http://www.pjbs.org

PJBS

ISSN 1028-8880

Pakistan Journal of Biological Sciences

ANSInet
Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

Pakistan Journal of Biological Sciences 16 (9): 421-425, 2013
ISSN 1028-8880 / DOI: 10.3923/pjbs.2013.421.425

Pregnancy in Mothers with Prosthetic Heart Valves

Rezvanie Salehi, Simin Taghavi, Shahla Imani and Mohamad Goldust
Tabriz University of Medical Sciences, Tabriz, Iran

Abstract: Prosthetic mechanical valves have a high risk condition for patients in pregnancy. The aim of this study was to evaluate the safety of pregnancy in mothers with prosthetic heart valves. In this cross sectional study, we compared incidence of thromboembolic attacks abortion and maternal and fetal complications in 19 patients with prosthetic heart valves. We reviewed medical records, also office visit and follow up of these women for 10 years. Between 10 years we studied 19 patients, 13 had mechanical heart valves with mean ages of 28.2±5.43, 4 cases with bioprosthetic valves with mean age of 25.4±4.12 and 2 cases of valve repaired 27.00±7.07. Seven women were uniparous 8 cases were in second pregnancy, one had 3rd and another one were gravid 4th . There was a mean interval between valve surgery and pregnancy of 7.65±6.07(1-23) years. Dominant underling disease for valve replacement was rheumatic. In conclusion bridge anticoagulation during pregnancy is safe for mother and fetus in women with mechanical heart valves.

Key words: Pregnancy, prosthetic heart valves, fetal outcomes

INTRODUCTION

Prosthetic mechanical valves which require anticoagulation during pregnancy have a high risk condition for patient (Roeder *et al*., 2011). Using of oral anticoagulants during pregnancy is controversial and many studies didn't show any agreement on the most suitable form of treatment for pregnant women, with mechanical prosthetic heart valves, who have a high risk of thromboembolism (Goldust *et al.,* 2013a; Lotti *et al.,* 2013; Suri *et al*., 2011). Warfarin derivatives carry the risk of embryopathy when given between the sixth and the 12th week of pregnancy but this complication can be prevented when heparin is substituted for oral anticoagulants in this period (Goldust *et al*., 2013b; Mohebbipour *et al*., 2012; Sin'kov *et al*., 2011). The risk of warfarin embryopathy with oral anticoagulation when used throughout pregnancy is approximately 6% but the frequency of warfarin embryopathy effect of decrease after replaced by heparin between 6 and 12 weeks' (Goldust *et al*., 2013c, d; McLintock, 2011). Using of heparin in all trimesters without warfarin has a risk of thrombotic attacks for mothers (Walfisch and Koren, 2010). Although, warfarin derivatives are relatively safe for the mother with a lower incidence of valve thrombosis than un-fractionated and low-molecular-weight heparin but carries the risk of embryopathy which is probably dose-dependent (Huisman, 2010; Sadighi *et al*., 2011; Vafaee *et al*., 2012). In the face of valve thrombosis during pregnancy, thrombolysis is the preferable therapeutic option. Bioprostheses and valve repair have a more favorable pregnancy outcome than mechanical prostheses but have high re-operation rate in young women and they do not an ideal alternative (Goldust *et al.,* 2012; Milan *et al*., 2011; Saeed *et al*., 2011). Other risks of prosthetic valves in pregnancy are included with a variety of complications, such as structural failure of the valve, infection, heart failure and bleeding due to anticoagulatio (Quinn *et al*., 2009). Valve thrombosis with the procoagulant state of pregnancy increases the risk of thrombus formation especially among women with first generations of mechanical valves. This risk is potentially a life-threatening complication event and depends upon the type and location of the prosthetic valve, as well as a number of other risk factors. Likes history of a prior thromboembolic event, atrial fibrillation, prosthesis in the mitral position and multiple prosthetic valves (Golfurushan *et al.,* 2011; McLintock *et al.,* 2009; Sadeghpour *et al.,* 2011). The patient should be informed about the risk of life threatening thromboembolic events and a thrombotic stroke exists regardless of the anticoagulant regimen utilized and although risks of fetal loss, bleedings and other complications (Goldust *et al.,* 2011; Martinez-Diaz, 2008). While warfarin seems to offer the best protection against thromboembolic events in women with mechanical heart valves during pregnancy but its freely passes the placenta and so associated with characteristic embryopathy and an increase in late fetal

Corresponding Author: Mohamad Goldust, Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran Tel: 00989111289630 Fax: 0098411336880

deaths and hemorrhagic sequelae (Jeejeebhoy, 2009). Un Fractionated Heparin (UFH) and Low Molecular Weight Heparin (LMWH) do not cross the placenta but require twice daily subcutaneous injections and are associated with higher rates of maternal valve thrombosis and thrombocytopenia (Mohamed, 2009). Other confound problem with heparin are the use of sub-therapeutic dose regimens or poor compliance in many (but not all) reported cases of valve thromboses or thromboembolism (Montavon *et al.,* 2008). The aim of this study was to assess the rate of maternal thrombotic and hemorrhagic complications and pregnancy outcomes and fetal complications in women with prosthetic heart valves in high risk pregnancy who received treatment with enoxaparin during 6 up to 12 of gestational ages week of pregnancy and then on 36 up to 37.

MATERIALS AND METHODS

In this cross sectional study that was conducted from June 2001 till June 2012 in Tabriz Madani hospital, we analyzed all medical records, also monthly office visit of cardiologist, gynecologist (fellowship of high risk pregnancy) and follow up of the women with prosthetic heart valves during pregnancy and also full echocardiography study in each trimester. This study was approved by ethic committee, Tabriz University of medical sciences; Written consent was obtained from all the patients. For 10 years maternal outcomes included thrombo embolic and hemorrhagic complications, fertility history include parity gravidity and abortion and bridge anticoagulation. Pregnancy and fetal outcomes included miscarriage, still birth, type of delivery, mod of anticoagulation, comorbidities, abortion and live birth, low birth weight, type of prosthetic valve and warfarin embryopathy. Data are expressed as mean values±SD or proportions. A paired t test was used to investigate the time-dependent variables and Student t test to compare 2 groups. A p-value<0.05 was accepted as significant. SPSS 16 software (SPSS, Chicago, Illinois) was used for statistical analysis.

RESULTS

Between 10 years, we studied 19 patients, 13 had mechanical heart valves with mean ages of 28.30±5.43 (19-38), 4 cases with bioprosthetic valves with mean age of 25.4±4.12(20-30) and 2 cases of valve repaired 27.00±7.07(22-32). Seven women were uniparous 8 cases were in second pregnancy, one had 3rd and another one were gravid 4th. There was a mean interval between valve surgery and pregnancy of 7.65±6.07(1-23) years. In mechanical heart valves cases, 10 cases from 13 had one valve replacement and 2 cases had double valve replacement. Bioprosthetic valves were only in four patients. The majority of patients had undergone isolated mitral valve replacement (11 cases) and also aortic valve replacement were in 2 cases. Most of the valves were bileaf let type (12/13) and one had cage and ball valve. Sinus rhythm was more common and atrial fibrillation was only in one case. The mean INR for bileaf let valves were 2.5-3.5 and 3-3.5 for cage and ball valve. Dominant underling disease for valve replacement was rheumatic (Table 1, Fig. 1).

Table 1: Analysis of type of valve

	MV				
Type of valve	Bileaflet	Cage	Av	Age±SD (Rang)	Dobble
Bioprosthetic	4		1	25.40±4.12 (20-30)	
Mechanical	13	1	3	28.30±5.43 (19-38)	2
Repair	2			27.00±7.07 (22-32)	

DISCUSSION

The management of anticoagulation during pregnancy is controversial and there is no ideal clear cut treatment option (Koch, 2008). Patients with prosthetic heart valve have highest risk of thromboembolism and pregnancy itself is a factor of hypercoagulability (pregnancy-induced hypercoagulability) as a physiologically adaptive mechanism to prevent postpartum hemorrhage, hence increases risk of embolization (Curtis *et al.,* 2008). Thromboembolic events are lower with modern valve as compared with old generation, because of improvement in design and materials. The prevalence decreased but not disappeared. There is general agreement about discontinuation of oral anticoagulant during first trimester of pregnancy to avoid the warfarin embryopathy (Khamooshi *et al.*, 2007). According to ACC/AHA guide lines in 2008 anticoagulant during pregnancy in women with prosthetic heart valve must ensure continuous, monitored, therapeutic anticoagulation. Women who elect to stop warfarin between 6-12 weeks of gestation to reduce the risk of fetal defect should receive continuous IV or dose adjusted subcutaneous (SQ) UFH or dose adjusted subcutaneous LMWH (Mischke, 2007). Adjusted- dose of LMWH is twice daily to maintain anti-Xa level between 0.7-1.24 mL^{-1} 4 h after administration. Unfractionated heparin (UFH, initiated in high doses 17,500-20/000 IU every 12 hours to achieve 6 hours post dose of a PTT at least twice control. Warfarin to achieve INR goals of 3(ranges = 2.5-3) (Roos-Hesselink *et al.*, 2007). Thromboembolic event rate of mechanical heart valves

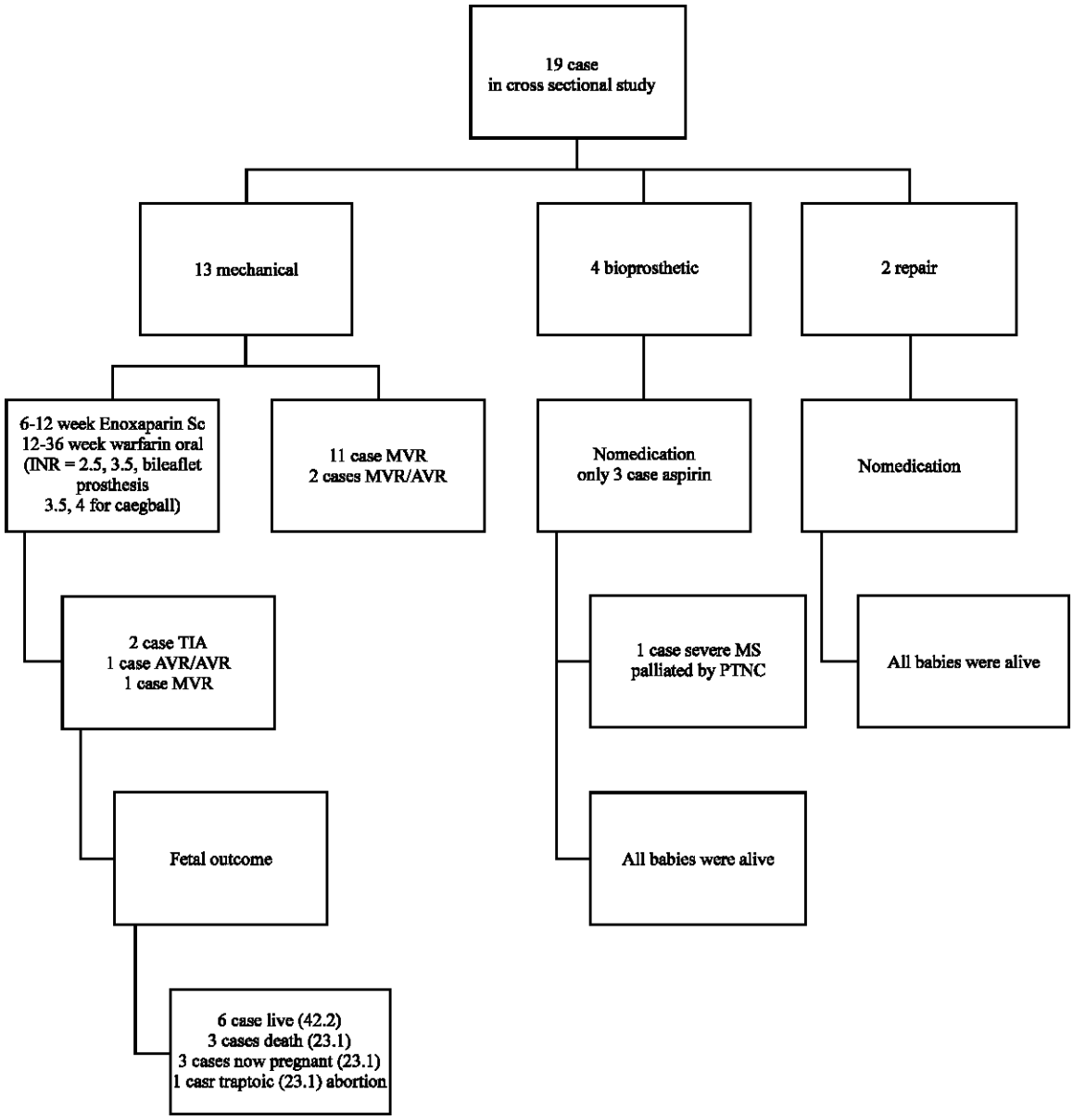

Fig. 1: Demographic diagram of study population

is 7.5-23% even with anticoagulation and mortality rate of 40 % (8-11,14). As we pointed earlier older mechanical valves and mitral valve position, have highest thromboembolic risk (Trzeciak *et al.,* 2006). Warfarin embryopathy seems to be dose related and warfarin should be safely used during pregnancy. Our study showed excellent results of bridge anticoagulation for mothers and even good outcome for fetus. These are in complete agreement with results of other studies (Varadarajan *et al.,* 2006). Salazar *et al.* (1996) used subcutaneous LMVH from 6-12 weeks and again in the last 2 weeks of pregnancy in 37 women with prosthetic heart valves, 2 died of fatal valve thrombosis of tilting disc mitral valve during pregnancy and another one died of anticoagulation-related gastrointestinal bleeding. (Salazar *et al.,* 1996). Fetal complications included 15 spontaneous abortion of first trimester with no incidence of warfarin induced embryopathy. In our study we hadn't mother's death due to thrombotic event or bleeding complication. This is may be due to close monitoring of patients with frequent visits and telephone call. Also giving of more information to the patients before and

during pregnancy was important in reducing of complication rate. Maximum doses of warfarin in our study was between 5-7.5 mg day^{-1} which is relatively low dose and absence of warfarin embryopathy in this study could be explained Geelani *et al.* (2005) from India reported 250 pregnancies in 245 women. In one group oral warfarin and in another group subcutaneous heparin used in first trimester. The incidences of spontaneous abortion were the same in both groups (Geelani *et al.*, 2005). We had not valve thrombosis in our study but in other studies thromboembolic rate was high in heparin group. The explanation may be related to poor compliance of patients to frequent heparin injection. In availability of measurement of anti-Xa in every centers or inadequate monitoring of aPTT maybe the cause of increase thrombosis in heparin group (Greer, 2005). Final dates of our study revealed no complication with bioprosthetic or repaired valves. This recommendation for women with childbearing age is choice of repair valve or bioprosthetic valve replacement.

CONCLUSION

According to this data bridge anticoagulation during pregnancy is safe for mother and fetus in women with mechanical heart valves.

REFERENCE

Curtis, S.L., J. Trinder and A.G. Stuart, 2008. Acute thrombosis of a prosthetic mitral valve in pregnancy in spite of adjusted-dose low-molecular-weight heparin and aspirin. J. Heart Valve Dis., 17: 133-134.

Geelani, M.A., S. Singh, A. Verma, A. Nagesh, V. Betigeri and M. Nigam, 2005. Anticoagulation in patients with mechanical valves during pregnancy. Asian Cardiovasc Thorac Ann., 13: 30-33.

Goldust, M., F. Golforoushan and E. Rezaee, 2011. Treatment of solar lentigines with trichloroacetic acid 40% vs. cryotherapy. Eur. J. Dermatol., 21: 426-427.

Goldust, M., E. Rezaee and S. Hemayat, 2012. Treatment of scabies: Comparison of permethrin 5% versus ivermectin. J. Dermatol., 39: 545-547.

Goldust, M., E. Rezaee and R. Raghifar, 2013a. Comparison of oral ivermectin versus crotamiton 10% cream in the treatment of scabies. Cutaneousv Ocul. Toxicol.

Goldust, M., M. Talebi, J . Majidi, M.A.R. Saatlou and E. Rezaee, 2013b. Evaluation of antiphospholipid antibodies in youths suffering from cerebral ischemia. Int. J. Neurosci., 123: 209-212.

Goldust, M., M.R. Ranjkesh, M. Amirinia, F. Golforoushan, E. Rezaee and M.A.R. Saatlou, 2013c. Sertaconazole 2% cream vs. hydrocortisone 1% cream in the treatment of seborrheic dermatitis. J. Dermatol. Treat., (In Press).

Goldust, M., S.B. Nejad, E. Rezaee and R. Raghifar, 2013d. Comparative trial of permethrin 5% vs. lindane 1% for the treatment of scabies. J. Dermatol. Treat., (In Press)

Golfurushan, F., M. Sadeghi, M. Goldust and N. Yosefi, 2011. Leprosy in Iran: An analysis of 195 cases from 1994-2009. J. Pak. Med. Assoc., 61: 558-561.

Greer, I.A., 2005. Venous thromboembolism and anticoagulant therapy in pregnancy. Gend. Med., 2: S10-S17.

Huisman, M.V., 2010. Further issues with new oral anticoagulants. Curr. Pharm. Des., 16: 3487-3489.

Jeejeebhoy, F.M., 2009. Prosthetic heart valves and management during pregnancy. Can. Fam. Phys., 55: 155-157.

Khamooshi, A.J., F. Kashfi, S. Hoseini, M.B. Tabatabaei, H. Javadpour and F. Noohi, 2007. Anticoagulation for prosthetic heart valves in pregnancy. Is there an answer? Asian Cardiovasc Thorac. Ann., 15: 493-496.

Koch, K.C., 2008. [Heart disease in pregnancy]. Dtsch. Med. Wochenschr., 133: 1684-1688.

Lotti, T., M. Goldust and E. Rezaee, 2013. Treatment of seborrheic dermatitis, Comparison of sertaconazole 2 % cream vs. ketoconazole 2% cream. J. Dermatol. Treat, 10.3109/09546634.2013.777154

Martinez-Diaz, J.L., 2008. Valvular heart disease in pregnancy: A review of the literature. Bol. Asoc. Med., 100: 55-59.

McLintock, C., 2011. Anticoagulant therapy in pregnant women with mechanical prosthetic heart valves: No easy option. Thromb. Res., 127: S56-S60.

McLintock, C., L.M. McCowan and R.A. North, 2009. Maternal complications and pregnancy outcome in women with mechanical prosthetic heart valves treated with enoxaparin. BJOG, 116: 1585-1592.

Milan, P.B., D.M. Nejad, A.A. Ghanbari, J.S. Rad and H.T. Nasrabadi *et al.*, 2011. Effects of *Polygonum aviculare* herbal extract on sperm parameters after EMF exposure in mouse. Pak. J. Biol. Sci., 14: 720-724.

Mischke, K., 2007. Management of pregnant women with artificial heart valves: Inconsistency in ESC publications. Eur. Heart J., 28: 2419-2420.

Mohamed, H., 2009. Antithrombotic therapy in patients with prosthetic heart valves. Libyan J. Med., 4: 54-56.

Mohebbipour, A., P. Saleh, M. Goldust, M. Amirnia, Y.J. Zadeh, R.M. Mohamadi and E. Rezaee, 2012. Treatment of scabies: Comparison of ivermectin vs. lindane lotion 1%. Acta Dermatovenerol. Croat, 20: 251-255.

Montavon, C., I. Hoesli, W. Holzgreve and D.A. Tsakiris, 2008. Thrombophilia and anticoagulation in pregnancy: Indications, risks and management. J. Matern. Fetal Neonatal. Med., 21: 685-696.

Quinn, J., K. von Klemperer, R. Brooks, D. Peebles, F. Walker and H. Cohen, 2009. Use of high intensity adjusted dose low molecular weight heparin in women with mechanical heart valves during pregnancy: A single-center experience. Haematologica, 94: 1608-1612.

Roeder, H.A., J.A. Kuller, P.C. Barker and A.H. James, 2011. Maternal valvular heart disease in pregnancy. Obstet. Gynecol. Surv., 66: 561-571.

Roos-Hesselink, J.W., F.J. Meijboom, F.W. Leebeek and C.J. de Groot, 2007. [Pregnancy and the mechanical prosthetic valve: Dilemmas about the choice of antithrombotic prophylaxis]. Ned. Tijdschr. Geneeskd., 151: 389-394.

Sadeghpour, A., R. Mansour, H.A. Aghdam and M. Goldust, 2011. Comparison of trans patellar approach and medial parapatellar tendon approach in tibial intramedullary nailing for treatment of tibial fractures. J. Pak. Med. Assoc., 61: 530-533.

Sadighi, A., A. Elmi, M.A. Jafari, V. Sadeghifard and M. Goldust, 2011. Comparison study of therapeutic results of closed tibial shaft fracture with intramedullary nails inserted with and without reaming. Pak. J. Biol. Sci., 14: 950-953.

Saeed, C.R., J.B. Frank, M. Pravin, R.H. Aziz, M. Serasheini and T.G. Dominique, 2011. A prospective trial showing the safety of adjusted-dose enoxaparin for thromboprophylaxis of pregnant women with mechanical prosthetic heart valves. Clin. Appl. Thromb. Hemost., 17: 313-319.

Salazar, E., R. Izaguirre, J. Verdejo and O. Mutchinick, 1996. Failure of adjusted doses of subcutaneous heparin to prevent thromboembolic phenomena in pregnant patients with mechanical cardiac valve prostheses. J. Am. Coll. Cardiol., 27: 1698-1703.

Sin'kov, S.V., I.B. Zabolotskikh, G.A. Penzhoian and V.P. Muzychenko, 2011. Thrombophilia and principle of thrombosis prevention in obstetrics. Anesteziol. Reanimatol., 1: 66-70.

Suri, V., A. Keepanasseril, N. Aggarwal, S. Chopra, R. Bagga and P. Sikka and R. Vijayvergiya, 2011. Mechanical valve prosthesis and anticoagulation regimens in pregnancy: A tertiary centre experience. Eur. J. Obstet. Gynecol. Reprod. Biol., 159: 320-323.

Trzeciak, P., L. Polonski and M. Zembala, 2006. Haemorrhagic and thrombo-embolic complications in patients with prosthetic valves-the under-appreciated problem with no safe solutions. Kardiol. Pol., 64: 1038-1042.

Vafaee, I., M.B. Rahbani Nobar and M. Goldust, 2012. Etiology of ocular trauma: A two years cros sectional study in Tabriz, Iran. J. Coll. Physicians Surg. Pak., 22: 344-344.

Varadarajan, P., D. Isaeff and R.G. Pai, 2006. Prosthetic valve thrombosis presenting as an acute embolic myocardial infarction in a pregnant patient: Issues on anticoagulation regimens and thrombolytic therapy. Echocardiography, 23: 774-779.

Walfisch, A. and G. Koren, 2010. The warfarin window in pregnancy: The importance of half-life. J. Obstet. Gynaecol. Can., 32: 988-989.