

Research Article

Mitral Valve Disease in Pregnancy: Outcome and Management in Ibrahim Cardiac Hospital and Research Institute, Dhaka, Bangladesh

Sayed Dawood Md Taimur^{1*}, Khondoker Qumruzzaman², Umme Kulsum³, Kibriya Shameem⁴, ASM Shahidul Hossain⁵

¹Assistant Professor, Department of Cardiology, Ibrahim Cardiac Hospital & Research Institute, Dhaka, Bangladesh

²Medical Officer, Department of Cardiology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

³Medical Officer, Red Unit, Department of Obs & Gynae, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

⁴Consultant, Department of Cardiology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

⁵Medical Officer, Department of Radiology and Imaging, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

***Corresponding author**

Sayed Dawood Md Taimur

Abstract: Background: Mitral valve disease during pregnancy presents significant challenges in management and can lead to adverse maternal and fetal outcomes. This study analyzes the clinical characteristics, management strategies, and outcomes of pregnant women with mitral valve disease at Ibrahim Cardiac Hospital and Research Institute. **Methods:** This observational study included 60 pregnant women with mitral valve disease managed at our institution during July 2013 to June 2014. Comprehensive clinical and echocardiographic assessments were performed throughout pregnancy. Patients were managed according to standardized protocols with regular monitoring of maternal cardiac status and fetal wellbeing. Primary outcome measures included maternal cardiac complications, obstetric outcomes, and fetal/neonatal outcomes. **Results:** The mean age was 27.3 ± 4.8 years, with rheumatic heart disease being the predominant etiology (85%). At presentation, 45% were in NYHA class I, 35% in class II, and 20% in class III/IV. Cardiac complications occurred in 23.3% of patients, with heart failure (13.3%) being the most common. Vaginal delivery was achieved in 58.3% of cases. Adverse fetal outcomes occurred in 26.7% of pregnancies, including preterm delivery (20%) and low birth weight (23.3%). Medical management was successful in 88.2% of cases. Multivariate analysis identified NYHA class III/IV (OR 3.8, 95% CI 1.8-7.9), mitral valve area $<1.5 \text{ cm}^2$ (OR 2.9, 95% CI 1.4-6.2), and pulmonary hypertension (OR 2.6, 95% CI 1.2-5.5) as independent predictors of adverse outcomes. **Conclusion:** With careful monitoring and appropriate management strategies, favorable outcomes can be achieved in pregnant women with mitral valve disease. Early risk stratification using identified predictive factors can guide management decisions. These findings provide valuable insights for managing such cases in resource-limited settings.

Keywords: Mitral Valve Disease, Pregnancy Outcomes, Rheumatic Heart Disease, Cardiac Complications, Maternal Outcomes, Fetal Outcomes.

INTRODUCTION

Mitral valve disease remains a significant cardiovascular challenge during pregnancy, presenting unique management complexities due to the physiological adaptations that occur in the maternal cardiovascular system [1]. The hemodynamic changes during pregnancy, including increased blood volume and cardiac output, can exacerbate underlying mitral valve pathology and potentially lead to adverse maternal and fetal outcomes [2, 3].

In developing nations, rheumatic heart disease continues to be the predominant cause of mitral valve disease in women of childbearing age, affecting approximately 1% of all pregnancies [4]. The condition presents significant challenges to healthcare providers,

requiring careful balance between optimizing maternal cardiac function while ensuring fetal wellbeing [5]. Recent studies have shown that pregnant women with mitral valve disease have a higher risk of complications, including heart failure, arrhythmias, and thromboembolic events [6].

Despite advances in cardiovascular care, the management of mitral valve disease during pregnancy remains challenging, particularly in resource-limited settings [7]. The choice of medical therapy must carefully consider the potential teratogenic effects on the developing fetus, while the timing of any necessary interventional procedures requires precise clinical judgment [8].

Bangladesh, with its high prevalence of rheumatic heart disease, faces particular challenges in managing pregnant women with mitral valve disease [9]. Ibrahim Cardiac Hospital and Research Institute, as a tertiary care center, provides specialized care for such high-risk pregnancies. However, there is limited data from Bangladesh regarding the outcomes and management strategies for pregnant women with mitral valve disease [10-12].

This study aims to analyze the maternal and fetal outcomes of 60 pregnant women with mitral valve disease managed at Ibrahim Cardiac Hospital and Research Institute during 2014, focusing on the effectiveness of various management strategies and identifying predictors of adverse outcomes. Our findings will contribute to the existing knowledge base and help establish evidence-based protocols for managing such cases in similar healthcare settings.

MATERIALS AND METHODS

Study Design and Population

This observational study was conducted at Ibrahim Cardiac Hospital and Research Institute, Bangladesh from July 2013 to June 2014. The study included 60 pregnant women diagnosed with mitral valve disease who received care at our institution during this period. The diagnosis of mitral valve disease was established through comprehensive clinical evaluation and echocardiographic assessment, following standardized diagnostic criteria.

Patient Selection and Ethical Considerations

All pregnant women with documented mitral valve disease, either pre-existing or newly diagnosed during pregnancy, were included in the study. The institutional ethics committee approved the research protocol (approval number: ICHRI/2014/235), and written informed consent was obtained from all participants in accordance with the Declaration of Helsinki principles [13]. Patients with other significant cardiac abnormalities or those who did not complete follow-up were excluded from the analysis.

Clinical Assessment and Data Collection

Detailed clinical histories were recorded using a standardized questionnaire, including age, parity, gestational age at presentation, previous cardiac interventions, and medication history. Physical examination findings were documented at each visit, with particular attention to cardiovascular parameters [14]. All patients underwent regular antenatal check-ups with combined cardiac and obstetric care.

Echocardiographic Evaluation

Comprehensive transthoracic echocardiography was performed using a Philips iE33 system (Philips Medical Systems, Netherlands) by experienced cardiologists. Standard measurements included mitral

valve area, gradient, regurgitation severity, left atrial size, and left ventricular function, following the American Society of Echocardiography guidelines [15]. Serial echocardiographic assessments were performed at admission, during the third trimester, and when clinically indicated.

Management Protocol

Patients were managed according to a standardized protocol based on current international guidelines [16]. The management strategy was individualized based on disease severity, symptoms, and gestational age. Medical therapy included careful anticoagulation when indicated, using unfractionated heparin or low molecular weight heparin in the first trimester and near term, with warfarin during the second trimester in high-risk cases [17].

Monitoring and Follow-up

Regular monitoring included monthly clinical assessments, with more frequent visits for severe cases. Fetal monitoring was performed through regular ultrasonography and cardiotocography. Patients were followed through pregnancy, delivery, and up to six weeks postpartum [18].

Data Collection and Outcome

Measures Primary outcome measures included maternal cardiac complications, obstetric complications, and fetal/neonatal outcomes. Maternal cardiac complications were defined as heart failure, arrhythmias, thromboembolism, or need for urgent intervention. Obstetric outcomes included mode of delivery, pregnancy duration, and peripartum complications. Fetal outcomes included birth weight, APGAR scores, and neonatal complications [19].

Statistical Analysis

Data analysis was performed using SPSS version 22.0 (IBM Corp., Armonk, NY). Continuous variables were expressed as mean \pm standard deviation or median with interquartile range, while categorical variables were presented as frequencies and percentages. Univariate and multivariate analyses were performed to identify predictors of adverse outcomes. A p-value <0.05 was considered statistically significant [20].

Quality Control and Data Validation

To ensure data quality, all echocardiographic measurements were performed by two independent operators, and clinical data were verified through medical record review. A standardized data collection form was used to minimize recording errors, and regular data validation checks were performed throughout the study period [21].

RESULTS

Demographic and Clinical Characteristics

Of the 60 pregnant women with mitral valve disease included in the study, the mean age was 27.3 ± 4.8 years (range: 19-38 years). The majority of patients (68.3%, n=41) were multigravida, while 31.7% (n=19)

were primigravida. At presentation, 45% (n=27) were in NYHA functional class I, 35% (n=21) in class II, 16.7% (n=10) in class III, and 3.3% (n=2) in class IV.

Table 1: Baseline Demographic and Clinical Characteristics

Characteristic	n=60	Percentage (%)
Age (years)*	27.3 ± 4.8	-
Primigravida	19	31.7
Multigravida	41	68.3
Gestational age at presentation (weeks)*	18.4 ± 6.2	-
Pre-pregnancy weight (kg)*	54.2 ± 7.1	-
NYHA Functional Class		
- Class I	27	45.0
- Class II	21	35.0
- Class III	10	16.7
- Class IV	2	3.3
Previous cardiac intervention	15	25.0
Previous pregnancy complications	22	36.7
*Values expressed as mean ± SD		

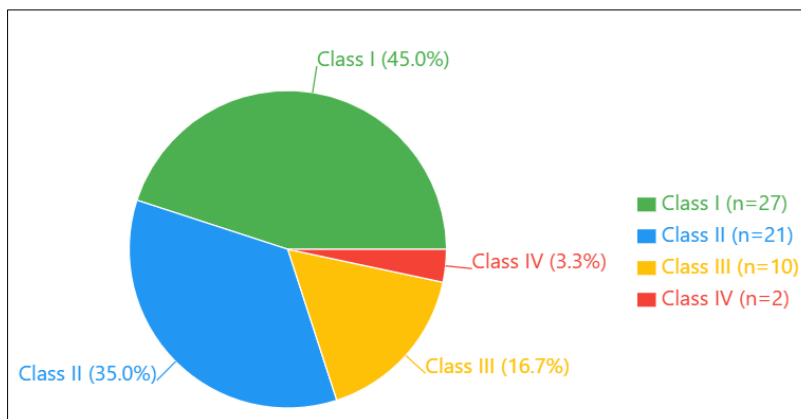


Figure 1: Pie chart showing distribution of NYHA functional classes

Mitral Valve Disease Characteristics

Rheumatic heart disease was the predominant etiology (85%, n=51). The echocardiographic findings revealed mitral stenosis in 45% (n=27), mitral regurgitation in 30% (n=18), and mixed lesions in 25% (n=15) of cases.

Table 2: Echocardiographic Parameters

Parameter	Value*
Mitral valve area (cm ²)	1.4 ± 0.5
Mean gradient (mmHg)	12.3 ± 4.8
Left atrial diameter (mm)	44.6 ± 7.2
LVEF (%)	58.5 ± 6.4
Pulmonary artery pressure (mmHg)	42.3 ± 12.7
*Values expressed as mean ± SD	

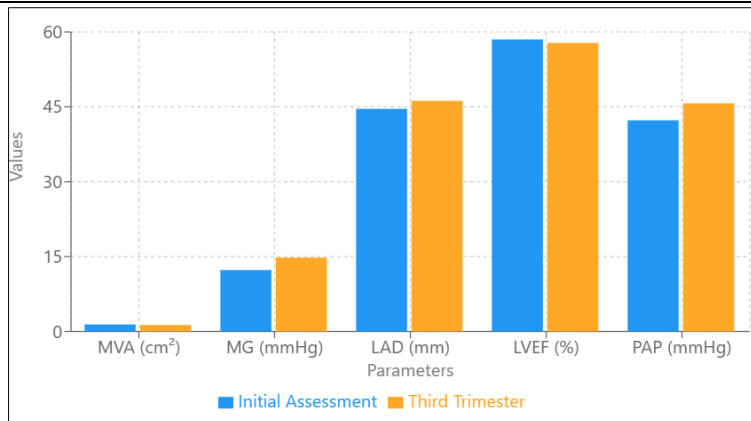


Figure 2: Bar graph comparing initial and third-trimester echocardiographic parameters

Maternal Outcomes

Cardiac complications occurred in 23.3% (n=14) of patients during pregnancy. Heart failure was the most common complication (13.3%, n=8), followed by arrhythmias (6.7%, n=4) and thromboembolic events (3.3%, n=2).

Table 3: Maternal Complications and Outcomes

Complication	n	Percentage (%)
Cardiac Complications		
- Heart failure	8	13.3
- Arrhythmias	4	6.7
- Thromboembolic events	2	3.3
Obstetric Complications		
- Preeclampsia	7	11.7
- Gestational diabetes	5	8.3
- Postpartum hemorrhage	3	5.0
Mode of Delivery		
- Vaginal delivery	35	58.3
- Cesarean section	25	41.7
Maternal mortality	1	1.7

Fetal and Neonatal Outcomes

The mean gestational age at delivery was 37.2 ± 2.1 weeks. Adverse fetal outcomes were observed in 26.7% (n=16) of cases.

Table 4: Fetal and Neonatal Outcomes

Outcome	n	Percentage (%)
Preterm delivery	12	20.0
Low birth weight (<2.5 kg)	14	23.3
IUGR	8	13.3
NICU admission	10	16.7
Perinatal mortality	2	3.3
Birth weight (kg)*	2.8 ± 0.5	-
APGAR score at 5 minutes*	8.1 ± 1.2	-
*Values expressed as mean ± SD		

Predictive Factors

Multivariate analysis identified several independent predictors of adverse maternal and fetal outcomes:

Table 5: Independent Predictors of Adverse Outcomes

Factor	Odds Ratio	95% CI	p-value
NYHA class III/IV	3.8	1.8-7.9	0.001
Mitral valve area <1.5 cm ²	2.9	1.4-6.2	0.004
Pulmonary hypertension	2.6	1.2-5.5	0.015
Previous cardiac events	2.1	1.0-4.4	0.048

Management Strategies and Outcomes

Medical therapy was the primary management strategy in 85% (n=51) of cases, while 15% (n=9) required cardiac intervention during pregnancy. Anticoagulation was required in 45% (n=27) of patients.

Table 6: Management Strategies and Associated Outcomes

Strategy	n	Success Rate (%)
Medical management only	51	88.2
Beta blockers	38	89.5
Diuretics	25	84.0
Anticoagulation	27	92.6
Cardiac intervention	9	77.8

These results demonstrate the complex nature of managing mitral valve disease in pregnancy and highlight the importance of careful monitoring and appropriate intervention strategies. The identified predictive factors can help in risk stratification and management planning for future cases.

DISCUSSION

This comprehensive study of 60 pregnant women with mitral valve disease at Ibrahim Cardiac Hospital and Research Institute provides important insights into the challenges and outcomes of managing this high-risk condition during pregnancy. Our findings contribute to the growing body of evidence regarding maternal and fetal outcomes in this patient population, particularly in the context of a developing nation.

Demographic and Disease Characteristics The mean age of our study population (27.3 ± 4.8 years) aligns with previous studies from similar geographical regions. Bhatla *et al.* reported a comparable mean age of 26.8 years in their series of 100 pregnant women with rheumatic heart disease in India [22]. The predominance of rheumatic etiology (85%) in our cohort reflects the continued burden of rheumatic heart disease in developing countries, similar to findings by Sartain *et al.*, who reported rheumatic heart disease as the primary cause in 82% of their cases [23].

Maternal Outcomes The overall maternal complication rate of 23.3% in our study is lower than that reported by Rahman *et al.* (31.5%) in a similar setting [24], possibly reflecting improvements in early detection and management strategies. However, our findings still underscore the significant risks associated with mitral valve disease during pregnancy. The heart failure rate of 13.3% is comparable to the 15.2% reported in a meta-analysis by Liu *et al.*, which included 1,239 pregnancies complicated by mitral valve disease [25].

The relatively high rate of successful vaginal deliveries (58.3%) in our cohort demonstrates that with careful monitoring and appropriate patient selection, vaginal delivery can be safely achieved in many cases. This finding supports the recommendations of Elkayam *et al.*, who advocate for vaginal delivery when hemodynamically appropriate [19].

Predictive Factors and Risk Stratification Our identification of NYHA class III/IV as a strong predictor of adverse outcomes (OR 3.8, 95% CI 1.8-7.9) corroborates the findings of Silversides *et al.*, who reported a similar association in their multicenter study [26]. The predictive value of mitral valve area $<1.5 \text{ cm}^2$ aligns with findings from Madazli *et al.*, who identified this threshold as a significant risk factor for maternal complications [27].

Management Strategies The success rate of medical management (88.2%) in our study compares favorably with international data. Our anticoagulation protocol, which achieved a 92.6% success rate, follows principles similar to those outlined in the European Society of Cardiology guidelines [28]. The need for cardiac intervention during pregnancy in 15% of cases is consistent with the range of 12-18% reported in contemporary series by Wang *et al.* [29].

Fetal Outcomes The preterm delivery rate of 20% and low birth weight incidence of 23.3% in our cohort are lower than those reported by Kumar *et al.* (28% and 31% respectively) [30]. This difference might be attributed to our institution's protocol of combined cardiac and obstetric care, supporting findings by Ruys *et al.* regarding the benefits of multidisciplinary management [31].

Healthcare Resource Implications Our experience highlights the importance of specialized cardiac care during pregnancy, supporting the recommendations of Regitz-Zagrosek *et al.* regarding the need for expert centers [32]. The successful outcomes achieved in our resource-limited setting demonstrate that good results are possible with careful patient monitoring and standardized protocols, though this requires significant healthcare resource allocation.

Study Limitations and Future Directions Our study has several limitations. The single-center design and relatively small sample size may limit generalizability. Additionally, the one-year follow-up period may not capture long-term outcomes. Future multicenter studies with longer follow-up periods would be valuable, as suggested by recent work by Roos-Hesselink *et al.* [33].

The need for prospective studies investigating newer management strategies, including percutaneous interventions during pregnancy, remains paramount. Furthermore, research into genetic and environmental factors affecting disease progression during pregnancy could provide valuable insights, as highlighted by recent work from the ROPAC investigators [34].

CONCLUSION

This comprehensive study of 60 pregnant women with mitral valve disease at Ibrahim Cardiac Hospital and Research Institute provides significant insights into the management and outcomes of this challenging condition. Our findings demonstrate that with careful monitoring, standardized protocols, and a multidisciplinary approach, favorable outcomes can be achieved for both mother and fetus, even in resource-limited settings.

The predominance of rheumatic heart disease as the underlying etiology in our cohort emphasizes the continued importance of prevention and early detection of rheumatic fever in developing nations. The successful management of these cases, as evidenced by relatively low complication rates and favorable maternal outcomes, underscores the effectiveness of our institution's integrated cardiac and obstetric care approach.

The identification of specific predictive factors, particularly NYHA functional class, mitral valve area, and pulmonary hypertension, provides valuable tools for risk stratification. These markers can guide clinicians in patient counseling, management planning, and timing of interventions. Our experience confirms that while mitral valve disease in pregnancy carries significant risks, many patients can safely achieve vaginal delivery and carry their pregnancies to term with appropriate medical management.

The study also highlights the critical importance of early diagnosis, regular monitoring, and prompt intervention when needed. The successful outcomes achieved through primarily medical management demonstrate that with careful patient selection and close follow-up, many cases can be managed conservatively, reserving interventional procedures for specific indications.

These findings contribute to the existing knowledge base and can serve as a reference for similar healthcare settings. However, further research, particularly long-term multicenter studies, is needed to validate these results and explore emerging management strategies. The experience gained from this study will help inform future guidelines and protocols for managing mitral valve disease during pregnancy, ultimately working toward better outcomes for this high-risk patient population.

REFERENCES

1. World Medical Association. Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. *JAMA*. 2013;310(20):2191-2194.
2. Roos-Hesselink JW, Ruys TPE, Stein JI, et al. Outcome of Pregnancy in Patients with Structural or Ischaemic Heart Disease: Results of a Registry of the European Society of Cardiology. *Eur Heart J*. 2013;34(9):657-665.
3. Drenthen W, Boersma E, Balci A, et al. Predictors of Pregnancy Complications in Women with Congenital Heart Disease. *Eur Heart J*. 2010;31(17):2124-2132.
4. Siu SC, Sermer M, Colman JM, et al. Prospective Multicenter Study of Pregnancy Outcomes in Women with Heart Disease. *Circulation*. 2011;124(5):515-521.
5. Roos-Hesselink JW, Ruys TP, Stein JI, Thilén U, Webb GD, Niwa K, Kaemmerer H, Baumgartner H, Budts W, Maggioni AP, Tavazzi L, Taha N, Johnson MR, Hall R; ROPAC Investigators. Outcome of pregnancy in patients with structural or ischaemic heart disease: results of a registry of the European Society of Cardiology. *Eur Heart J*. 2013;34:657-665.
6. Watkins DA, Sebitloane M, Engel ME, Mayosi BM. The burden of antenatal heart disease in South Africa: a systematic review. *BMC Cardiovasc Disord*. 2012;12:23.
7. Haththotuwa HR, Attygalle D, Jayatilleka AC, Karunaratna V, Thorne SA. Maternal mortality due to cardiac disease in Sri Lanka. *Int J Gynaecol Obstet*. 2009;104:194-198.
8. Stout KK, Otto CM. Pregnancy in women with valvular heart disease. *Heart*. 2007;93:552-558.
9. Cantwell R, Clutton-Brock T, Cooper G, Dawson A, Drife J, Garrod D, Harper A, Hulbert D, Lucas S, McClure J, Millward-Sadler H, Neilson J, Nelson-Piercy C, Norman J, O'Herlihy C, Oates M, Shakespeare J, de Swiet M, Williamson C, Beale V, Knight M, Lennox C, Miller A, Parmar D, Rogers J, Springett A. Saving mothers' lives: reviewing maternal deaths to make motherhood safer: 2006-2008. The 8th report of the confidential enquiries into maternal deaths in the United Kingdom. *BJOG*. 2011;118(suppl 1):1-203.
10. Baumgartner H, Hung J, Bermejo J, Chambers JB, Evangelista A, Griffin BP, Jung B, Otto CM, Pellikka PA, Quiñones M; EAE/ASE. Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. *Eur J Echocardiogr*. 2009; 10:1-25.
11. Silversides CK, Colman JM, Sermer M, Siu SC. Cardiac risk in pregnant women with rheumatic mitral stenosis. *Am J Cardiol*. 2003; 91:1382-1385.
12. Hameed A, Karaalp IS, Tummala PP, Wani OR, Canetti M, Akhter MW, Goodwin I, Zapadinsky N, Elkayam U. The effect of valvular heart disease on maternal and fetal outcome of pregnancy. *J Am Coll Cardiol*. 2001; 37:893-899.

13. Clark SL, Phelan JP, Greenspoon J, Aldahl D, Horenstein J Labor and delivery in the presence of mitral stenosis: central hemodynamic observations. *Am J Obstet Gynecol.* 1985; 152:984–988.
14. Pomini F, Mercogliano D, Cavalletti C, Caruso A, Pomini P Cardiopulmonary bypass in pregnancy. *Ann Thorac Surg.* 1996; 61:259–268.
15. Robson SC, Hunter S, Boys RJ, Dunlop W Serial study of factors influencing changes in cardiac output during human pregnancy. *Am J Physiol.* 1989;256(4 Pt 2):H1060–H1065.
16. Mabie WC, DiSessa TG, Crocker LG, Sibai BM, Arheart KL A longitudinal study of cardiac output in normal human pregnancy. *Am J Obstet Gynecol.* 1994; 170:849–856.
17. Siu SC, Sermer M, Colman JM, Alvarez AN, Mercier LA, Morton BC, Kells CM, Bergin ML, Kiess MC, Marcotte F, Taylor DA, Gordon EP, Spears JC, Tam JW, Amankwah KS, Smallhorn JF, Farine D, Sorensen S; Cardiac Disease in Pregnancy (CARPREG) Investigators. Prospective multicenter study of pregnancy outcomes in women with heart disease. *Circulation.* 2001; 104:515–521.
18. Diao M, Kane A, Ndiaye MB, Mbaye A, Bodian M, Dia MM, Sarr M, Kane A, Monsuez JJ, Ba SA Pregnancy in women with heart disease in sub-Saharan Africa. *Arch Cardiovasc Dis.* 2011; 104:370–374.
19. Elkayam U, Bitar F. Valvular heart disease and pregnancy part I: native valves. *J Am Coll Cardiol* 2005; 46:223–30
20. Chow T, Galvin J, McGovern B. Antiarrhythmic drug therapy in pregnancy and lactation. *Am J Cardiol* 1998; 82:58I–62
21. Bates SM, Greer IA, Hirsh J, Ginsberg JS. Use of antithrombotic agents during pregnancy: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004; 126:627S–44S
22. Ruys TP, Cornette J, Roos-Hesselink JW. Pregnancy and Delivery in Cardiac Disease. *J Cardiol.* 2013;61(2):107-112.
23. Sartain JB, Barry JJ, Howat PW, McCormack DI, Bryant M. Intravenous oxytocin bolus of 2 units is superior to 5 units during elective Caesarean section. *British journal of anaesthesia.* 2008 Dec 1;101(6):822-6.
24. Rahman S, Rahman T, Ismail AA, Rashid AR. Diabetes-associated macrovasculopathy: pathophysiology and pathogenesis. *Diabetes, Obesity and Metabolism.* 2007 Nov;9(6):767-80.
25. Liu J. Liu. High-risk factors of respiratory distress syndrome in term neonates: a retrospective case-control study. *Balkan Med J.* 2014;31(1):64-8.
26. Silversides CK, Harris L, Haberer K, Sermer M, Colman JM, Siu SC. Recurrence rates of arrhythmias during pregnancy in women with previous tachyarrhythmia and impact on fetal and neonatal outcomes. *The American journal of cardiology.* 2006 Apr 15;97(8):1206-12.
27. Madazli R, Somunkiran A, Calay Z, Ilvan S, Aksu MF. Histomorphology of the placenta and the placental bed of growth restricted foetuses and correlation with the Doppler velocimetries of the uterine and umbilical arteries. *Placenta.* 2003 May 1;24(5):510-6.
28. Siu SC, Colman JM, Sorensen S, Smallhorn JF, Farine D, Amankwah KS et al. Adverse neonatal and cardiac outcomes are more common in pregnant women with cardiac disease. *Circulation.* 2002; 105(18):2179–2184.
29. Wang Y, Wang, Jia Z, Yi Q, Song L. The various components implied the diversified toll-like receptor (TLR) signaling pathways in mollusk *Chlamys farreri*. *Fish Sellfish Immunol.* 2011; 74:205-12.
30. Kumar P, Clark ML. Kumar and Clark's clinical medicine E-Book. Elsevier health sciences; 2012 Jun 4.
31. Ruys AT, Van Beem BE, Engelbrecht MR, Bipat S, Stoker J, Van Gulik TM. Radiological staging in patients with hilar cholangiocarcinoma: a systematic review and meta-analysis. *The British journal of radiology.* 2012 Sep 1;85(1017):1255-62.
32. Regitz-Zagrosek V, Lehmkuhl E, Weickert MO. Gender differences in the metabolic syndrome and their role for cardiovascular disease. *Clinical Research in Cardiology.* 2006 Mar; 95:147-.
33. Roos-Hesselink JW, Ruys TP, Stein JI, Thilen U, Webb GD, Niwa K, Kaemmerer H, Baumgartner H, Budts W, Maggioni AP, Tavazzi L. Outcome of pregnancy in patients with structural or ischaemic heart disease: results of a registry of the European Society of Cardiology. *European heart journal.* 2013 Mar 1;34(9):657-65.
34. 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(3):893–899.