

Studies have showed severe mitral stenosis an independent risk factor for adverse fetal outcomes, including preterm birth and low birth weight.<sup>23</sup> The mechanism may be inability to increase cardiac output because of underlying stenotic lesion the uteroplacental blood flow is compromised which may lead to fetal growth retardation.<sup>33</sup> Priya H L et al study showed 50% of babies had a birth weight ranging from 2.5 to 3.5 kg, which is considered appropriate for the term neonate.<sup>34</sup> However almost 30% of the term newborn were of low birth weight (<2.5 kg). This suggests that cardiac disease itself could be one of the risk factors for low birth weight.

### 5.1. Limitation

The study followed up women till 7 days postpartum. There is risk for adverse outcomes beyond 7 days postpartum, so rate of maternal deaths and event rate attributable RHD would likely to be underestimated because of insufficient follow-up. Around 38% of patients had delivery at local hospital which might lead to under-reporting of events during peri and postpartum outcome. The number of patients included are small and larger studies are needed to assess the predictors of maternal and fetal outcome.

## 6. Conclusion

Women with rheumatic heart disease carry a high risk both for mother and fetus. Early diagnosis, close follow-up during pregnancy, early recognition of deterioration in symptoms and timely cardiac intervention can lead to good maternal or fetal outcome. Multidisciplinary evaluation by cardiologists and obstetrician, proper pre-conception and antenatal care are the key measures to improve the outcomes of these patients.

### What is already known?

Rheumatic heart disease is a most common cardiac disorder during pregnancy in Indian women and has adverse effect on both mother and fetus.

### What this study adds?

Regular monitoring and follow up during pregnancy improve the clinical outcome. Timely cardiac intervention in form of BMV during pregnancy improves maternal and fetal outcome. Cardiac surgery in form of MVR combined with LSCS during delivery is a safe and feasible option in patients having severe valvular heart disease, not amenable for percutaneous intervention who cannot tolerate the hemodynamic changes during post-partum period.

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