ORIGINAL ARTICLE

Fetomaternal Outcome in Mild to Moderate Mitral Stenosis

HUMAIRA BASHIR[1], ASMA AKHTAR[2], SAIRA AYUB[3], *FAIZA AAMER*[4]

ABSTRACT

Maternal heart diseases comprise 0.2% to 3% of all pregnancies and are responsible for 10% to 25% of maternal deaths. In developing countries like Pakistan rheumatic heart disease is very common whereas mitral stenosis is the most common valvular lesion. This study was designed to find out fetomaternal outcome of pregnancy in women having mild-moderate mitral stenosis.

Keywords: Valvular heart disease, mitral stenosis, congestive heart failure, preterm delivery, intrauterine growth restriction

INTRODUCTION

Heart diseases are the most important non obstetrical causes of maternal death during pregnancy. Maternal heart diseases comprise 0.2% to 3% of all pregnancies[1] and are responsible for 10% to 25% of maternal deaths[2]. Women with valvular heart disease had a high rate of clinical deterioration and a marked increase in morbid events during pregnancy, including congestive heart failure (CHF), arrhythmias and need to either initiate or increase cardiovascular drug therapy or to hospitalize patients during pregnancy.

Although rheumatic heart disease is decreasing worldwide, it is still an important cause of valvular problems[3]. In developing countries like Pakistan[4,5] rheumatic heart disease is very common whereas mitral stenosis (MS) is the most common valvular lesion (90%)[6].

Profound hemodynamic alterations occur during pregnancy, labour and in the postpartum period.[7] These changes begin during the first five to eight weeks of pregnancy and reach their peak late in the second trimester.[8] Blood volume increases by 40-50%[9], cardiac output by 30-50%,[10] heart rate by 10-15 beat/minute[11] in addition to rise in stroke volume and decline vascular peripheral resistant.[12,13] These changes return to pre-pregnancy baseline within 3-4 weeks following delivery[14]. Pregnancy has a deleterious effect on stenotic lesions[15].

Problems associated with mitral stenosis in pregnancy are due to further narrowing of mitral valve and the haemodynamic change that take place[16]. Increase in intravascular volume can lead to an increase in transmitral gradient and left atrial pressure and also cause pulmonary oedema[17]. Maternal mortality for patients with MS is significantly higher (6.8%) for those who are New York Heart Association (NYHA) class 3 and 4 than patients who are NYHA class 1 and 2(0.4%), particularly during labour and delivery[18].

Majority of pregnant women with mitral stenosis are diagnosed during pregnancy. Formerly asymptomatic patients become symptomatic due to hemodynamic changes associated with pregnancy and the development of symptoms is the reason for their first cardiac evaluation[19].

The presenting symptoms of mitral stenosis are dyspnea on exertion, orthopnea and paroxysmal nocturnal dyspnea. Physical examination of patient with mitral stenosis show pulse pressure which may be reduced, mitral facies with plethoric cheeks, raised JVP, basal crepts, S1 loud and mid diastolic murmur at mitral area with no radiation. Diagnosis is confirmed by ECG (P mitral and low voltage), and echocardiograph (mitral valve area less than 4 cm^2). Predictors of adverse maternal outcome include;

- Severity of mitral stenosis (valve < 1.5 cm^2)
- Functional class of heart disease as determined by level of activity that lead to dyspnea (New York Heart Association Class III & IV)[14].

Fetal outcome depends on the degree of maternal well being. Fetal mortality is not exceptionally high in patients with NYHA class I and II, however if there is associated pulmonary hypertension there is a risk of abortions, intrauterine growth restriction (IUGR), preterm delivery and early neonatal death[20].

In one study, the risk of maternal complications during pregnancy raised from 26% in mild mitral stenosis (defined as mitral valve area > 1.5 cm^2) to 38% in moderate mitral stenosis (mitral valve area 1.1–1.5 cm^2) and up to 67% in severe mitral stenosis (mitral valve area < 1.0 cm^2).[21] So if mitral stenosis is diagnosed early and managed properly with multidisciplinary approach, involving trained obstetrician, cardiologist, anesthetist, pediatrician and nurse, it result in successful fetomaternal outcome in majority of cases[22].

[1,2,3]*Senior Registrar in Nishter Hospital Multan*
[4]*Associate Prof. Biochemistry FMH Lahore*
Correspondence to Dr. Humaira Bashir Email: drhumaira_irfan@hotmail.com Cell: 03346057354

In one study, frequency of mild and moderate mitral stenosis was 41% and 39% respectively. In this study maternal outcome in terms of congestive heart failure in mild and moderate mitral stenosis was 11% and 61% respectively. Fetal outcome in terms of preterm delivery and IUGR in mild and moderate mitral stenosis was 5% & 28% and 16% and 27% respectively[23].

This study was planned to determine magnitude of fetomaternal outcome during pregnancy with mild to moderate mitral stenosis so that guideline could be made to handle these cases efficiently.

MATERIALS AND METHODS

This case series was carried out in Labour Ward Department of Obstetrics & Gynaecology, Nishtar Hospital Multan which is a tertiary care hospital. This study was started after the approval of synopsis and completed in six months duration six months from 19th January 2012 to 28th February 2012 and 1st June 2012 to 17th October 2012. Sample size was determined according to formula:

$$n = \frac{Z^2\, pq}{d^2}$$

Here n is the sample size, confidence level is 95%, p is anticipated population proportion (16+27)/2=22% and d is margin of error=7%, so the sample size is ≈135 patients. Non probability purposive sampling technique was used.

Inclusion Criteria:

1. Pregnant women (18–40 years) with mild and moderate mitral stenosis.
2. Gestational amenorrhea 20-40 weeks calculated by last menstrual period and early dating scan.
3. Parity 0–4.

Exclusion Criteria:

1. Mitral stenosis previously corrected with surgical intervention.
2. Prosthetic mitral valve replacement.
3. Patients with medical disorders like anemia, hypertension, diabetes mellitus.

Data collection procedure: A proforma was specifically designed containing demography of the patient to record findings of this study. One hundred and thirty five cases of mitral stenosis fulfilling the inclusion criteria were recruited from outdoor and labor ward of obstetric and gynecology department Nishtar Hospital Multan. Study was conducted with permission of ethical committee of institution. After taking an informed consent, detailed medical and obstetrical history including general physical examination, pericardial examination and abdominal examination was done under supervision of consultant gynecologist having 5 years post fellowship experience. Investigations like obstetrical ultrasonography and echocardiogram were done to see fetal well being and maternal condition. Patients were monitored till delivery and outcome variable i.e. congestive heart failure, preterm delivery and IUGR were noted on the proforma by the researcher along with demography of the patient. Final outcome was measured at the end of delivery.

Data Analysis: Data were entered and analyzed by SPSS version 10. Descriptive statistics were used to calculate mean±SD for gestational age and birth weight of the fetus. Frequencies and percentages were calculated for fetomaternal outcome associated with mitral stenosis in pregnancy i.e. congestive heart failure, parity, preterm delivery and IUGR.

Effect modifiers like age, gestational age and parity were controlled by stratification and chi-square test was applied to see effect of these outcome variables. p-value ≤ 0.05 was taken as significant.

RESULTS

In present study, there were 135 patients with mild to moderate mitral stenosis evaluated for fetomaternal outcome. Mean gestational age was 37.04±2.74 weeks. Mean age of mothers was 29.09±4.43 years (Table 6) and age range was 18–40 years. There were 10(7.4%) women of the age of ≤ 20 years, 9(6.7%) women between 21 to 25 years, 88(65.2%) women between 26 to 30 years, 15(11.1%) women between 31 to 35 years, and 13(9.6%) women between 36 to 40 years as shown in Table 1.

There were 39(28.9%) primigravidae, 13(9.6%) nullipara, 58(43%) primipara and 25(18.5%) women of para 2–4 (Table 2).

There were 23(17.0%) preterm deliveries, and 112 (83.0%) term deliveries (Table 3).

Regarding maternal outcome, congestive heart failure was observed in 43 patients (31.9%) as shown in Table No.4 and fetal outcome showed preterm deliveries in 23 (17.0%) and intrauterine growth restriction 30(22.2%) cases (Table 5).

Out of the total 10 patients ≤ 20 years, 1(10%) had congestive heart failure, 2(20%) had preterm delivery and 3(30%) had intrauterine growth restriction. Out of the total 9 patients between 21–25 years, 6(66.7%) had congestive heart failure, 4(44.4%) had preterm delivery and 0(0%) had intrauterine growth restriction. Out of the total 88 patients between 26–30 years, 28(31.8%) congestive heart failure, 11(12.5%) had preterm delivery and 20(22.7%) had intrauterine growth restriction. Out of the total 15 patients between 31–35 years, 5(33.3%) had congestive heart failure, 5(33.3%) had preterm delivery and 4(26.7%) had intrauterine growth restriction. Out of the total 13 patients between 36–40 years, 3(23.1%) had congestive heart failure, 1(7.7%)

had preterm delivery and 3(23.1%) had intrauterine growth restriction as shown in Table No. 10. Age had no significant effect on occurrence of CHF between age groups (p=0.64). Preterm delivery was significantly high in age group 26–30 years (p=0.036). There was no significant difference among age groups regarding IUGR (p=0.165).

Out of the total 39 primigravida, 12(30.8%) had congestive heart failure, 7(17.9%) had preterm delivery and 8(20.5%) had intrauterine growth restriction. Out of the total 13 nullipara, 4(30.8%) had congestive heart failure, 3(23.1%) had preterm delivery and 1(7.7%) had intrauterine growth restriction. Out of the total 58 primipara, 15(25.9%) congestive heart failure, 11(18.9%) had preterm delivery and 12(20.7%) had intrauterine growth restriction. Out of the total 25 Para 2–4, 12(48%) had congestive heart failure, 2(8%) had preterm delivery and 9(36%) had intrauterine growth restriction (Table 8).

Parity had no significant effect on the occurrence of CHF (p=0.172), preterm delivery (p=0.432) and IUGR (p=0.288).

Out of the total 23 pregnancies < 37 weeks gestation, 1(4.4%) had congestive heart failure, 23(100%) had preterm delivery and 1(4.4%) had intrauterine growth restriction. Out of the total 112 term pregnancies, 42(37.5%) had congestive heart failure, 0(0%) had preterm delivery and 29(25.9%) had intrauterine growth restriction (Table 9).

Gestational age had no significant effect on the occurrence of CHF (p=0.255) and IUGR (p=0.534). Preterm deliveries were significantly more (p<0.0001) in gestational age < 37 weeks.

Table 1: Age Distribution of the patients (n=135)

Age (in years)	n	%age
≤ 20	10	7.4
21 – 25	9	6.7
26 – 30	88	65.2
31 – 35	15	11.1
36 – 40	13	9.6
Total	135	100%

Table 2: Parity distribution of patients (n=135)

Parity	n	%age
Primigravida	39	28.9
Nullipara	13	9.6
Primipara	58	43.0
Para 2–4	25	18.5
Total	135	100%

Table 3: Gestational age distribution of patients (n=135)

Gestation	n	%age
Preterm pregnancy (<37 weeks)	23	17.0
Term pregnancy	112	83.0
Total	135	100%

Table 4: Maternal Outcome (n=135)

Congestive heart failure	n	%age
Yes	43	31.9
No	92	68.1
Total	135	100

Table 5: Fetal Outcome

Variable	n	%age
Preterm delivery (<37 weeks)	23	17.0
Intrauterine growth restriction	30	22.2

Table 6: Descriptive Statistics

Variable	Mean ± S.D.
Age (in years)	29.09±4.43
Gestational age (in weeks)	37.04±2.74

Table 7: Age distribution of the patients in relation to outcome

Age (years)	n	Outcome (Maternal & Fetal)					
		Congestive heart failure	p-value	Preterm delivery	p-value	Intrauterine growth restriction	p-value
≤ 20	10	1(10%)	p=0.064	2(20%)	p=0.036	3(30%)	p=0.165
21–25	9	6(66.7%)		4(44.4%)		0(0%)	
26–30	88	28(31.8%)		11(12.5%)		20(22.7%)	
31–35	15	5(33.3%)		5(33.3%)		4(26.7%)	
36–40	13	3(23.1%)		1(7.7%)		3(23.1%)	
Total	135	43		23		30	

Table 8: Parity distribution of the patients in relation to outcome

Parity	n	Outcome (Maternal & Fetal)					
		Congestive heart failure	p-value	Preterm delivery	p-value	Intrauterine growth restriction	p-value
Primi-gravida	39	12(30.8%)	p = 0.172	7(17.9%)	p = 0.432	8(20.5%)	p = 0.288
Nullipara	13	4(30.8%)		3(23.1%)		1(7.7%)	
Primipara	58	15(25.9%)		11(18.9%)		12(20.7%)	
Para 2–4	25	12(48%)		2(8%)		9(36%)	
Total	135	43		23		30	

Table 9: Gestational age distribution of the patients in Relation to Outcome

Gestation (in weeks)	n	Outcome (Maternal & Fetal)					
		Congestive heart failure	p-value	Preterm delivery	p-value	Intrauterine growth restriction	p-value
< 37	23	1(4.4%)	p = 0.255	23(100%)	p < 0.0001	1(4.4%)	p = 0.534
37 and more	112	42(37.5%)		0(0%)		29(25.9%)	
Total	**135**	**43**		**23**		**30**	

DISCUSSION

Heart diseases are the most important non obstetrical causes of maternal deaths during pregnancy. Pregnant patient with heart disease is a unique challenge to the obstetrician, dealing with high risk pregnancies and requires a thorough understanding

of the impact of pregnancy on the haemodynamic response to the patient's cardiac lesion. The prevalence of pregnancy with rheumatic heart disease has decreased in developed countries in last two decades. Rheumatic heart disease is still the leading cause of death due to heart disease in young woman in the developing world.

Women with valvular heart disease have an increased risk of adverse outcomes in pregnancy. Mitral stenosis is the most common, potentially lethal heart condition in pregnancy. Maternal risks are increased with severity of the lesion. Pregnant women with valvular heart disease have been reported significantly higher incidence of adverse fetomaternal outcome like congestive heart failure, preterm delivery, and IUGR. An increased incidence of congestive heart failure in patients with valvular heart disease is not surprising owing to the marked hemodynamic changes normally occurring during gestation. Perinatal outcome was also more adverse in the valvular heart disease as moderate and severe mitral stenosis have a clear effect on fetal outcomes.

Present study was conducted to find fetomaternal outcome of pregnancy in case of mild–moderate mitral stenosis. Age is an important factor because complications are associated with advanced age. Mean age of mothers was 29.09±4.43 years. Majority of the patients 88(65.2%) were between 26 to 30 years of age. Congestive heart failure was observed in 43 patients (31.9%), preterm deliveries in 23(17%) and intrauterine growth restriction in 30(22.2%) cases. Almost similar results have been observed in national and international literature.

Afshan Hameed et al **p-value** [23] in a case-control study comparing women who had mitral stenosis with well matched controls found an increased incidence of preterm delivery (28% in moderate stenosis v 6% in controls, 44% in severe stenosis v 11% in controls) and intrauterine growth restriction (27% in moderate stenosis v 0% in controls, 33% severe stenosis v 0% in controls). Regarding maternal outcome, congestive heart failure in 11% (2/19) cases as compared to 10% (0/19) controls in mild stenosis (p=0.5) while in moderate patients 61%(11/18) cases versus 0%(0/18) controls had CHF (p=0.01).

Nada Salih Ameen and Nawfal Fawzi Anwer have reported that mild mitral lesion revealed congestive heart failure 0%(0/45), preterm deliveries 13.3%(6/45), in moderate mitral lesion congestive heart failure 37.5%(3/8), and preterm deliveries 12.5%(1/8) and in severe mitral lesion congestive heart failure 69.2%(9/13) and preterm deliveries 15.4%(2/13).

Malhotra M et al[5] have evaluated maternal and fetal outcome in valvular heart disease and found congestive heart failure (5.1% vs. 0%, P<0.001) in cases and controls respectively. Perinatal outcome was also more adverse in the valvular heart disease group than in the control group, with increased preterm delivery rate (48.3% vs. 20.5%) and reduced birth weight (2434±599 g vs. 2653±542 g; P<0.001).

Tasnim Tahira and Sumera Tahir[90] assessed pregnancy outcome in cardiac disease. In their study 50 patients (67.6%) were in 20-25 years. Mitral stenosis was the most common lesion present in 40 patients (60.6%). Preterm delivery was 18.9% and there were 18% SGA babies. Stillbirth was in 2 patients (3%).

Syeda Batool Mazhar and Gul-e-Irum[12] evaluated fetomaternal outcome in pregnancy with cardiac disease. In their study 28(65.3%) had rheumatic heart disease and mitral valve disease was the commonest. The mean age was 27.50±5.17 years. Six infants (14.3%) had intrauterine growth restriction, 2(4.8%) perinatal deaths occurred due to prematurity while there was 1(2.4%) intrauterine death.

Farhana Asghar and Hina Kokab[4] evaluated outcome of pregnancy complicated by heart disease. Rheumatic heart disease was the common etiology (66%) and mitral valve was involved in all cases in their study. In 42% cases mitral stenosis was the isolated lesion. Congestive cardiac failure was observed in 10(21.2%) patients and preterm delivery in 7 patients (14%).

Tayyiba Wasim et al[24] evaluated foetomaternal outcome of pregnancy with cardiac disease in five year study. Majority of patients were young age, 102 patients were less than 30 years of age out of 160 (63.75%). 55 were primigravida and 65% were diagnosed with cardiac lesions during pregnancy. Seventy five patients were para 2-4 and rest had more than 4 babies. Thirty six percent patients were diagnosed to have cardiac lesions for the first time during pregnancy. Acquired valvular heart defects were found in 132 (82%) patients with mitral stenosis being the commonest lesion (55%). Pre-maturity was found 20(14%), foetal death (IUGR + Foetal distress) 10(7%). Ten cases (6.25%) of pregnant peripartum cardiomyopathy patients were seen. Six mothers (3.8%) expired in the 5 year study period.

Syeda Sayeeda et al[25] conducted a two years study on pregnant women with cardiac disease in a tertiary care centre at Bangladesh. The incidence of IUGR was 19.75% and 17.5% delivered at preterm.

Akhter N et al[26] evaluated maternal and fetal outcome in valvular heart disease in pregnancy in a multicenter prospective study carried out over a period of 5 years at Bangladesh. The incidence of preterm birth and small for gestational age newborn was 11.69% and 13.36% respectively. There was one (1.67%) maternal death. They concluded that

pregnancy in women with valvular heart disease is associated with remarkable unfavourable effect on maternal and fetal outcome which are related to severity of disease.

In one study Nargis Akhter et al[27] found outcome of pregnancy in women with mitral stenosis. Preterm deliveries were 6(12%).Small for gestational age babies were 7(14%). Stillbirth was 1 (2%) and there were 4(8%) cases of atrial fibrillation.

Lin JH et al[28] revealed 18 of preterm labor medically (28%, 18/65), 4 of fetal growth restriction (6%, 4/65) in groups of NYHA class III and IV in their study. They concluded that pregnant women with rheumatic heart disease of moderate-severe mitral stenosis, severe pulmonary hypertension and atrial fibrillation are at high risk of heart failure.

Naila Yasmeen et al[29] evaluated feto-maternal outcome in patients with cardiac disease in pregnancy. They found cardiac failure in 6(15%) patients. Preterm labour was seen in 10(25%) patients. 10 (25%) babies were growth restricted.

CONCLUSION

- Among the complications, congestive heart failure had a high frequency of 31.9% followed by intrauterine growth restriction 22.2% and preterm deliveries 17%.
- Preterm delivery in patients with mitral stenosis was significantly high in age group 26–30 years.

REFERENCES

1. Montoya ME, Karnath BM, Ahmad M. Endocarditis during pregnancy. South Med J 2003;96:1156-7.
2. Dobbenga-Rhodes YA, Preive AM. Assessment and evaluation of women with cardiac disease during pregnancy. J Perinant Neonatal Nurs. 2006;20: 295-302.
3. Karamermer Y, Roos-Hesselink JW. Mitral stenosis before, during and after pregnancy. ICRJ. 2007;1(1):2-5.
4. Asghar F, Kokab H. Evaluation and outcome of pregnancy complicated by heart disease. J Pak Med Assoc. 2005;55:416-9.
5. Malhotra M, Sharma JB, Tripathi R, Arora P. Maternal and fetal outcome in valvuler heart disease. Int J Gynaecol Obstet. 2004; 84:11-6.
6. Presbitero P, Boccuzzi GG, de Groot CJM, Roos-Hesselink JW. Pregnancy and heart disease. In: Camm AJ, Lüscher TF, Serruys PW, editors. The ESC textbook of cardiovascular medicine. Oxford: Blackwell Publishing; 2006. p. 607-24.
7. Abbas AE, Lester SJ, Connolly H. Pregnancy and cardiovascular system. Int J Cardiology. 2005;98:179-89.
8. Ueland K. Intrapartum management of cardiac patient. Clin Perinatol. 2001;8:155-62.
9. Hunter S, Robson SC. Adaption of maternal heart disease in pregnancy. Brit Heart J. 1998;68:540-3.
10. Siu SC, Semer M, Harrison DA. Risk and predictors for pregnancy related complications in women with heart disease. Circulation. 1999;102:278-9.
11. Siu SC, Semer M, Colman JM. Prospective multicenter study of pregnancy outcome in women with heart disease. Circulation. 2001;104:515-21.
12. Mazhar SB, Gul-e-Irum. Fetomaternal outcome in pregnancy with cardiac disease. J Coll Physicians Surg Pak. 2005;15(8):476-80.
13. Reimold SC, Rutherford JD. Clinical practice. Valvular heart disease in pregnancy. N Engl J Med. 2003;349(1):52-9.
14. Barbosa PJ, Lopes AA, Feitosa GS, Almeida RV, Silva RM, Brito JC, et al. Prognostic factors of rheumatic mitral stenosis during pregnancy and puerperium. Arq Bras Cardiol. 2000;75:215-24.
15. Siu SC, Colman JM. Heart disease and pregnancy. Heart. 2001;85:710-5.
16. Weiss BM. Managing severe mitral valve stenosis in pregnant patients--percutaneous balloon valvuloplasty, not surgery, is the treatment of choice. J Cardiothorac Vasc Anesth. 2005;19: 277-8.
17. Nobuyoshi M, Arita T, Shirai S, Hamasaki N, Yokoi H, Iwabuchi M, et al. Percutaneous balloon mitral valvuloplasty: a review. Circulation. 2009;119:e211-9.
18. de Souza JA, Martinez EE Jr, Ambrose JA, Alves CM, Born D, Buffolo E, et al. Percutaneous balloon mitral valvuloplasty in comparison with open mitral valve commissurotomy for mitral stenosis during pregnancy. J Am Coll Cardiol. 2001;37:900-3.
19. 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.
20. Presbitero P, Somerville J, Stone R, Aruta E, Spiegelhatter D, Rabajdi F. Pregnancy in cyanotic congenital heart disease. Outcome of mother and fetus. Circulation. 1994;89:2673-6.
21. Silversides CK, Colman JM, Sermer M, Siu SC. Cardiac risk in pregnant women with rheumatic mitral stenosis. Am J Cardiol. 2003;91:1382-5.
22. Trinidad D, Cox RA. Heart diseases during pregnancy. P R Health Sci J. 2006;25:259-65.
23. Hameed A, Karaalp IS, Tummala PP, Wani OR, Canetti M, Akhter MW, et al. The effect of valvular heart disease on maternal and fetal outcome of pregnancy. J Am Coll Cardiol. 2001;37:893-9.
24. Wasim T, Amer W, Majrroh A, Siddiq S. Foetomaternal outcome of pregnancy with cardiac disease. J Pak Med Assoc. 2008;58:175-8.
25. Sayeeda S, Wahid F, Begum F, Zaman MM. A two years study on pregnant women with cardiac disease in a tertiary care centre. Bangladesh J Obstet Gynaecol. 2008;23(1):8-14.
26. Akhter N, Rahman F, Salman M, Anam K, Begum N, Naher S, et al. Valvular heart disease in pregnancy: maternal and fetal outcome. Mymensingh Med J. 2011;20(3):436-40.
27. Akhter N, Rahman F, Salman M, Anam K, Akther P, Naher SH, et al. Outcome of pregnancy in women with mitral stenosis. University Heart Journal. 2010;6(2):74-7.
28. Lin JH, Ling WW, Liang AJ. Pregnancy outcome in women with rheumatic heart disease. Zhonghua Fu Chan Ke Za Zhi. 2007;42(5):315-9.
29. Yasmeen N, Aleem M, Iqbal N. Feto-maternal outcome in patients with cardiac disease in pregnancy. Pak J Med Health Sci. 2011;5(4):748-51.