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Pregnancy outcomes in patients with cardiac valve replacement

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Abstract
Pregnant women who have mechanical heart valves need anticoagulant therapy. One must consider the danger of bleeding and embryopathy when deciding whether to use oral anticoagulants in comparison to the risk of valve thrombosis. Anticoagulation management is of the utmost importance when managing a pregnant lady who has a prosthetic heart valve. Due to a lack of prospective data, it is not possible to provide precise suggestions for every patient. Managing women of reproductive age with a mechanical heart valve is a significant problem for medical professionals. Warfarin is deemed a safe and efficient anticoagulant for patients with artificial heart valves. Treating a pregnant woman can be challenging, especially in the first trimester, because the medication can pass through the placenta and harm the fetus. Administering Heparin in the first trimester reduces the occurrence of embryopathy but raises maternal morbidity and death.

Keywords: Pregnant women, cardiovascular disease, anticoagulant therapy

Introduction
Cardiovascular disease is a significant medical issue that can occur during pregnancy. It is a prevalent indirect obstetric factor contributing to maternal mortality. Cardiac disease complicates around 1% of pregnancies. The whole care team for the mother and fetus may find it difficult to handle these situations. The cardiovascular system undergoes numerous changes throughout pregnancy. The alterations ultimately result in increased cardiac workload. Pregnancy and heart disease impose significant strain on the heart [1].

There are serious risks to both the mother and the fetus when a woman whose heart has a mechanical valve becomes pregnant. Women who have mechanical valves during their pregnancies are at a much greater risk of complications, according to a modified WHO risk classification III [2]. Maternal mortality or severe morbidity, including but not limited to: prolonged hospitalization (more than one day), heart failure due to valve thrombosis or dysfunction, cerebrovascular accident, or complications with bleeding (intra-abdominal bleeding, vaginal hematoma, wound hematoma, primary postpartum hemorrhage, secondary postpartum hemorrhage) requiring transfusion or return to surgery, were considered poor maternal outcomes [3]. A poor fetal outcome was characterized as any form of pregnancy loss (miscarriage or termination of pregnancy), stillbirth, neonatal mortality, fetal abnormalities, Apgar score below 7 at 5 minutes, or admission to the neonatal unit [4].

Incidence of maternal death
Heart disorders during pregnancy account for 16% of maternal mortality in Egypt. Cardiovascular disease throughout gestation ranks as the fourth most common reason for death in pregnant women., behind hemorrhage, sepsis, and hypertensive conditions. Cardiac disease observed during pregnancy is typically related to heart valves and is commonly caused by rheumatic fever. Rheumatic fever is declining in developed nations but remains a significant issue in the developing world. Immigrants, particularly those without awareness of the hazards associated with heart disease during pregnancy or of any existing cardiac conditions, are considered a high-risk group. Mitral stenosis is the most prevalent abnormality, however its occurrence is decreasing [5].

Cardiac Remodeling during pregnancy
Pregnancy causes a 28% increase in left ventricular wall thickness and a 52% rise in left ventricular wall mass relative to values before pregnancy.

A recent study using cardiac magnetic resonance imaging found a 40% rise in right ventricular mass [6].

Risk assessment

Factors include operation type, valve prosthesis, anticoagulation status, and anticoagulant medication all play a role in the risk of complications during pregnancy in people who have had heart surgery. Symptoms, cardiac function, and functional capacity are other factors that impact the result [7].

Patient factors

At all times, cardiac specialists should be keeping tabs on these patients. Talk to them about how to plan a pregnancy and how to report a missed period as soon as possible. It is crucial to check the woman's obstetric history, confirm the pregnancy with an ultrasound, and verify the pregnancy status with a urine pregnancy test. Assessment of pregnant women with prosthetic heart valves should encompass details regarding her functional capacity before pregnancy, current medication regimen, a comprehensive clinical evaluation, and specifics of the valvular prosthesis [8].

An assessment by a cardiologist using an electrocardiogram (ECG) and an echocardiogram study can aid in assessing the risk related to the heart's condition. Pregnancy, labor, and delivery result in elevated hemodynamic load. Counsel the patient and her family about the high-risk pregnancy status, emphasizing the necessity of regular monthly or every two weeks antenatal visits and the various complications of pregnancy that may arise. [9].

Prosthesis-related factors

Individuals with mechanical heart valves experience a higher frequency of thromboembolic accidents. Device thrombosis is the leading cause of maternal mortality in patients with artificial heart valves. [10].

Drug-related factors

The fetal problems associated with maternal anticoagulant medication are teratogenicity and fetal loss. Using additional cardiovascular medications during pregnancy can also harm the fetal outcome [10].

Valves

Mechanical

Patients with mechanical valves often need to take oral anticoagulants due to the prevalence of these types of valves. Patients choosing to transition to unfractionated heparin (UFH) should do so while under medical supervision because the threat of valve thrombosis is higher [11].

Biological

Tissue valve prosthesis reduces thromboembolism risk and anticoagulant requirements during pregnancy in women of reproductive age, although it is associated with structural valve deterioration (SVD) [12].

Valve Repair

Patients who have undergone valve repair and are in normal heart rhythm do not take oral anticoagulants. However, those who have had balloon mitral valvuloplasty (BMV) should be assessed for their heart condition, focusing on detecting restenosis or moderate regurgitation related to BMV [10].

Anticoagulants and Pregnancy

Oral anticoagulants

The oral anticoagulant drug coumadin, often known as warfarin, was the most widely prescribed after its approval for use in the 1960s. The main difference between phenprocoumon and acenocoumarol (Acitrom), two examples of vitamin K antagonists (VKA), is their half-life [13].

Heparin

Heparin, including both UFH and low-molecular-weight heparin (LMWH), does not pass through the placenta during pregnancy and does not lead to birth defects [10].

Factors such as changing dosage requirements, difficulties in monitoring heparin levels throughout pregnancy, and patient adherence may contribute to the higher rates of maternal cardiac problems and thromboembolic complications (TECs) associated with heparins compared to VKA [14].

Aspirin

Systemic embolism is less common when aspirin is taken. During the second and third trimesters, taking 80-100 mg of aspirin can improve the antithrombotic effects. Physicians and patients should collaborate in making choice on anticoagulation [15].

Maternal Adverse Outcomes

1. **Maternal mortality**

   Maternal mortality is interpreted as death occurring throughout pregnancy and within 1 week following birth [16].

2. **Heart failure**

   Pregnancy's increased physiological requires, such as elevated volume of blood and cardiac output, can lead to the initiation or worsening of heart failure in individuals with ventricular dysfunction or abnormalities with natural or artificial heart valves [10].

   Diuretics do not cause birth defects in babies. Diuretics impact the plasma volume expansion in normal pregnancy but do not have a deleterious effect on fetal growth [17].

3. **Arrhythmia**

   A woman's arrhythmia treatment options are determined by the arrhythmia's severity, duration, and how well it is tolerated. Weighing the possible benefits of the treatment in lowering or preventing arrhythmia against the risks to the mother and fetus is an important aspect of the decision-making process. This is especially true during organogenesis, that typically ends by the end of the first trimester for most organs [18].

   In the acute phase, vagus nerve stimulation or intravenous adenosine can be used to control supraventricular arrhythmias. Any tachyarrhythmia with hemodynamic instability can be safely treated with electrical cardioversion [19]. The main drugs that are suggested to prevent supraventricular tachycardia are digoxin and a selective β-blocker [17].

   Amiodarone is indicated for usage only after other drugs or therapies have been ineffective, and when tachyarrhythmia results in hemodynamic instability. Verapamil and diltiazem, which are calcium channel-blocking medicines, are generally believed to be harmless [20].

4. **Thromboembolic complications**

   Pregnancy is linked to a higher occurrence of thromboembolism such as valve thrombosis, stroke, or transient ischemic episodes due to a hypercoagulable state [10].

   Heparin can be used for tiny, non-obstructive blood clots. Possible therapies for obstructive valve thrombosis include surgical intervention and thrombolysis, both of which pose

significant risks on both the fetus and the mother [10].

5. **Pregnancy induced hypertension (preeclampsia and eclampia)**
   The latest guidelines for hypertension indicate the use of methyldopa, labetalol, and nifedipine (the only calcium channel blockers that have been studied in sufficient detail during pregnancy). It is important to use caution when using β-blockers with diuretics, as the former may retard fetal development, especially in the early phases of pregnancy. To lower the blood pressure of pregnant women, methyldopa should be taken initially [21].
6. **Maternal bleeding complications**
   Major bleeding is defined as bleeding that results in a hemoglobin loss of at least 1 g/dL (or 0.62 mmol/L), requiring a blood transfusion, or causing damage to vital organs such as a hemorrhagic stroke or retinal bleeding. Postpartum hemorrhage is identified by significant blood loss, which is defined as over 500 mL after vaginal delivery or over 1000 mL after cesarean delivery. It can occur right after birth and up to one day after delivery [16].

The incidence of significant blood loss in pregnant women with artificial heart valves was documented to be 2.5%. This risk is comparable in both heparin and warfarin therapy. Warfarin needs to be replaced with heparin around 35–36 weeks of pregnancy to prevent bleeding complications after delivery. Inducing labor or cesarean section should be scheduled around 38 weeks [22].

Fetal Adverse Outcomes

1. Miscarriage is the loss of a woman's pregnancy before 24 weeks.
2. Fetal mortality refers to fetal loss occurring after 24 weeks of gestation [16]. The most common foetal challenge facing pregnancies involving women who have mechanical heart valves is spontaneous abortion [10].
3. Embryopathy:

It is easy for warfarin to pass the placenta. Osteocalcin and matrix Gla protein carboxylation of glutamic acid residues modulates calcium deposition; vitamin K is a cofactor for this process. Anticoagulant medication administered during the initial three months of pregnancy may result in a decrease in osteocalcin and Gla matrix protein production, causing nasal hypoplasia and visible spots on X-rays of nearby growth plate sites (chondroplasia punctata). Exposure during the second and third trimesters can lead to central nervous system and eye issues include optic atrophy, cataracts, blindness, microphthalmia, intraventricular hemorrhage, microcephaly, seizures, and growth/mental retardation. Warfarin embryopathy is most likely to occur from the sixth to ninth weeks of pregnancy. There is a heated dispute around the occurrence of coumarin embryopathy. A correlation between warfarin dosage and fetal problems has been documented [23].

- **Low birth weight:** Birth weight below 2500 grams.
- **Preterm labor:** Delivery prior to 37 weeks of pregnancy. Neonates are susceptible to preterm, cerebral bleeding, and warfarin embryopathy [24].

Management Plan for patients with heart valve replacement during pregnancy

Pregnant women undergoing heart surgery necessitate specialized clinical experience and coordinated care from a team consisting of a cardiac surgeon, cardiologist, obstetrician, and anesthetist. Patients need to be thoroughly informed about the maternal and fetal hazards linked to therapeutic anticoagulation during pregnancy [10].

Pregnancy should be avoided for patients classified as functional class 3 or 4 on the NYHA scale. The safety comparison between surgical and medicinal approaches for terminating a pregnancy due to diagnosed missed abortion is uncertain due to limited information [25]. Surgical approach is favored for its ability to permit the treatment to be completed in a more organized manner to get optimal results. Surgical termination is brief and has a low probability of failure, with the possibility of reducing anesthetic risks by using general anesthesia [26]. Medical abortion appears to be riskier because of pain, severe bleeding, time taking and the potential for failure [27].

Anticoagulation Issues

Candidates for anticoagulation treatment

For patients with artificial heart valves, anticoagulation is a lifelong necessity. Postpartum hypercoagulability requires a larger maintenance dose of oral anticoagulant on a continuous basis [28].

Anticoagulant monitoring during pregnancy

People using oral anticoagulants should have their prothrombin time (PT) tested regularly to check their anticoagulation status. When individuals taking oral anticoagulants have their prothrombin times (PT) standardized using the international normalized ratio (INR), their anticoagulation levels can be consistently assessed. Throughout the initiation phase, monitor 4–5 times weekly; throughout the stable phase, monitor every 4 weeks. During the transition phase, it is important to closely monitor patients and consider concomitant heparin therapy. Estimating the INR may result in an overestimation of the desired amount of oral anticoagulation, therefore regular monitoring is recommended [29].

The anticoagulant impact of unfractionated heparin (UH) can be accurately assessed using the activated partial thromboplastin time (aPTT) test, which is readily accessible. The anticoagulant impact of LMWH is not indicated by the aPTT. Evaluating the action of LMWH involves measuring the antifactor Xa level, a procedure that is not widely accessible [10].

Anticoagulant Management at the time of delivery

Discontinue warfarin at the 36th week and switch to appropriate heparin therapy, with targeted labor induction at the 38th week [30].

Endocarditis prophylaxis

Antibiotic prophylaxis is essential for prevention and should be tailored to the specific procedure the patient will undergo. Prophylaxis must primarily target Enterococcus faecalis by administering ampicillin 2G iv together with gentamycin 80 mg 30 minutes before the surgery, It is advisable to administer a second dose 6 hours following the surgery [10].

Conclusion

In conclusion, managing maternal and fetal outcomes during pregnancy in women with heart conditions, particularly those with artificial heart valves, requires a multidisciplinary approach and careful planning. Maternal adverse outcomes such as maternal mortality, heart failure, arrhythmia, thromboembolic complications, pregnancy-induced hypertension, and maternal bleeding complications need specialized treatments and considerations to balance the health and safety of both the

mother and fetus. This includes cautious use of medications, monitoring of the patient's condition, and timely interventions such as switching anticoagulants closer to delivery.

Fetal adverse outcomes, including miscarriage, fetal mortality, embryopathy, low birth weight, and preterm labor, highlight the necessity for vigilant prenatal care and appropriate management of anticoagulation therapy to mitigate risks associated with warfarin and other medications.

A comprehensive management plan for pregnant women with heart valve replacements involves coordinated care from cardiologists, obstetricians, cardiac surgeons, and anesthetists. Education on the risks of therapeutic anticoagulation during pregnancy is crucial. Specific recommendations include avoiding pregnancy for high-risk patients, regular monitoring of anticoagulation levels, and appropriate prophylactic measures to prevent endocarditis.

Overall, the goal is to ensure the best possible outcomes for both mother and child through careful monitoring, timely medical interventions, and a well-coordinated care team.

Conflict of Interest
Not available

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