Case Report

Prosthetic heart valve thrombosis in pregnancy: a case series on acute management

S Foolchand, H Ramnarain

Abstract

Rheumatic heart disease is one of the leading causes of valve dysfunction, resulting in prosthetic valve implantation. Changes in physiology and the haemodynamics of pregnancy increase the susceptibility of thrombosis to the prosthetic valve in the pregnant woman. Valve redo surgery carries a considerable risk of maternal and perinatal morbidity and mortality. Women of reproductive age should be well counselled regarding compliance with anticoagulation, contraception and pre-pregnancy planning.

Cardiovascular disease (CVD) is one of the leading causes of morbidity and mortality worldwide,[1] and remains one of the top five causes of maternal death in South Africa.[2] Cardiac disease accounted for 34.3% of maternal deaths in the sub-category of medical and surgical conditions as a cause of maternal mortality in the Sixth Triennial report.[2] The burden of rheumatic heart disease and its sequelae contribute to a large proportion of women presenting with CVD in low- and middle-income countries (LMIC) such as South Africa.[1] The increased risk of heart failure secondary to valve degeneration may be abrogated by valve-replacement surgery,[1] resulting in a marked improvement of an individual's quality of life as well as life expectancy.[3]

Mechanical and biological prosthetic (bio) heart valves are used in replacement surgery depending on clinical presentation, preference of the patient and availability of the various types of prosthetic valves.[3] However, bio prosthetic valves often result

Department of Obstetrics and Gynaecology, University of KwaZulu-Natal, Grey's Hospital, Pietermaritzburg, South Africa
S Foolchand, MB ChB, FCOG (SA), Certificate Maternal-Foetal Medicine, foolchand.s@gmail.com

Department of Obstetrics and Gynaecology, University of KwaZulu-Natal, Inkosi Albert Luthuli Central Hospital, Durban, South Africa
H Ramnarain, MB ChB, FCOG (SA)

in re-operation due to dysfunction, especially when implanted in younger patients.[3] Mechanical valve prostheses are more commonly used in South Africa. These operations are generally performed on younger women in the reproductive age group and the implications of surgery and especially the use of warfarin (an oral anticoagulant) and its potential problems associated with pregnancy are often poorly understood.

The use of warfarin is lifelong, which poses the risk of teratogenicity in pregnancy, particularly in the first trimester, and foetal wastage later in the pregnancy.[3,4] The use of unfractionated heparin is associated with adverse effects on the mother.[4] Reports also include the risk of postpartum haemorrhage at delivery in patients who have been anticoagulated.[5]

Cardiac surgical intervention in pregnancy historically carries a greater risk to both mother and foetus. A recent meta-analysis, assessing maternal and foetal outcomes after cardiac surgeries during pregnancy involving cardiopulmonary bypass (CPB), found the following in women: per 100 pregnancies, the pooled unadjusted estimate of maternal mortality was 11.2 (95% CI: 6.8–17.8), pregnancy loss was 33.1 (95% CI: 25.2–41.2), maternal complications were 8.8 (95% CI: 2.8–24.2) and neonatal complications were 10.8 (95% CI: 4.2–25.2).[6]

Thrombosis of prosthetic valves is a medical/surgical emergency and all healthcare workers attending to pregnant women with prosthetic valves should have a high index of suspicion for valve thrombosis and resultant valve dysfunction. It can be life-threatening and appropriate management reduces maternal and foetal adverse outcomes.[7] Pregnant women are at greater risk for valve thrombosis due to poor compliance secondary to risk of possible foetal affectation, poor knowledge of healthcare workers in counselling patients on the different anticoagulation regimes in pregnancy, resource limitations in terms of assessments and monitoring, poor access to healthcare, nausea and vomiting during pregnancy, and a reduction in fibrinolysis and anti-thrombin III, contributing to the prothrombotic nature of pregnancy.[5]

Open-heart surgery carries considerable risk, especially in early pregnancy.[8] Therefore, CVD is considered a significant non-obstetric cause of maternal mortality.[9] In resource-limited countries such as South Africa, the management of such patients is challenging due to the obstetric risks and complications of anticoagulant therapy.[9]

The following are six cases of pregnant patients on anticoagulant therapy with malfunctioning prosthetic mitral valves, seen during the period of a year at two tertiary institutions in KwaZulu-Natal, requiring emergent valve replacement.

Case reports

Patient 1

A 30-year-old patient, P3G4, presented at 15 weeks' gestation. She had a routine echocardiography, which revealed dysfunction of a single mitral leaflet. This was confirmed by fluoroscopy. The patient had defaulted on multiple follow-up appointments and obtained warfarin from her local clinic. She had utilised an intra-uterine contraceptive device for contraception, which was removed due to abnormal bleeding, and no further contraception was offered to the patient. She was discussed in a multi-disciplinary team (MDT) involving cardiothoracic surgery/cardiology/maternal–foetal medicine/high-risk obstetrics.

The patient elected to have a valve redo and a 25-mm ON-X valve was inserted. The patient recommended oral anticoagulation after a period of intravenous heparin post operatively and the foetal heart was confirmed. She had an uneventful vaginal delivery of a 3-kg female neonate with good apgars.

Patient 2

A 20-year-old P0G1 presented at 21 weeks' gestation to her local hospital with a history of mitral valve prosthesis at age six years. She had defaulted on follow up at cardiology since 2017 and had stopped taking warfarin at least eight months previously. Screening of her valves confirmed that one leaflet was stuck. She was counselled in a MDT about valve redo surgery and the complications to her herself and the foetus.

At surgery, a thrombus and pannus were noted, which were impeding the valve leaflet movement. Her valve was replaced with a 25-mm ON-X prosthesis. She had an uneventful postoperative course and the foetal heart was confirmed on ultrasound pre- and post surgery. She went into spontaneous labour and delivered a 2.75-kg female with good apgars.

Patient 3

A 26-year-old primigravida was referred in active labour with hypertension and cardiac failure. Her warfarin was stopped by her local clinic mid-second trimester and the patient was not referred for tertiary care. The patient rapidly progressed and delivered vaginally. Valve screening showed suspicion of a stuck valve. She was assessed by the MDT and counselled for an emergent redo valve surgery.

The intra-operative findings included the mitral valve leaflet stuck in an open position with thrombus formation around the valve hinge. The valve was replaced with a 25-mm ON-X prosthetic valve. She recovered well post operation and was discharged to her referral centre for follow up, with counselling on contraception, compliance with anticoagulation therapy and pre-pregnancy assessment should she contemplate future pregnancies.

Patient 4

A 24-year-old patient, P1G2, presented with an anembryonic pregnancy. She had had a previous stillbirth at 28 weeks' gestation, most likely due to warfarin exposure. Screening of her valves revealed a stuck mitral valve leaflet.

The patient agreed to a suction curettage and valve-redo surgery. On day seven post evacuation, she had her mitral valve explanted and replaced with a 27/29-mm ON-X mechanical prosthesis as the mitral valve prosthesis was thrombosed with a large clot on both the left atrial and ventricle sides. The aortic valve was inspected and found to be incompetent and a 21-mm ON-X mechanical aortic prosthesis was implanted. The patient had an uneventful recovery and was counselled on compliance, contraception and booking at the pre-pregnancy clinic when planning her next pregnancy.

Patient 5

A 19-year-old primigravida in her first pregnancy presented to cardiology with a stuck mitral valve and poor compliance with warfarin. She was counselled and admitted for intravenous heparin and review by cardiothoracic surgery for possible mitral valve-redo surgery.

At surgery, the mitral valve leaflet was seen to be thrombosed at the hinge. She had her mitral valve prosthesis replaced with a 27/29-mm ON-X prosthesis and her native aortic valve replaced with a 21-mm ON-X mechanical valve due to severe aortic valve disease. She made an uneventful postoperative recovery.

The high-risk obstetrics unit was consulted immediately post operation as there was now a suspicion that she was pregnant. Subsequent ultrasound assessment revealed an 18-week intra-uterine gestation with an absent foetal heart pulsation. She was counselled and had a termination of pregnancy with misoprostol. The patient was counselled on contraception and the importance of a pre-pregnancy planning for the future. She was returned to the care of the cardiothoracic team.

Patient 6

A 27-year-old patient, P2G3, was referred at 29 weeks' gestation. She had a history of poor compliance. Although asymptomatic, screening revealed a stuck mitral valve leaflet. She was extensively counselled by a MDT and consented to valve-redo surgery.

The patient had her mitral valve prosthesis redone with the foetus *in utero*. At surgery the leaflet was noted to be thrombosed and the valve was replaced with a 27/29-mm ON-X mechanical prosthetic valve. The patient did not consent to foetal monitoring during surgery and an intra-uterine foetal death was noted post procedure. She underwent induction while still on intravenous heparin and delivered a 1.2-kg stillbirth vaginally. She was bridged onto oral anticoagulation and discharged via the cardiothoracic ward on optimal oral anticoagulation and contraception.

Discussion

The cases outlined above reinforce the areas of concern in the management of pregnant women with cardiac prosthetic valves. Maternal mortality as a result of valve thrombosis ranges between two and 15%, even on heparin therapy.[8] Pregnant women are at increased risk for valve thrombosis, which may be exacerbated by the physiological changes of pregnancy.[8]

Pregnancy is a hypercoagulable state due to the increase in factors VII, VIII and X.[7] The formation of a thrombus or pannus at the valve impacts on its functionality, leading to stenosis or regurgitation.[10] Management of patients with thromboses is complex due to the risk of perinatal morbidity and mortality.

Poor compliance and follow up contributed significantly to the presentation of the above patients. Compliance failure is a well-known problem to all healthcare workers in our country and reasons include lack of insight into the need for anticoagulation, poor follow up, the reluctance or failure of medical professionals outside of obstetrics and gynaecology to actively advocate contraceptive use in women of reproductive age, lack of resources and knowledge regarding the management of anticoagulation in pregnancy, as well as financial constraints on the part of the patient.

The use of subcutaneous low-molecular weight heparin in pregnant women with mechanical prosthetic valves without meticulous anti-Xa monitoring is not an option and cannot be emphasised enough. The administration of anticoagulants and thrombolytic agents during pregnancy increases the risk of sub-placental bleeding and embolism.[8]

The index of suspicion for valve thrombosis must be high for all pregnant women with mechanical heart valves. Patients may present with worsening dyspnoea, palpitations or cardiac failure, new murmurs, and new symptoms of cardiac or respiratory compromise.

A detailed clinical examination and transthoracic echocardiography (TTE) should be the basic assessment for all pregnant women with mechanical prosthetic valves,[11] irrespective of symptoms, as some may be asymptomatic, similar to our second patient. TTE should be the imaging used as first line, as a normal prosthetic heart valve function seen on TTE is reassuring.

The echocardiographic signs of obstructive valve thrombosis include reduced valve mobility, presence of thrombus, abnormal trans-prosthetic flow, central prosthetic regurgitation, elevated trans-prosthetic gradients, and reduced effective prosthetic area (as seen in patient 2).[12] The 2017 guidelines from the American Heart Association recommends urgent multimodality imaging in patients with suspected mechanical heart valve thrombosis to assess valvar function, leaflet motility and the presence and extent of thrombus.

Surgery is considered in the presence of a thrombus.[7] CPB surgery has implications for both the patient and her foetus. Surgery carries a risk of up to 30% for foetal mortality. Over the years, techniques have been introduced to decrease the risk to the foetus, such as avoiding hypothermia during bypass,[13] maintenance of a high flow rate (> 2.5 l/min/m^2), mean arterial pressure > 70–75 mmHg,[14] maintenance of the haematocrit above 28%, avoiding maternal hypoglycaemia and hypoxia, as well as by placing the patient in the left lateral recumbent position during CPB to avoid inferior vena cava compression by the uterus.[15,16]

Pulsatile flow has been suggested as being more beneficial in pregnant women than in non-pregnant women as it decreases vasoconstriction (in foetal lamb studies) by decreasing the activation of the foetal renin–angiotensin–aldosterone axis, which may reduce uterine contractions.[17] CPB can induce uterine contractions, especially during the cooling and rewarming phases.[18]

In the above case series, the patients were assessed, managed and counselled for valve-redo surgery, which was carried out successfully. The implications for both the mother and foetus were also discussed as surgical mortality rates are between five and 36%.[19] Therefore, the prosthetic type, and imaging and surgical risks (co-morbidities, age) are considered.[19] Follow up is imperative after prosthetic heart valve-replacement surgery.[20]

Conclusion

Women of reproductive age with prosthetic valves should be counselled adequately for potential risks. Prosthetic valve dysfunction in pregnancy increases the risk of adverse outcomes for both mother and foetus. Therefore, careful management is warranted to ensure positive outcomes and improvement in quality of life.

Clinicians taking care of reproductive-age women should enquire on a menstrual history and fertility desires. Patients with medical or surgical disorders should be referred for pre-pregnancy counselling and assessment. All women with mechanical prosthetic cardiac valves should be counselled on the various anticoagulant regimes available, with advantages and disadvantages discussed in detail, preferably prior to stopping contraception or planning a pregnancy. The options should include oral anticoagulants, unfractionated heparin or low-molecular weight heparin. Pregnant women with mitral valve prostheses should have a detailed history/examination and a TTE at the first antenatal consultation. The frequency of TTE depends on symptoms and available resources.

These women should also be managed in a tertiary institution. There should be a high index of suspicion for valve dysfunction. Those with a suspicion of valve malfunction should be urgently seen by a MDT consisting of cardiology/cardiothoracic/high-risk obstetrics/neonatology (if relevant) and anaesthetics. Patients requiring urgent valve-redo surgery should be counselled extensively on the surgery and possible foetal and maternal outcomes. Measures to decrease foetal loss at CPB should be instituted in all pregnant women.

References

1. Namara KM, Alzubaidi H, Jackson JK. Cardiovascular disease as a leading cause of death: how are pharmacists getting involved? *Integr Pharm Res Pract* 2019; **8**: 1–11.

2. Pattinson RC. Saving Mothers 2011–2013: The Sixth Report of the National Committee for Confidential Enquiries into Maternal Deaths in South Africa. Pretoria: Government Printer, 2014.

3. Barbarash L, Rutkovskaya N, Barbarash O, Odarenko Y, Stasev A, Uchasova E. Prosthetic heart valve selection in women of childbearing age with acquired heart disease: a case report. *J Med Case Rep* 2016; 1–5.

4. Rozestraten FFJ, Wilcox I, Lalande S, Simmons LA. A case report: mechanical mitral valve thrombosis in pregnancy. *Eur Heart J Case Rep* 2019; **3**: 1–5.

5. Van Kuilenburg JT, Verheugt FWA, van Dijk APJ. Prosthetic heart valve thrombosis, anticoagulation and pregnancy: a case report and review of literature. *Neth Heart J* 2007; **15**: 306–309.

6. Jha N, Jha AK, Chauhan RC, Chauhan NS. Maternal and fetal outcome after cardiac operations during pregnancy: a meta-analysis. *Ann Thoracic Surg* 2018; **106**(2): 618–626.

7. Akgüllü C, Eryılmaz U, Güngör H, Zencir C. Management of mechanical valve thrombosis during pregnancy, case report and review of the literature. *Int J Cardiovasc Acad* 2017; **3**: 79–82.

8. Cardoso G, Aguiar C, Andrade MJ, Patrício L, Freire I, Serrano F, *et al*. Prosthetic mitral valve thrombosis in pregnancy: from thrombolysis to

anticoagulation. *Rev Port Cardiol* 2015; **34**: 71.e1–71.e5.

9. Kariv S, Azibani F, Baard J, Osman A, Soma-Pillay P, Anthony J, *et al*. Haemorrhage and other complications in pregnant women on anti-coagulation for mechanical heart valves: a prospective observational cohort study. *Cardiovasc J Afr* 2018; **29**: 289–295.

10. Coffey S, Cairns BJ, Lung B. The modern epidemiology of heart valve disease. *Heart* 2016; **102**: 75–85.

11. Zoghbi WA, Chambers JB, Dumesuil JG, Foster E. Recommendations for the evalaution of prosthetic valves with echocardiogarphy and doppler untrasound. *J Am Soc Echocardiogr* 2009; **22**: 975–1014.

12. Roudaut R, Serri K, Lafitte S. Thrombosis of prosthetic heart valves: Diagnosis and therapeutic considerations. *Heart* 2007; **93**: 137–142.

13. John AS, Gurley F, Schaff HV, Warnes CA, Phillips SD, Arendt KW, *et al*. Cardiopulmonary bypass during pregnancy. *Ann Thorac Surg* 2011; **91**: 1191–1197.

14. Chandrasekhar S, Cook CR, Collard CD. Cardiac surgery in the parturient. *Anesth Anal* 2009; **108**: 777–785.

15. Parry AJ, Westaby S. Cardiopulmonary bypass during pregnancy. *Ann Thorac Surg* 1996; **61**: 1865–1869.

16. Kole SD, Jain SM, Walia A, Sharma M. Cardiopulmonary bypass in pregnancy. *Ann Thorac Surg* 1997; **63**: 915–916.

17. Hawkins JA, Paape Kl, Adkins TP, Shaddy RE, Gay WAJ. Extracorporeal circiulation in the fetal lamb. Effects of hypothermia and perfusion rate. *J Cardiovasc Surg* (Torino) 1991; **32**: 295–300.

18. Becker RM. Intracardiac surgery in pregnant women. *Ann Thorac Surg* 1983; 36: 453–458.

19. Lim WY, Lloyd G, Bhattacharyya S. Mechanical and surgical biopros-thetic valve thrombosis. *Heart* 2017; **103**: 1934–1941.

20. Sucha D, Symersky P, van den Brink RBA, Tanis W, Laufer EM, Meijs MFL, *et al*. Diagnostic evaluation and treatment strategy in patients with suspected prosthetic heart valve dysfunction: The incremental value of MDCT. *J Cardiovasc Comput Tomogr* 2016; **10**: 398–406.