

Pregnancy and prosthetic heart valves: A case series

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ABSTRACT

Objectives: To assess the problems faced by pregnant women with prosthetic cardiac valves in terms of maternal and neonatal outcomes.

Settings: Tertiary-level teaching hospital.

Population: All pregnant women with prosthetic cardiac valves visiting the hospital in the period between January 2008 and September 2012.

Method: Retrospective observational case series study.

Results: Among the women presenting for antenatal visits to the hospital in the study period, eight were found to have prosthetic cardiac valves. All cases had rheumatic origin of their cardiac lesion. Five cases had a mitral valve replacement. One had aortic and two had double-valve replacement. All patients had mechanical valves and were on anticoagulant regimen. Among them, one patient developed valve thrombosis and another developed embolic transient ischemic attack while in labor. Two patients developed symptomatic arrhythmia requiring treatment, while one patient had pneumonia with parapneumonic effusion. Three cases had abortions, while the other five pregnancies delivered live babies. All deliveries took place by lower segment Caesarean section (LSCS) for indications other than the cardiac condition. One pregnancy was complicated by intrauterine growth restriction and oligohydramnios. No patient developed any complications during the LSCS. There were no cases of warfarin embryopathy observed.

Conclusion: Maternal complications tend to be higher in pregnant women with prosthetic cardiac valves requiring strict adherence to anticoagulant regimens and specialized treatment in tertiary care centers.

Key words: Anticoagulation; prosthetic cardiac valves; warfarin.

Introduction

Cardiovascular disorders affect approximately 0.3%–3.5% of all pregnancies.^[1] The physiological changes in the cardiovascular system brought about by pregnancy tend to accentuate the condition causing further worsening and an increased propensity for cardiac failure particularly during the midtrimester, labor, and immediate postpartum period.^[2] With the high prevalence of rheumatic heart disease in India,^[3] the prevalence of prosthetic cardiac valves use is also in the same measure. Pregnancy in women with this

condition presents with its unique set of problems as regards the maternal and fetal outcome due to the condition itself and the use of anticoagulants pertinent to it.

In women with prosthetic cardiac valves, on one hand while the functional class is improved with placement of the artificial valve remedying the cardiac lesion in question, a fresh set of

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How to cite this article: Barnali B, Ranjan S. Pregnancy and prosthetic heart valves: A case series. Trop J Obstet Gynaecol 2019;36:277-82.

Access this article online	
Website: www.tjogonline.com	Quick Response Code 
DOI: 10.4103/TJOG.TJOG_68_18	

problems is created with regard to anticoagulation measures needed in case of metallic valves.^[4] Pregnancy on account of its hypercoagulability renders the dose of anticoagulants being taken insufficient and inadequate while the choice of the drugs also becomes a dilemma considering the effect of the drugs on the fetus. While warfarin has been found to have good anticoagulation, it is fraught with risks of teratogenesis and maternal hemorrhage, while heparin, both unfractionated and low-molecular weight, having minimal fetal effects is often found not to cope up with the increased demands of pregnancy.^[5] The fetal outcomes in these complicated pregnancies also tend to be below par with affected maternal cardiovascular system also compromising the uteroplacental circulation. There is also the risk of development of anomalies due to the use of warfarin which has lifelong consequences for the fetuses born alive.^[6] All these problems make it mandatory for such pregnancies to be monitored and treated for complications in a tertiary healthcare setting which may improve if not totally abdicate the effects of the underlying condition on the maternal and fetal outcome.

India is a country with grave problems of poverty and illiteracy which adds onto these serious problems. Even after guidelines issued by the American Association of Cardiologists regarding the anticoagulation regimens to be followed in pregnancy,^[4] their compliance and adherence becomes difficult both due to ignorance and financial reasons.

We undertake this study to assess the problems faced by pregnant women with prosthetic cardiac valves and the challenges faced while treating them.

Materials and Methods

It was a retrospective observational study conducted in the obstetrics and gynecology and cardiology departments of a tertiary care center. Being a retrospective study, no ethical clearance was required to be obtained for the same. The Hospital records for the period of January 2008-September 2012 were studied, and all pregnant patients found to have prosthetic cardiac valves were included. The patient's records were observed for the problems faced due to pregnancy, the cardiac condition, the anticoagulation regimens followed, and delivery. Patients were analyzed for New York Heart Association (NYHA) class at the time of conception, anticoagulation during pregnancy, ECHO findings at the time of presentation, outcome of pregnancy, and cardiac and obstetric complications.

Results

In the given study period, 144 patients were found to have cardiac disease complicating their pregnancies. Among them,

eight patients were found to have prosthetic cardiac valves and hence were suitable for the study. None of the patients had bioprosthetic valves which are associated with fewer complications on account of no need for anticoagulation. All the patients had cardiac valve replacement due to a lesion of rheumatic origin which is more common in a country like India. Only one patient had an uncomplicated pregnancy while all the other patients had either maternal or fetal complications. Most complications were due to cardiac reasons than obstetric ones. The cases are summarized as follows:

Case I: Mrs. S, a 24-year-old primigravida at 7+ weeks, presented to the hospital with complaints of breathlessness on exertion. The patient had severe pulmonary arterial hypertension, moderate pulmonary regurgitation/tricuspid regurgitation, and severe aortic root and subvalvular obstruction. The patient was in NYHA Class II in sinus rhythm and not in failure. She had undergone aortic valve replacement and transpulmonary patent ductus arteriosus closure 10 years back. She was on tablet warfarin and aspirin and had conceived on the same. Electrocardiogram done showed right bundle branch block and right ventricular hypertrophy. Ultrasound pelvis was suggestive of missed abortion.

After stopping warfarin and changing over to heparin for better coagulation control, suction evacuation of pregnancy was done. Warfarin was restarted following the procedure.

The patient improved symptomatically and was discharged. She was advised against future conception and levonorgestrel intrauterine system was recommended for the same.

Case II: Mrs. S, a 31-year-old G2MTP1, presented to the hospital at 24+ weeks for antenatal checkups. She had mitral regurgitation and aortic regurgitation and had undergone aortic and mitral valve replacement 3 years back. She was in NYHA Class I in sinus rhythm and not in failure at the time of presentation. She had conceived while on tablet aspirin, warfarin, and ramipril.

In view of its fetotoxic effects, ramipril was stopped immediately.^[7] As the patient had presented in second trimester, warfarin and aspirin were continued. Anomaly scan done showed no evidence of anomalies in the fetus. She continued to have regular checkups in the hospital and her coagulation parameters were regularly monitored. Ultrasound later in pregnancy showed adequate interval growth of the fetus. At the onset of third trimester, warfarin was stopped and low-molecular-weight heparin (LMWH) was started.

At the onset of labor, as epidural analgesia was provided, heparin was stopped. However, the patient complained of headache after sometime. She was diagnosed to have embolic transient ischemic attack and heparin was restarted. In view of nonprogress of labor, emergency lower segment Caesarean section (LSCS) was finally done and the patient delivered a healthy female baby with a weight of 3.1 kg. Post delivery, the patient was restarted on warfarin and discharged.

Case III: Mrs. S, a 34-year-old primigravida at 27+ weeks, referred to the hospital from a secondary care center in view of impaired glucose tolerance test. She had undergone mitral valve replacement 2 years back. She had history of embolic stroke 1 year back leading to hemiparesis with weakness persisting. She was on tablet warfarin and clopidogrel with penicillin prophylaxis at the time of conception. Warfarin had been changed to unfractionated heparin from 6 to 14+ weeks. The patient was in NYHA Class I in sinus rhythm at the time of presentation.

The patient was put on diabetic diet in view of her blood sugar levels. She also received steroid prophylaxis at 28+ weeks. Warfarin was changed over to heparin from 33+ weeks. She underwent elective LSCS at 36+ weeks in view of intrauterine growth restriction, oligoamnios, and gestational diabetes mellitus. She delivered a male baby weighing 2.28 kg. There were no complications postnatally.

Case IV: Mrs. J, a 28-year-old G3Ab2 at 6+ weeks, presented to the hospital with chest pain and palpitations. She had undergone mitral valve replacement 9 years back. The patient had stopped warfarin preconceptionally and had conceived on heparin. She was in NYHA Class IV in atrial fibrillation and failure at the time of presentation. She was started on beta blockers, diuretics, and digoxin. Ultrasound pelvis showed a live fetus of 6+ weeks. She was advised medical termination of pregnancy, but she refused.

The patient developed severe abdominal pain and breathlessness 2 days later. She was found to have bradycardia and hypotension. She was administered inotropes but had a cardiac arrest and could not be revived.

Case V: Mrs. M, a 28-year-old G3P2L1ID1 at 34+ weeks, referred from a secondary care center with polyhydramnios. The patient had undergone mitral valve replacement 4 years back. She had conceived on warfarin and metipril and was in NYHA Class I and sinus rhythm at the time of presentation.

Warfarin was changed over to Heparin and steroid prophylaxis was given. Growth scan showed adequate interval growth. The patient underwent elective LSCS with sterilization at term in view

of cephalopelvic or fetopelvic disproportion (CPD). She delivered a female baby of 2.7 kg. She developed arrhythmia on the second postop day and was treated with diltiazem and adenosine. She was started back on warfarin at the time of discharge.

Case VI: Mrs. M, a 32-year-old primigravida, presented at 5+ weeks for antenatal checkups. She had undergone mitral valve replacement 6 years back and had conceived while on warfarin, penicillin, and losartan. The patient was in NYHA Class I and sinus rhythm at the time of presentation.

In view of fetotoxicity, losartan was changed to torsemide and warfarin was switched over to heparin till 15+ weeks and then restarted back. The patient was monitored regularly with scans and blood coagulation parameters which remained within the normal range. She was found anemic at 21+ weeks which was resolved with double-dose iron. Steroid prophylaxis was given at 28+ weeks and growth scan was normal. Heparin was restarted again at 34+ weeks. The patient delivered a healthy male baby of 2.8 kg at term by elective LSCS done in view of floating head at term. There were no complications postnatally.

Case VII: Mrs. S, a 33-year-old primigravida, presented at 32+ weeks with breathlessness. The patient had undergone mitral valve replacement 8 years ago. She had conceived on warfarin and aspirin and was in NYHA Class II and sinus rhythm at the time of presentation. She had regular checkups in a secondary care center previously.

She was diagnosed to have right-sided lobar pneumonia and parapneumonic effusion which was treated with antibiotics. Growth scan was normal. The patient was switched over to heparin at 35+ weeks and underwent elective LSCS at term in view of CPD. She delivered a healthy female baby of 3.2 kg. There were no complications postnatally.

Case VIII: Mrs. I, a 35-year-old G2MTP1 at 6+ weeks, presented for antenatal checkups. She underwent mitral valve replacement 2 years back and had conceived on warfarin. She was in NYHA Class I and sinus rhythm at the time of presentation. The patient was started on unfractionated heparin 5000 U sc bd. However at 10+ weeks, she took a lower dose of heparin than prescribed for 3 days and reported back with bleeding per vaginum. She was found to be with inevitable abortion. Suction evacuation was done and she was started on heparin eighth hourly. The patient developed chest pain and breathlessness the next day. ECHO was suggestive of valve thrombosis. She was started on streptokinase but the thrombus persisted. She had cardiac arrest the next day and was declared dead after failed cardiopulmonary resuscitation.

The ECHO findings of the patients are summarized as follows [Table 1]:

Table 1: Echocardiography findings of the patients

Patient	Ejection fraction	Other findings
Case I	77%	Severe PAH, severe aortic valve gradient, good prosthetic valve function
Case II	60%	Good prosthetic valve function, trivial AR
Case III	61%	Good prosthetic valve function, no clot/valve motion abnormality
Case IV	67%	No prosthetic valve clot, right ventricular systolic dysfunction
Case V	64%	Good prosthetic valve function
Case VI	60%	Good prosthetic valve function, normal biventricular systolic function
Case VII	58%	Good prosthetic valve function, normal biventricular systolic function
Case VIII	45%	Prosthetic valve thrombosis

Discussion

The first successful human heart valve replacement was reported in 1960.^[8] Since then, the procedure has been performed and has been proved to be life-saving in many individuals. With the increased life span of the patients receiving prosthetic valves, new set of unique clinical problems began to emerge, notably pregnancy in women of childbearing age.

In our present case series, the women were in the age group of 24–35 years and had no other comorbidities except for mechanical prosthetic cardiac valves which may have influenced their outcomes. Hence, there is no bias with regard to the events in the pregnancies of these women which were solely due to their condition.

None of the women in the series had a bioprosthetic heart valve, obviating the chance to study the effects of pregnancy on them. This is largely on account of their high cost precluding their availability in a developing country like India. There is also concern about the increased chances of structural valve deterioration with increasing age which also makes them not the preferred choice in young individuals. Limited studies are available about the outcome of pregnancies in women with bioprosthetic valves with mixed results.^[4]

All women had rheumatic origin of their cardiac lesions that were mostly in the mitral valve or both mitral and aortic valves which is the same as for studies conducted in developing countries in comparison to the developed ones where congenital lesions are more common. This, however, has no effect on the anticoagulation protocols used in the management of these pregnancies. In a study by Sillesen *et al.*, patients with corrected congenital aortic lesions tended to tolerate pregnancies better than others.^[9] In our series, only one patient with a mitral valve lesion developed cardiac failure.

The NYHA Class of most of these patients was either I or II at presentation. The only patient in Class IV died in the first trimester. But as she had stopped her warfarin preconceptually on medical advice, it indicates she was in a better class at the time of her conception. This shows that the NYHA classification may not have much bearing on the ultimate prognosis of the patient though it may be used preconceptually to decide whether a patient is fit for pregnancy or not.

As per the current guidelines proposed by the American College of Cardiologists and chest physicians,^[4] it is recommended to stop warfarin in the first trimester, that is, from 6 to 12 weeks to prevent warfarin embryopathy and replace it with heparin, but most patients in the series continued warfarin well upto the third trimester. This was because these patients were getting their checkups done at secondary care centers where this protocol was not followed and presented late at the center of study. No cases of warfarin embryopathy were observed among the patients who delivered live babies. This is comparable to studies by Tounsi *et al.*^[10] and Suri *et al.*^[11] which found a very low incidence of anomalies in babies where patients continued taking warfarin in the first trimester. Most studies have found a higher risk of fetal loss in patients on warfarin throughout pregnancy; however, in our series, this has happened with only one patient. The two other patients who had fetal loss had been started on heparin. The fact that these two had maternal loss as well makes warfarin appear a much preferential treatment than heparin.

Most of these patients were on a dose of warfarin <5 mg/day which is associated with less incidence of embryopathy which as per the guidelines can be continued in the first trimester. However, as per a meta-analysis done by D'souza *et al.*, this still remains unconfirmed.^[12] As per this study, the risk of foetopathy if warfarin is resumed in the second trimester still remains around 1.4% evidenced by some studies where babies born had hydrocephalus or intracerebral bleed, but no such observation was made here. One of the patients was also continued on an angiotensin converting enzyme inhibitor, a known cause of fetal congenital anomalies, and the baby was born normal. This shows these drugs tend to exhibit more of an all or none phenomenon than cause anomalies in the fetuses. In a developing country like India, warfarin is a much more attractive option among patients on account of its affordability, oral intake, and inexpensive test for monitoring. Our observations hence show that warfarin can be continued as a treatment option in poor patients with prosthetic cardiac valves despite its slightly high risk of fetal anomalies and loss.

As found by most studies, maternal outcome was better in patients on warfarin. In our series, it was found that maternal complications were more than the fetuses. But the two maternal losses took place in patients on heparin, one patient stopped it precepcionally while the other took lower doses than prescribed. This makes warfarin a better drug of choice in patients with more chance of loss of follow-up or compliance at the risk of fetal loss.

As per D'Sousa *et al.*^[12] and Steinberg *et al.*,^[13] the use of LMWH throughout the pregnancy is associated with best outcome in terms of fetuses. However, only one patient in this series could afford the same. Also, the continuous use of LMWH requires the monitoring of anti-Xa heparin levels which may be too expensive and not readily available in all laboratories. Also, as these studies do not show a better maternal outcome with LMWH, it is not yet feasible to start this kind of regimen in India.

Unlike other cardiac conditions where the chances of failure and complications tend to be more in the second trimester, the two deaths occurring in the first trimester show this condition is high risk throughout pregnancy. Also, even though all patients in the series developed problems, the only patient among the ones with a live birth who had regular antenatal checkups (ANCs) in the study center from the first trimester had the least amount of complications. This makes it imperative that all patients with prosthetic heart valves should be managed in a tertiary care center.

Most studies included their own booked patients, but most patients in our study were referred either in the second or third trimester or when complications had set in. The one patient who checked in the first trimester but died due to valve thrombosis was found to be noncompliant. Hence, patients need to be referred at the earliest for treatment in a tertiary care center with the presence of a cardiologist and intensive care unit apart from specialist gynecologist and neonatologist.

Unlike most studies, we did not encounter any cases of fetal intracerebral bleed or hemorrhagic complications in any of the patients in our series. Earlier, it was recommended to go for vaginal delivery in patients with cardiac disorders in view of anesthetic complications.^[5] But now with the availability of better and safer anesthetic and cardiology facilities, cesarean delivery in these patients has become a plausible alternative. As per the Van Hagen study on the European cardiology registry data,^[14] bleeding complications were more in patients with cardiac valves particularly at the time of delivery. Hence, vaginal delivery

should be preferred unless cesarean delivery is needed for obstetric indications. In our series, all mothers have undergone cesarean delivery for obstetric reasons and none of them had any such complication which indicates the safety of caesarean delivery in this particular group of patients.

The most paramount point established by our series is the need of strict compliance. Both patients who died in our series had refused to go with the medical advice offered. In a developing country like India with rampant ignorance, illiteracy, and low economic status, this can be a major problem. Patients are required to be counseled thoroughly on the need of compliance with their visits, treatment regimes, and doses. Most studies recommend an individualized regimen rather than strict adherence to the guidelines suggested after a discussion with the patient herself.^[15,16,17,18] However, the factors enunciated above may make it particularly difficult for a protocol through patient discussion. Decisions may sometimes hence be needed to be taken empirically.

Limitations

Despite extensive searching, we were not able to find the type of mechanical valves used by these patients. It is assumed since almost all of them were on low dose of warfarin, they were probably using the low thrombogenic valves which are more prevalent now. However, as the cardiology guidelines do not take into account the type of valve while deciding on the anticoagulation drugs used and most studies too have not found a correlation between the type of valves and outcomes of these patients, we do not feel it is of significant consequence.

Conclusion

Maternal complications tend to be high in pregnant patients with prosthetic cardiac valves requiring specialized care in a tertiary care center with the availability of cardiology and specialized anesthetic services. No anticoagulation regimen is without any risks and it is better to give individualized treatment for the same with regular monitoring. The need for compliance cannot be overemphasized and patients should be counseled regarding the same.

Acknowledgement

We would like to thank Dr. Lavanya Rai, Dr. Pratap Kumar, and Dr. Anjali M for their valuable inputs in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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