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Pulmonary arterial hypertension in pregnancy

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ABSTRACT

Pulmonary hypertension is a medical condition characterized by elevated pulmonary arterial pressure and secondary right heart failure. Pulmonary arterial hypertension is a subset of pulmonary hypertension, which is characterized by an underlying disorder of the pulmonary arterial vasculature. Pulmonary hypertension can also occur secondarily to structural cardiac disease, autoimmune disorders, and toxic exposures. Although pregnancies affected by pulmonary hypertension and pulmonary arterial hypertension are rare, the pathophysiology exacerbated by pregnancy confers both high maternal and fetal mortality and morbidity. In light of new treatment modalities and the use of a multidisciplinary approach to care, maternal outcomes may be improving.

Introduction

Pulmonary hypertension (PH) is a medical condition characterized by elevated pulmonary arterial pressure and secondary right heart failure. PH commonly occurs secondarily to an underlying medical condition such as heart or lung disease. More rarely, PH can occur as a primary condition and is included in a group of disorders termed pulmonary arterial hypertension (PAH). As the name suggests, PAH is directly caused by an underlying disorder of the pulmonary arterial vasculature. A narrowing of the pulmonary arterial bed occurs due to the "imbalance" of vasoactive mediators such as endothelin-1, prostacyclin, and nitric oxide.[1] A mean pulmonary artery pressure greater than or equal to 25 mmHg at rest defines PH.

PH has recently been reclassified into subgroups by the World Health Organization based on underlying etiology, natural history, and response to treatment[2] (Table). Group 1 is more specifically termed pulmonary arterial hypertension (PAH). This group includes what was known previously as primary PH or idiopathic PH but now also includes related secondary disorders that have a similar clinical course, such as drug-related or those secondary to a connective tissue disease. Although rare, primary or idiopathic PH is a rapidly progressing disease. Mean survival is between 2.8 and 5 years, especially in younger patients.[3–5] PH associated with connective tissue diseases such as lupus or scleroderma also carries a very poor prognosis.[6] Group 1 also includes those patients with congenital heart disease such as a ventricular septal defect (most common), atrial septal defect, or a patent ductus arteriosus. These cardiac defects cause left-to-right shunting of blood flow, leading to chronic overperfusion of the pulmonary vasculature and increased pulmonary arterial pressures. Over time, right heart hypertrophy occurs, eventually leading to reversal of shunting. The right-to-left shunting of deoxygenated blood leads to systemic hypoxemia. This pathophysiology is known as Eisenmenger's syndrome.

PH is a progressive condition that results in right ventricular strain and eventual right heart failure. Increased pulmonary vascular resistance (PVR) and pressure causes an increase in right ventricular afterload. With acute changes of the PVR, the thin-walled right ventricle is challenged to

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Table – Pulmonary hypertension classification.

Group 1	Pulmonary arterial hypertension a. Idiopathic pulmonary arterial hypertension b. Associated with other diseases (such as systemic sclerosis, HIV, schistosomiasis, and portal hypertension) or congenital heart disease c. Drug/toxin induced
Group 2	Pulmonary hypertension due to left heart disease a. Systolic or diastolic dysfunction b. Valvular disease
Group 3	Pulmonary hypertension due to lung disease, hypoxia, or both a. COPD b. Sleep apnea c. Interstitial lung disease d. Chronic exposures to high altitude
Group 4	Chronic thromboembolic pulmonary hypertension
Group 5	Unclear/multifactorial mechanism

accommodate the increased cardiac output, and this leads to acute right heart failure. In chronic PH, the right ventricle hypertrophies lead to increased oxygen consumption, poor contractility, and again eventual failure. The right ventricular malfunction also affects the left ventricular filling, causing a decreased cardiac output and oxygen delivery.[7]

Pregnancies affected by PH are rare with an incidence of 1.1/100,000 women.[8] Recently, pregnancies affected by PH have seen an improvement in survival due to newer treatment modalities and the utilization of a multidisciplinary approach to treatment. Despite these improvements, the consequences of PH are exacerbated by the physiologic changes of pregnancy, which contribute to a high maternal mortality reaching 30–56%.[9] Unfortunately, fetal risks are also high with an increased risk of growth restriction, increased risk of preterm delivery, and increased perinatal mortality.[10] Given the poor maternal and fetal outcomes, women with a diagnosis of PH are encouraged to use highly effective contraceptive methods and in the case of a pregnancy to strongly consider an early termination. Women who choose to continue a pregnancy in this high-risk setting should be cared for in a tertiary care center under the supervision of a multidisciplinary team with strong critical care team support.

Physiologic changes of pregnancy and effects of pulmonary arterial hypertension

Every organ system is affected by the physiologic changes of pregnancy. The cardiovascular system is especially burdened by an increase in blood volume up to 50%, peaking at 32 weeks of gestation with 4700–5200 ml.[3] Both heart rate and stroke volume are increased in pregnancy, resulting in an increased cardiac output by 30–50% by the early third trimester.[3] To compensate for this increased blood flow requirement, progesterone and other mediators with vasodilatory properties cause a decrease in both pulmonary vascular resistance and systemic vascular resistance. Unfortunately, in women with existing pulmonary arterial hypertension, the underlying pulmonary vascular disease hinders the normal pulmonary vasodilatary mechanisms in pregnancy. There are abnormal responses to vasoactive substances including progesterone. This leads to a paradoxical increase in pulmonary arterial pressures in these women as cardiac output increases. This dangerous combination of increased cardiac output demand and increased pulmonary vascular resistance leads to right heart failure. Furthermore, progesterone effects also increase the tidal volume, causing a mild respiratory alkalosis and a decreased functional residual capacity.[7] Most morbidity and mortality from PH occurs in the second and early in the third trimester and immediately postpartum, when hemodynamic changes are at the greatest.

Peripartum and postpartum changes

Labor may involve fluid shifts that increase the cardiac output, causing increased strain on the right heart and the pulmonary vascular bed.[11] This poses a problem to women who have difficulty in increasing their cardiac output. Similar to during pregnancy, the postpartum period is also complicated by significant hemodynamic changes. Both cardiac output and stroke volume increase after delivery while the heart rate decreases by 15%.[12] After delivery the uteroplacental blood flow shifts into the intravascular space, which is largely responsible for the resultant increase in both cardiac output and stroke volume. The relief of uterine compression on the vena cava increases the cardiac preload as well. Additionally, hemodynamic alterations occur with blood loss, approximately 500 ml in a vaginal delivery and 1000 ml in a cesarean delivery, which causes a decrease in preload. Lastly, there is a quick increase in the systemic and pulmonary vascular resistance immediately after delivery. These hemodynamic changes are only a few that make postpartum management difficult in patients with PH.[7]

Clinical presentation

Unfortunately, normal pregnancy-related symptoms may mask the presenting symptoms of PH. Notably, fatigue and shortness of breath are the most common symptoms. Chest pain from myocardial ischemia may be present.[13] Right-sided heart failure may cause increased dizziness, syncope, and edema of the lower extremities.[13]

Management in pregnancy

Thromboembolic/hypercoagulable state

Pregnancy is a hypercoagulable state due to a multitude of factors. Physically, the enlarged uterus causes increasing compression of the iliac veins and the vena cava, leading to venous stasis. Hormonal changes such as increased progesterone also increase venous stasis via their vasodilatory effects. Additionally, there are hematologic changes that exacerbate the hypercoagulable state, such as an increase in clotting factors, a resistance to activated protein C, and a decrease in protein S.[14] Also, fibrin is decreased in the setting