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PREGNANCY AND ACCOMPANYING CHRONIC CONDITIONS

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Introduction

The prevalence of chronic conditions, such as cardiovascular diseases, diabetes mellitus, asthma, mental and malignant diseases, is continually increasing worldwide. It is estimated that in developed countries, half of adults over 20 years old have at least one chronic condition. The simultaneous occurrence of two or more chronic conditions, i.e., multimorbidity, is a growing concern for public health, with prevalence increasing from 25% in 2003 to 32% in 2016. In the general population, there is a correlation between the number of chronic conditions and the rate of hospitalization, the risk of death and the magnitude of attributed healthcare costs.

The impact of multimorbidity on maternal outcomes during pregnancy and postpartum is less understood, but it is considered that chronic diseases, especially cardiovascular diseases, chronic hypertension and diabetes mellitus, are major contributors to increased maternal mortality rates and severe maternal morbidity (1).
The number of women suffering from chronic somatic conditions, who desire to become pregnant, become mothers and have children, is constantly increasing. All accompanying chronic conditions create an unfavorable environment for the development of pregnancy, exacerbating complications that arise during pregnancy, childbirth and the postpartum period. Complications from chronic conditions are a key driver of increased obstetric morbidity and mortality worldwide.

The prevalence of accompanying conditions in pregnant patients is quite high. According to the strictiest estimations, accompanying conditions are diagnosed in 15-20% of the patients, while some reports from various obstetric hospitals indicate that up to 70% of pregnant patients have accompanying conditions. It is estimated that even one in five women enters pregnancy with two or more chronic conditions (2).

The most common accompanying conditions include heart diseases, hypertension, renal disease, diabetes mellitus, gastrointestinal tract diseases and hepatobiliary system diseases. Recently, there has been an increase in pregnant patients with malignant diseases.

When existing risk factors from the mother are present, the gestational period can become complex and challenging. Pregnant individuals with pre-existing medical conditions should be closely monitored to reduce the possibilities of complications during pregnancy.

High rates of negative maternal outcomes in women with multimorbidity would indicate the need for improved preventive efforts to address modified risk factors during the preconception period and patient-centered support during the perinatal period.

This presentation will cover accompanying heart diseases in pregnancy as the most common cause of morbidity and mortality, as well as their anesthetic management.

Accompanying Heart Diseases in Pregnancy

Accompanying heart diseases are the most common cause of non-obstetric morbidity and mortality in pregnant patients, accounting for 26.5% of all pregnancy-related deaths. The mortality and morbidity associated with accompanying heart diseases are highest among women of color and those with a lower socioeconomic status. In the past, rheumatic heart disease was the most common form of heart disease in pregnant women and still prevails in some developing countries. However, in developed countries, congenital heart diseases are the most common type of heart disease complicating pregnancy, largely due to advances in the treatment of congenital heart diseases, allowing affected individuals to reach reproductive maturity and attempt pregnancy.

A large American study showed a significant increase in the number of deliveries by mothers with congenital heart diseases from 6.4 to 9 per 10,000 deliveries from 2000 to 2010. These deliveries had a higher-than-expected rate of medical and obstetric complications. Nevertheless, the primary cause of cardiac death during pregnancy is acquired heart disease, including cardiomyopathy, coronary artery disease and aortic disorders. Additionally, more women are delaying childbirth until the fourth and fifth decades of life, which, combined with other accompanying conditions, complicates pregnancy**.**

Congenital Heart Diseases in Pregnancy

Advancements in pediatric cardiac surgery have enabled over 85% of children with congenital heart diseases to reach reproductive maturity. The risk of pregnancy for both the mother and the fetus in this population depends on the anatomical and physiological classification of the type of congenital heart disease, as defined by the American College of Cardiology/American Heart Association (ACC/AHA) guidelines from 2018 for the treatment of adults with congenital heart diseases. The risk of cardiovascular complications during pregnancy and the peripartum period depends on the type of underlying defect, the degree and severity of residual hemodynamic lesions, and comorbidities.

According to the Registry for Pregnancy and Cardiac Diseases (ROPAC), among 5,739 pregnancies in 53 countries from 2007 to 2018, congenital heart disease was the most prevalent form of structural heart disease (57%). The number of high-risk pregnancies increased from 0.7% in the period 2007-2010 to 10.9% in the period 2015-2018 (5).

Pregnant Patients with Congenital Heart Diseases:
Risk and Physiological Changes

Pregnant patients with congenital heart diseases may face an increased risk during individual pregnancies, but if they survive, the overall risk of pregnancy is generally not cumulative. Thus, consecutive pregnancies generally carry the same, not higher, risk, assuming that cardiovascular status remains stable.

The impact of physiological changes during pregnancy, especially circulatory and respiratory physiology, can have detrimental effects on mothers with congenital heart diseases and their developing fetuses. There are two main hemodynamic changes that can influence this: a decrease in systemic vascular resistance and an increase in cardiac minute volume.

Women with pre-existing heart disease are exposed to an increased risk of thromboembolism during pregnancy. A large study involving 688 pregnancies in women with congenital heart diseases showed an incidence of 2% for thromboembolic events, compared to the expected rate of 0.05-0.10% for uncomplicated pregnancies (6).
For all patients with congenital heart disease, an assessment of the risk of pregnancy and childbirth should be conducted. The guidelines from the American College of Cardiology/American Heart Association (ACC/AHA) and the European Society of Cardiology for managing congenital cardiovascular diseases during pregnancy recommend the modified classification of the World Health Organization (WHO) as the best predictive model for cardiovascular risk. The modified WHO classification includes risk based on the mother's cardiovascular condition and provides guidance on the frequency of prenatal cardiology and obstetric monitoring.

The risk for pregnancy is classified into four categories. Category 4 includes conditions associated with very high risk for the mother and/or fetus during pregnancy. These conditions are significant pulmonary arterial hypertension of any cause, severe mitral stenosis, severe symptomatic aortic stenosis, bicuspid aortic valve with aortic diameter >50mm, Marfan syndrome with aortic dilation >45mm, severe systemic ventricular systolic dysfunction (left ventricular ejection fraction <30%, NYHA III-IV) and severe maternal coarctation. Pregnancy is contraindicated in these patients.

In addition to the modified WHO classification, there are other scoring systems for risk assessment and predicting adverse cardiac events in pregnant women. These include CARPREG (Cardiac Disease in Pregnancy) and ZAHARA (Pregnancy in women with congenital heart disease II).

Some experts recommend obtaining levels of brain natriuretic peptide (BNP) during pregnancy in women with congenital heart diseases considered at risk for developing heart failure. An elevated level of NT-proBNP (>128pg/mL) in the 20th week of pregnancy can be an independent risk factor for cardiovascular events during pregnancy in women with congenital heart diseases. A negative BNP is useful to exclude heart failure.

The option of terminating the pregnancy should be discussed with women for whom pregnancy poses a significant risk to either the mother or the fetus**.**

Impaired cardiovascular stability of the mother (Category 4), maternal cyanosis and maternal medications, expose the fetus to risks that jeopardize normal intrauterine growth and development, significantly increasing fetal morbidity and mortality. Offspring of women with congenital heart diseases are also at an increased risk of congenital heart defects.

For women with congenital heart diseases, vaginal delivery is recommended, and cesarean section should be reserved for obstetric indications. Successful operation before pregnancy is crucial for reducing risks to both the mother and the fetus. The risks of pregnancy post-operation are mainly determined by the presence, type and degree of cardiac and vascular residues, as well as their consequences.

Given the heterogeneity of these diseases, individual assessment and appropriate counselling by a specialized adult congenital heart disease specialist are recommended for women with congenital heart diseases who are considering pregnancy**.**

Acquired Heart Diseases in Pregnancy

Women with acquired heart diseases are at risk of cardiac complications during pregnancy. Their risk can be assessed by evaluating the severity of their valvular lesions and the degree of ventricular dysfunction. The most common acquired heart diseases in women of reproductive age include cardiomyopathies, valvular disease, pre-existing coronary artery disease, arrhythmias, prior myocardial infarction, and rarely, patients with a transplanted heart.

In the case of cardiomyopathies, the ventricular dysfunction in these patients can have various etiologies: previous viral infections, HIV infection, peripartum cardiomyopathy, drug-induced cardiomyopathy, or idiopathic causes.

For most of the pregnant women with acquired heart diseases, vaginal delivery is recommended as it poses a lower risk to the heart compared to cesarean section. Cesarean section should be reserved for standard obstetric indications.

Patients with valvular heart disease (VHD) are highlighted as a specific group. Hemodynamic changes during pregnancy, including an increase in heart rate and cardiac output, can result in heart decompensation in women with valvular heart disease (VHD). Generally, stenotic valvular lesions are less well-tolerated during pregnancy compared to regurgitant lesions. The risk of complications varies depending on the type and severity of the underlying VHD.

Whenever possible, women with valvular heart disease (VHD) should undergo a risk assessment and counselling before conception. If already pregnant, a comprehensive risk assessment should be conducted at the first antenatal visit. The most of women with mild forms of VHD will fare well during pregnancy. However, women with mitral stenosis, even in mild cases, face a risk of cardiac complications associated with pregnancy. Those with mechanical heart valves are also at a high risk of cardiac complications related to pregnancy. Women with severe mitral stenosis, symptomatic severe aortic stenosis, and VHD associated with severe left ventricular systolic dysfunction or significant pulmonary hypertension, should be advised to avoid pregnancy due to the high risk of cardiovascular and fetal complications. All patients with moderate or high-risk VHD should be referred to specialized centers for high-risk pregnancy and heart disease.
In general, vaginal delivery with appropriate analgesia/anesthesia is preferred for women with valvular heart disease (VHD). However, in patients with severe valvular lesions (severe aortic stenosis), planned cesarean section is sometimes indicated.

AnestheticTreatment for Pregnant Women with High-risk Cardiovascular Disease

Anesthetic treatment for pregnant women with high-risk cardiovascular disease requires an understanding of the cardiac anatomy and pathophysiology of the individual patient, how the physiological changes associated with pregnancy and childbirth affect the patient, and the hemodynamic changes that can be induced by the choice of analgesic or anesthetic techniques. Understanding the hemodynamic changes during pregnancy and childbirth, allows the anesthesiologist to anticipate decompensation during the birthing period in patients with cardiovascular lesions and to choose appropriate anesthetic monitoring and techniques to minimize this risk. Ideally, an individualized management plan is developed in the period before childbirth by a multidisciplinary team consisting of a gynecologist-obstetrician, cardiologist and anesthesiologist. Interdisciplinary communication and preparation are crucial as peripartum obstetric and cardiac complications may require prompt intervention.

Although the most of pregnant women with cardiovascular diseases experience favorable outcomes, some may undergo a deterioration of cardiopulmonary status before or during childbirth or in the early postpartum period. Plans for emergency situations related to obstetric complications are developed by a multidisciplinary team, involving the planning for emergency cesarean section, postpartum hemorrhage, and management of cardiopulmonary complications or cardiac arrest. In high-risk patients, scheduling induction rather than waiting for spontaneous labor can ensure that appropriate specialists are readily available, but this decision is multidisciplinary. Induction of labor, if needed, is generally safe. Regarding the mode of delivery, vaginal delivery is generally preferred unless there is an obstetric indication for a cesarean section.

"Cardiac Vaginal Delivery" - In maternal "cardiac delivery" with epidural analgesia, fetal descent during the majority of the second stage is achieved solely through uterine contractions without the aid of maternal bearing down. When the fetal head reaches the pelvic floor, an operative vaginal delivery (either forceps or vacuum extraction) is performed. This avoids the physiological changes associated with maternal pushing (Valsalva maneuver or increased intrathoracic pressure resulting in decreased venous return, reduced preload and decreased cardiac output). However, prolonged passive second stage and instrumented vaginal delivery may increase the risk of neonatal injury, perineal trauma and maternal bleeding. Thus, the appropriateness of "cardiac delivery" remains controversial.

The medications commonly used in the delivery room can have various implications in patients with high-risk cardiovascular diseases. It is noteworthy that oxytocin, which is most commonly used in obstetrics, may have effects on blood pressure. Oxytocin reduces mean arterial pressure and total peripheral vascular resistance, potentially causing a slight increase in pressure in the pulmonary artery. These changes need to be considered, and oxytocin must be administered cautiously in patients with specific cardiovascular lesions, as it may lead to unexpected decompensation when the load is reduced. In these patients, oxytocin is administered as a diluted solution through continuous intravenous (iv) infusion using an infusion pump at rates of 2.5–7.5IU/hour or 7.5–15IU/hour for cesarean deliveries. Importantly, oxytocin should not be administered iv as a bolus in patients with cardiovascular diseases.

Maintaining adequate intravascular volume and avoiding dehydration during delivery is crucial. Allowing moderate amounts of clear fluids to be administered during delivery is recommended. Aggressive fluid administration should be avoided, especially in patients with associated preeclampsia**.**

General principles of anesthetic management for a high-risk cardiac patient include:

- Placement of filters on all ivcatheters in every patient with a known intracardiac or extracardiac shunt to prevent paradoxical air embolism.
- Preparation of vasoactive drugs: Bolus ivdoses of phenylephrine and ephedrine should be immediately available, as well as an infusion of phenylephrine. On the other hand, nitroprusside and nitroglycerin are usually avoided immediately after delivery, as these uterine relaxants may lead to uterine atony and postpartum hemorrhage.
- Monitoring: Continuous pulse oximetry during active labor, continuous ECG recording, and continuous arterial blood pressure monitoring are recommended for high-risk cardiac patients during labor. Other invasive cardiovascular monitoring (central venous pressure, transesophageal echocardiography) may be used in selected patients**.**

Analgesia during childbirth:
Non-neuraxial analgesia is considered essential. If neuraxial analgesia is not an option, the advisability of vaginal delivery may need to be reevaluated. During childbirth, neuraxial analgesia is recommended for most of the women with high-risk cardiovascular diseases, specifically epidural analgesia, epidural with dural puncture, or combined spinal-epidural (CSE) with low doses.

The primary physiological benefit of neuraxial labor analgesia in high-risk cardiac patients is the reduction of peaks in cardiac output during labor, as these increases are largely a result of catecholamine release due to pain and anxiety. Therefore, it is best to place the epidural early in labor. Ideally, the epidural block should be dense enough to minimize each successive pain.

For patients in active labor with intense pain, a combined spinal-epidural (CSE) using intrathecal opioids without a local anesthetic in the intrathecal space may have an advantage over just the epidural technique due to a faster onset of analgesia with minimal hemodynamic effects.

Administration of a test dose with epinephrine is avoided in cardiac patients because a small ivdose of epinephrine can result in catastrophic events (e.g., severe tachyarrhythmias or hypertension with cardiovascular deterioration).

Anesthesia for Cesarean section

Neuraxial anesthesia techniques are preferred for most of the patients undergoing Cesarean section, including those with cardiovascular pathology (9).
For the most of high-risk cardiac patients, a low-dose combined spinal-epidural or slowly titrated epidural anesthetic may be the best choice. Benefits of the low-dose combined spinal-epidural (CSE) technique include a faster onset of neuraxial block, allowing the anesthesiologist to adequately maintain preload and additional afterload, while still achieving the reliability of the

intrathecal local anesthetic block. Although there are limited data on deliveries in high-risk cardiac patients with this technique, intrathecal doses of local anesthetics, as opposed to epidural alone, can significantly contribute to good surgical anesthesia. A study involving four patients with high-risk cardiovascular diseases delivered by Cesarean section with CSE showed that CSE was safe and effective. Administration of a low intrathecal dose is followed by slow loading of the epidural catheter with a local anesthetic (e.g., 2% lidocaine without epinephrine) to achieve a surgical level of T6.
Epidural technique for Cesarean section - with or without CSE, the placement of the epidural catheter is followed by titration (3 to 5mL every five minutes) of a substance such as 2% lidocaine. With such titration, along with appropriate monitoring and caution, severe cardiovascular instability is unlikely.

In high-risk cardiac patients, an intra-arterial catheter should be placed before giving epidural anesthesia. Always have a phenylephrine infusion prepared to immediately start titrating phenylephrine to treat hypotension. Other vasopressors should also be ready, although the choice depends on the patient's underlying cardiac abnormality. Moving the uterus to the left immediately after placing the epidural, hydration and rapid fluid overload should be avoided in patients with cardiac weakness. For these patients, reduced crystalloid volumes and slow administration are appropriate during the onset of the block, and the administration of a vasopressor agent may be necessary.
Spinal anesthesia is usually avoided in high-risk patients, primarily due to the rapid onset of sympathectomy with a sudden decrease in systemic vascular resistance and preload, potentially resulting in life-threatening hypotension (severe aortic stenosis, severe mitral stenosis, cyanotic congenital heart disease with right-to-left shunting, severely dilated cardiomyopathies with low ejection fraction, hypertrophic cardiomyopathy).

Some anesthesiologists avoid any neuraxial technique in such highly risky patients. However, carefully and closely monitored epidural anesthesia, or low-dose combined spinal-epidural (CSE) anesthesia for Cesarean section, has been reported to be well-tolerated, even in women with severe aortic stenosis or hypertrophic cardiomyopathy(11).
Occasionally, general anesthesia is required for Cesarean section in patients with high-risk cardiovascular diseases. The pathophysiology and desired hemodynamic goals for the specific cardiovascular lesion of the patient are considered when choosing anesthetic agents. Maintaining the mother's hemodynamic stability is a priority, and for sustaining stability in patients with high-risk cardiovascular diseases, a very slow titration induction is typically indicated. A reasonable approach to induction involves the use of a short-acting hypnotic (etomidate, ketamine, or propofol in divided doses, titrated for effect) with boluses or an infusion of phenylephrine, succinylcholine, and opioids (although opioids are generally avoided in Cesarean sections) for blunting the sympathetic response to laryngoscopy and intubation.

For maintenance of general anesthesia, sevoflurane or desflurane is administered at approximately 1 MAC and nitrous oxide is avoided. Sometimes there is a need for urgent cardiovascular intervention, such as mechanical circulatory support, including veno-arterial extracorporeal membrane oxygenation (ECMO) or insertion of an intra-aortic balloon pump, ventricular assist device, or cardiothoracic surgical procedures.

The intensity of postpartum monitoring is determined based on the patient's underlying cardiovascular disease and any obstetric or cardiac events that occurred during delivery.

Treatment for a birthing woman with high-risk cardiovascular diseases involves a high-risk heart team for pregnancy, consisting of cardiologists, obstetricians and anesthesiologists, working together to develop an individualized treatment plan. Interdisciplinary communication and preparation are crucial because peripartum obstetric and cardiac complications may require emergency intervention.

Anesthetic management for a pregnant woman with high-risk cardiovascular diseases requires a thorough pre-anesthetic evaluation, considerations for monitoring, as well as an assessment of the risks and benefits of neuraxial techniques or general anesthesia. Additionally, methods to minimize the postpartum risk while providing optimal anesthetic care should be implemented.

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