



Cardiovascular Editorial

Pregnancy with Mechanical Heart Valves – A Complete Interplay of Dose and Anticoagulation

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The formidable challenge in managing anti-coagulants in pregnant women with mechanical heart valves requires consistent counseling and communication between the medical specialist and pregnant women. In our scenario, medical specialist needs to interact with family members also and convince them about anticoagulation management and various risks the pregnant women are exposed to.

The WHO recognizing the pregnancy in women with mechanical heart valves as high-risk category (Class III) with maternal mortality rate of 1% and valve thrombosis close to 5%, obstetric morbidity such as hemorrhage, pre-term birth, and fetal complications including growth restriction, miscarriage, and still birth.^[1]

There is an increase in blood volume (30–50%) and cardiac output with substantial reduction in systemic vascular resistance and decrease in blood pressure with normal pregnancy. The hypercoagulable state in pregnancy requires appropriate anticoagulation strategy and adequacy of anticoagulation is hampered by the increased renal clearance and volume of distribution associated with pregnancy. Further with COVID-19 still on horizon which is again, a prothrombotic state has increased the risk for complications in pregnant women with mechanical valves. Thus, the medical specialist requires clear understanding of the physiological changes and management of anticoagulation in pregnancy with mechanical heart valves.

The uneven distribution of health facilities and inadequate guidelines based on small retrospective studies with incomplete data increases the challenge to manage anticoagulation manifold.

The appropriate anticoagulation choices decrease the risk for mother and fetus in pregnancy with prosthetic heart valves. The embolic event should raise suspicion of valve thrombosis in such cases. The reported risk of thromboembolism is 7–23%/patient/year and half of these episodes arise from valve thrombosis and in the absence of adequate anticoagulation risk increases up to 25% during pregnancy with mechanical heart valves.^[2] The risk of thromboembolism increases further with atrial fibrillation.^[3] TEE, fluoroscopy, and gated cardiac CT are the essential tools in evaluating patients with suspected valve thrombosis.^[4]

The maternal safety and fetal safety require the choice of anticoagulant with uninterrupted therapeutic anticoagulation during pregnancy with mechanical heart valves.

Warfarin is the preferred choice for preventing thrombotic complications but it crosses the placenta and causes miscarriage; spontaneous abortion; warfarin embryopathy; or fetal intracranial hemorrhage, particularly at dose >5 mg daily and when given during first trimester.^[5]

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During pregnancy, the warfarin dose needs constant monitoring to achieve therapeutic international normalized ratio (INR) and the dose may change. Warfarin embryopathy is characterized by the skeletal abnormalities such as nasal bone hypoplasia and stippled epiphyses with 5–7% embryopathy rate during first trimester.^[6]

The neurological sequelae and increased risk of fetal hemorrhage^[7] are associated with warfarin use during second and third trimester.^[7]

Although unfractionated heparin or low molecular weight heparin (LMWH) does not cross the placenta and is not teratogenic, either type provides less protection against thrombotic events,^[8] particularly when improperly closed, monitored, or administered.

In this issue of IJCWD, Rao *et al.* studied the issues related to fertility and pregnancy outcomes in women after surgery for valvular heart diseases. The attempt is being made to collate, analyze, and strategize the management of anticoagulants in pregnant women with mechanical heart valves in India. The authors reported 63% of women conceived after heart valve surgery.

The role of preconception counseling and decision being shared between the women; family members; and her physician during first contact after pregnancy and choice of anticoagulant is not clear. The authors reported fetal loss of 9% with 5 mg/day of warfarin during first trimester. They have not made any strong correlation between the dose of warfarin and spontaneous abortion.

The requirement of low dose of warfarin ≤ 5 mg/day throughout pregnancy poses the lowest combined risk to mother and fetus.^[5,9] One should be cautious as many studies have not found improved fetal outcomes on low-dose warfarin in pregnancies with mechanical heart valves.^[10]

Van Hagen *et al.* reported a 1.4% risk of maternal mortality and multiple significant morbidities including a 23% risk of hemorrhage and an 18.4% risk of fetal loss. Valve thrombosis occurred in 4.7% with 20% of maternal mortality. Strikingly half of valve thrombosis occurred during first trimester with all women switching to same form of heparin. There was no significant difference in occurrence of valve thrombosis in mitral or aortic position.^[11]

In the present study, the authors reported six abortions, three because of warfarin and three because of heparin. As the dose of warfarin used is not more than 5 mg/day and body surface area differs in our patient as compared to Western population, this finding needs further investigation.

The current American Heart Association/American College of Cardiology guidelines suggest that, during first trimester, the dose of warfarin should be 5 mg/day or less (Class IIa) to achieve the target INR.^[1] There is >30% risk of fetal loss

or embryopathy with warfarin dose of >5 mg/day. Thus, the dose of adjusted LMWH be used in the first trimester (aiming for a 4–6-h post-dosing anti-Xa level of 0.8–1.2 IU/mL). However, Van Hagen *et al.* data suggest 50% incidence of mechanical valve thrombosis during transition from UKA to LMWH in the first trimester.^[1]

In general, pregnant women will need higher than expected doses of LMWHs to achieve target anticoagulation with an overall mean dose increases to 1.3 mg/kg every 12 h, in comparison with 1 mg/kg every 12 h.^[12]

Low dose aspirin is safe during pregnancy in women with mechanical heart valves if needed for prevention of pre-eclampsia.

In the present study, it is difficult to draw conclusions. It requires multicentric studies to reach out the conclusion so that thoughtful consideration for monitoring anticoagulation levels must be accepted by the mother; heart care team; and maternal fetal medicine team so as to achieve optimize maternal and fetal outcomes. Comprehensive and candid preconception counseling about the risks of pregnancy with a mechanical heart valve is important.

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