DOI: https://doi.org/10.17816/rmmar643161

Pulmonary Hypertension in Pregnancy

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ABSTRACT

Pregnancy complicated with pulmonary hypertension is a severe and dangerous condition. Due to changes in the maternal cardiovascular system, the symptoms of pulmonary hypertension during pregnancy may be more severe compared with those in non-pregnant women. This review describes effective treatment methods, including preconception counseling and monitoring, overall care, labor and postpartum care, contraception, maternal and fetal outcomes, and principles of diagnostics and management. The review was performed in line with the PRISMA guidelines across eLibrary and PubMed databases in 2024. The search queries were легочная артериальная гипертензия у беременных (pulmonary hypertension in pregnancy), осложнения беременности и родов при легочной артериальной гипертензии (complications of pregnancy and labor in pulmonary hypertension), прегравидарная подготовка у пациенток с легочной артериальной гипертензией (preconception care in patients with pulmonary hypertension), контрацепция у пациенток с легочной артериальной гипертензией (contraception in patients with pulmonary hypertension), анестезия при родоразрешении беременных с легочной артериальной гипертензией (anesthesia in labor in pregnant women with pulmonary arterial hypertension). The review included the studies of any design published in these databases over the past decade. The initial search identified 235 articles, yielding 89 titles after removal of duplicates, abstracts, and summaries without an available full-text version. After removal of 56 articles that did not meet the inclusion criteria, 33 full-text articles were analyzed and included in the review. It was found that pulmonary hypertension in pregnancy is a rare condition associated with a high complication rate and mortality. The study data obtained in recent years demonstrate better survival rates in the patients with such condition. The management and delivery of pregnant women with comorbid pulmonary hypertension are difficult. For successful outcomes, they require a personalized and multidisciplinary approach. All women with pulmonary hypertension should avoid pregnancy due to the high risk of maternal mortality. Close maternal and fetal observation by a multidisciplinary team during pregnancy and labor is recommended in case of pregnancy maintenance. There is no current consensus on drug and dose selection for women with pulmonary hypertension. The choice of the abortion time, labor time, and anesthesia is based on individual needs and risk assessment. The possible association between pulmonary hypertension and pre-eclampsia deserves special attention and further study.

Keywords: pregnancy; pulmonary hypertension; maternal mortality; risk assessment; pre-eclampsia; pregnancy maintenance; abortion.

To cite this article
Rudaeva EV, Mozes VG, Kashtalap VV, Elgina SI. Pulmonary Hypertension in Pregnancy. *Russian Military Medical Academy Reports*. 2025;44(1):103–112. DOI: https://doi.org/10.17816/rmmar643161

Received: 18.12.2024 **Accepted**: 19.01.2025 **Published**: 31.03.2025

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УДК 616.131-008.331.1-055.26
DOI: https://doi.org/10.17816/rmmar643161

Легочная гипертензия при беременности

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АННОТАЦИЯ

Беременность, осложненная легочной артериальной гипертензией, является тяжелым и опасным состоянием. Изменения в сердечно-сосудистой системе матери предполагают, что легочная артериальная гипертензия во время беременности может проявляться более тяжелыми симптомами по сравнению с таковыми у небеременных. В данном обзоре освещены эффективные методы лечения, включая консультирование и мониторинг на прегравидарном этапе наблюдения, общий уход, роды и послеродовый период, вопросы контрацепции, исходы для матери и плода, принципы диагностики и ведения. Проведен обзор литературы в соответствии с рекомендациями PRISMA. Обзор публикаций проведен в 2024 г. в базах eLibrary и PubMed. Использовались следующие поисковые запросы: «легочная артериальная гипертензия у беременных», «осложнения беременности и родов при легочной артериальной гипертензии», «прегравидарная подготовка у пациенток с легочной артериальной гипертензией», «контрацепция у пациенток с легочной артериальной гипертензией», «анестезия при родоразрешении беременных с легочной артериальной гипертензией». В обзор включены исследования любого дизайна, опубликованные в указанных базах за последние 10 лет. Первично было отобрано 235 работ, из которых после удаления дубликатов, тезисных публикаций и резюме статей без доступной полнотекстовой версии осталось 89. После удаления 56 статей, которые не соответствовали критериям включения, было проанализировано 33 полнотекстовых статей. Установлено, что легочная артериальная гипертензия во время беременности встречается редко и связана с высокой частотой осложнений и летальности. Получены данные об улучшении выживаемости таких пациенток в последние годы. Беременные с сопутствующей патологией в варианте легочной артериальной гипертензии сложны в ведении и родоразрешении, требуют индивидуального и мультидисциплинарного подхода для достижения успешных результатов. Все пациентки с легочной артериальной гипертензией должны избегать беременности ввиду высокого риска материнской смертности. При пролонгировании беременности показано тщательное наблюдение за матерью и плодом во время беременности и в родах многопрофильной командой специалистов. В настоящее время нет единого мнения по выбору лекарств и дозировки для женщин с легочной артериальной гипертензией. Сроки прерывания беременности, родов и выбор анестезии обусловлен индивидуальными потребностями и оценкой риска. Потенциальная связь между легочной артериальной гипертензией и преэклампсией заслуживает особого внимания и дальнейшего изучения.

Ключевые слова: беременность; легочная артериальная гипертензия; материнская смертность; оценка риска; преэклампсия; пролонгирование беременности; прерывание беременности.

Как цитировать

Рудаева Е.В., Мозес В.Г., Кашталап В.В., Елгина С.И. Легочная гипертензия при беременности // Известия Российской военно-медицинской академии. 2025. Т. 44, № 1. С. 103–112. DOI: https://doi.org/10.17816/rmmar643161

Рукопись получена: 18.12.2024 **Рукопись одобрена:** 19.01.2025 **Опубликована:** 31.03.2025

ЭКО•ВЕКТОР

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INTRODUCTION

The incidence of cardiovascular disease during pregnancy continues to increase and is one of the most common causes of maternal mortality. Pulmonary arterial hypertension (PAH) is a high-risk pathology associated with a 3-year mortality rate and an incidence rate of 55%. PAH is extremely rare, treatment-resistant, and more frequently affects women, particularly those of reproductive age. In a recent review of cardiac diseases during pregnancy, PAH accounted for only 1% of cases but had the highest mortality rate. Advances in pulmonary vasodilator therapy, combined with earlier recognition and treatment of conditions such as congenital heart disease (CHD), have improved life expectancy, enabling most affected women to reach reproductive age [1].

Pregnancy induces physiological changes in the cardiovascular system, including a 45% increase in circulating blood volume and cardiac output, decreased systemic vascular resistance, and heightened maternal volume receptor sensitivity and sympathetic activation, resulting in a 25% increase in heart rate [2].

Hemodynamic changes during pregnancy are influenced by hormonal shifts; progesterone activates the renin–angiotensin–aldosterone system, which leads to sodium retention and volume expansion, inducing additional strain on the cardiovascular system [3].

The physiological effects of pregnancy on pulmonary circulation are similar to those observed in systemic circulation under normal conditions. Increased progesterone levels promote pulmonary vasodilation and recruitment of previously unperfused pulmonary arterioles. In PAH, the thin-walled and compliant pulmonary vasculature becomes thickened and chronically vasoconstricted. These maladaptive pulmonary arteries are unable to accommodate increased cardiac output and plasma volume, resulting in further increase of pulmonary vascular resistance (PVR) and right ventricular (RV) deformation, making the RV susceptible to ischemia and failure. Consequently, left ventricular dysfunction may occur due to interventricular dependence and compression related to cardiac chamber remodeling. In PAH, the most critical period before delivery is between 20 and 30 weeks of gestation, when cardiac output peaks. During labor, sympathetic stimulation related to pain, fluid shifts, and changes in intrathoracic pressure from the Valsalva maneuver in the second stage further increases PVR. This may cause rapid preload-dependent RV changes, potentially leading to catastrophic cardiovascular collapse [1–3].

In pregnant patients with PAH, the risk of RV failure significantly increases during labor and the early postpartum period, influenced by physiological changes in pressure and volume in the cardiovascular system. During labor, each uterine contraction displaces up to 500 mL of blood into the maternal circulation, increasing circulating blood volume, cardiac output, and arterial pressure by up to 25%. In the postpartum period, cardiac output may further increase due to autotransfusion from uterine involution and reabsorption of physiologic edema from the lower extremities. Additional cardiovascular strain may be caused by obstetric bleeding, anesthesia, analgesia, or purulent-septic complications. Mortality risk in PAH is highest immediately postpartum, whereas normalization of physiological parameters may take 3–6 months [3].

This study aimed to analyze the available literature on optimizing management of pregnant patients with PAH.

METHODS

The study was conducted in two stages. The first stage involved a literature search in *eLIBRARY.RU* and *PubMed*. The following search queries were used: легочная артериальная гипертензия *у* беременных *(pulmonary arterial hypertension in pregnancy)*, осложнения беременности *и* родов при легочной артериальной гипертензии *(pregnancy and delivery complications in pulmonary arterial hypertension)*, прегравидарная подготовка *у* пациенток *с* легочной артериальной гипертензией *(preconception care in patients with pulmonary arterial hypertension)*, контрацепция *у* пациенток *с* легочной артериальной гипертензией *(contraception in patients with pulmonary arterial hypertension)*, and анестезия при родоразрешении беременных *с* легочной артериальной гипертензией *(anesthesia for delivery in pregnant women with pulmonary arterial hypertension)*. Studies of any design published in the specified databases over the past 10 years were reviewed. Initially, 235 publications were identified. After removing duplicates, conference abstracts, and article summaries without full-text availability, 89 publications remained.

The second stage comprised reviewing the publications and excluding those that did not meet the inclusion criteria. Eligible studies addressed the management of patients with PAH during preconception care, pregnancy, labor, and the postpartum period and those examining the feasibility of pregnancy and contraception in this population.

RESULTS

Pathophysiology and Classification

When the pathological cycle of PAH begins, it becomes difficult to interrupt. Three primary processes contribute to increased PVR: sustained pulmonary vasoconstriction; cellular proliferation within the intimal, medial, and adventitial layers of the pulmonary vasculature; and in situ thrombosis that impedes pulmonary capillary flow. Consequently, vascular remodeling reduces the availability

of endogenous vasodilators, namely, nitric oxide and prostacyclin, while promoting overexpression of endothelin-1, a potent vasoconstrictor. These changes lead to RV dilation, increased afterload, and abnormal ventricular remodeling. Ultimately, RV dysfunction and failure develop, which are the principal survival determinants in PAH. An adaptive mechanism that may counteract these changes is preserved RV function. In the absence of therapy for PAH, the RV cannot compensate for the increased venous return, which leads to its dilation [4].

According to the 2022 Russian clinical guidelines for pulmonary hypertension, including chronic thromboembolic pulmonary hypertension, PAH (or pulmonary hypertension [PH]) is a hemodynamic and pathophysiological condition characterized by a mean pulmonary arterial pressure (mPAP) ⩾25 mmHg at rest, measured by right heart catheterization. In 2022, the European Society of Cardiology (ESC) and European Respiratory Society (ERS) updated their clinical guidelines and defined PAH as mPAP >20 mmHg. Additional diagnostic criteria include a pulmonary artery wedge pressure ⩽15 mmHg and PVR >2 Wood units [5].

The disease corresponds to risk category 4 in the modified World Health Organization (mWHO) classification for cardiovascular complications in pregnant women with heart disease. It is associated with high maternal and perinatal mortality; therefore, pregnancy is contraindicated in patients with PAH. Although advancements in PAH therapy have led to decreased maternal mortality, the rate remains high, requiring a highly individualized approach in managing such pregnancies [4, 6, 7].

In an analysis of 125 pregnancies in women with PAH between 1978 and 1996, maternal mortality was 36% in those with Eisenmenger syndrome, 30% in those with primary PAH, and 56% in those with secondary PAH [8]. Over the past decade, maternal mortality in patients with PAH has decreased to 3.6%–7.2%; however, the highest rates are still observed in patients with Eisenmenger syndrome and secondary PAH. Considering the high risk of adverse outcomes, pregnancy is contraindicated in patients with PAH. Upon diagnosis, pregnancy termination or early delivery should be considered based on gestational age and maternal condition [8].

Despite these risks, the number of pregnancies in women with PAH has increased in recent years. This is primarily attributed to improved treatment options, which have enabled more women with PAH to survive into reproductive age [2, 9].

Moreover, there has been an active search for predictors of adverse outcomes to enable individualized risk assessment in patients with PAH. This is particularly relevant for pregnant women with PAH because it helps estimate the possibility of maternal and fetal complications and informs clinical management strategies. In addition to well-established risk factors, predictors of poor outcomes in PAH include first pregnancy (odds ratio [OR], 3.70; 95% CI, 1.15–12.5; p=0.03), general anesthesia use (OR, 4.37; 95% CI, 1.28–16.5; p=0.02), rapid progression of PAH-related syndromes (OR, 3.044; 95% CI, 1.042–8.895; p <0.05), brain natriuretic peptide plasma level ⩾300 pg/mL (OR, 5.543; 95% CI, 1.403–21.896; p <0.05), severe PH with mPAP ⩾80 mmHg (OR, 6.769; 95% CI, 2.748–16.677; p <0.05), mWHO functional class 3–4 (OR, 6.053; 95% CI, 2.638–13.886; p <0.05), and a history of pulmonary hypertension prior to pregnancy (OR, 5.434; 95% CI, 1.298–22.738; p <0.05). However, these predictors were identified in studies with small sample sizes [10].

In addition, systolic pulmonary arterial pressure has been recognized as an independent risk factor, with a threshold value of 56 mmHg. In a multivariate analysis of 249 pregnant women (214 with PAH and 35 with PH due to left heart disease), preexisting PH, delivery at ⩾28 weeks of gestation, and severe disease with pulmonary arterial pressure >80 mmHg were identified as independent predictors of cardiac complications [7, 10].

Preconception Counseling

Preconception counseling is critical in managing women of reproductive age with PAH, as it directly contributes to risk mitigation. Patients with PAH should be advised to use reliable and safe contraception; however, difficulties may be encountered in clinical practice. Combined hormonal contraceptives are associated with increased risk of venous thromboembolism (VTE) and may be used only in patients with PAH receiving anticoagulant therapy. Progestin-only contraceptives, which are recommended for this population, involve risks. In a meta-analysis by Mantha et al. in 2012 (8 randomized controlled trials), injectable progestins were associated with a twofold increased risk of VTE compared with oral formulations, indicating the need for further research regarding their safety. Additionally, patients using progestin-only contraceptives and receiving bosentan—an endothelin receptor antagonist—should use additional contraception methods because the drug decreases the area under the curve of estrogen and progesterone concentrations by 14% and 31%, respectively [1, 3, 7].

Insertion of intrauterine contraceptive devices may cause vasovagal reactions, which can result in serious adverse events such as acute reductions in cardiac output and cardiovascular collapse in women with PAH. Barrier methods are unreliable, and sterilization, although effective, is irreversible and carries anesthetic risk [7].

Women with PAH who are planning to get pregnant should undergo genetic screening and counseling, as recommended by the 2022 Russian clinical guidelines on the management of normal pregnancy and ESC/ERS clinical practice guidelines. If a patient has heritable PAH and

BMPR2 gene mutation is identified, the risk of the child inheriting this mutation and developing PAH should be discussed with her. Moreover, it is crucial to consider the etiology of PAH in women who are planning pregnancy or are already in early gestation, as treatment of the underlying disease may involve drugs with teratogenic effects [11].

If PAH is diagnosed or suspected, patients should be referred to a specialized cardiology center for further evaluation and treatment. The multidisciplinary team should comprise obstetrician–gynecologists, cardiologists, and anesthesiologist–intensivists. During labor, these patients require the involvement of hematologists, cardiac anesthesiologists, intensive care specialists, neonatologists, and extracorporeal membrane oxygenation (ECMO) teams. Antenatal anesthetic planning should include documentation for planned and emergency deliveries.

Terminating pregnancy in patients with PAH may be decided at any stage of gestation [12–14]. Medical termination of pregnancy in the first trimester of pregnancy is considered the safest. It is critical that women are part of the overall decision-making process during counseling. Patients who decide to continue the pregnancy require regular follow-up by a cardiologist in collaboration with an obstetrician–gynecologist, with increasing frequency as gestation progresses [15].

Diagnosis

Functional status is a crucial component of assessment. The World Health Organization functional class (WHO-FC) is the most reliable prognostic indicator of survival in PAH, and any deterioration in functional status should prompt immediate evaluation. Other prognostic indicators include the 6-minute walk test, which is simple to perform and interpret. Additionally, it is recommended to assess perceived exertion using the Borg scale at the end of the test [14, 15].

Brain natriuretic peptide (BNP/NT-proBNP, a peptide hormone and its inactive N-terminal fragment) is the most commonly used biochemical marker in PAH. BNP levels typically double during pregnancy but usually remain within the normal range, making BNP an indicator of worsening cardiac function. Although no specific biochemical marker for PAH has been identified, BNP remains the most prognostically informative biomarker [12, 14].

Transthoracic echocardiography (TTE) is the first-line noninvasive test for PH diagnosis. Doppler measurements and the modified Bernoulli equation are used to calculate tricuspid regurgitation velocity and estimate PAP in suspected PH. Tricuspid valve blood flow velocity and other TTE parameters are used to evaluate the probability of PH [9, 15]. Regular TTE monitoring is crucial for evaluating PAH-related outcomes, including right atrial and RV function, the degree of tricuspid regurgitation, and left ventricular remodeling and dysfunction. These findings support treatment planning and delivery management in comprehensive care. The frequency of echocardiographic assessment increases in the third trimester, depending on the patient's functional status, and is performed by a cardiologist [15].

In most patients, PAH is diagnosed before delivery. Diagnosis may be challenging because symptoms are often nonspecific and subtle, leading to delayed recognition. Particular attention should be given to pregnant women with a family history or comorbidities such as coronary artery disease, HIV infection, or connective tissue disease. Caution should be exercised in patients complaining of excessive exertional dyspnea, fatigue, or signs of right heart failure. These patients should be urgently referred to specialized cardiology centers for further evaluation.

Electrocardiography (ECG) may be normal, particularly in mild cases of PAH. In more severe cases, ECG may show RV dilatation and hypertrophy or supraventricular arrhythmias such as atrial fibrillation or atrial flutter. Ventricular arrhythmias rarely occur in PAH. The diagnostic workup include identifying the presence, severity, and etiology of PH and evaluating the extent of right heart dysfunction [13, 15].

According to ESC/ERS guidelines, echocardiographic assessment of PH probability should include findings from at least two different categories (types A and B). Structural abnormalities observed on TTE in severe PAH include RV hypertrophy, right atrial enlargement, tricuspid regurgitation, and interventricular septal displacement. Moreover, echocardiography allows differentiation between PH and PAH with CHD findings and for excluding signs of left heart disease. To exclude lung diseases or thromboembolic diseases, spirometry and ventilation-perfusion (V/Q) scanning or pulmonary computed tomography angiography should be performed [16, 17].

Right heart catheterization remains the gold standard for diagnosing PAH. It allows for establishing the diagnosis, assessing disease severity, and determining therapeutic interventions. Particularly, it is useful in patients with mixed-etiology PH, which is common especially in CHD. The risk of complications from catheterization during pregnancy is low when performed at specialized cardiology centers. To minimize fetal radiation exposure, appropriate shielding should be employed, fluoroscopic exposure should be limited to focused areas, and radial artery access should be preferred over femoral access to avoid pelvic irradiation [1, 3, 16, 18].

Treatment Methods

Targeted therapies have improved the survival and life expectancy of patients with PAH. These therapies act on three biological pathways. Endothelin-1 causes

vasoconstriction of the vascular smooth muscle by binding to endothelin-A receptors. Bosentan, ambrisentan, and macitentan are widely used endothelin receptor antagonists. However, they are contraindicated in pregnancy owing to teratogenicity and their category X classification [3, 7, 13].

The nitric oxide and prostacyclin (PGI_2) pathways are downregulated in PAH, resulting in decreased production of cyclic guanosine monophosphate and cyclic adenosine monophosphate (cAMP), respectively. This promotes vasoconstriction and abnormal cellular proliferation. Phosphodiesterase-5 (PDE5) inhibitors target the nitric oxide pathway. Studies have recommended sildenafil, an oral selective PDE5 inhibitor, as a first-line agent in pregnant patients with WHO-FC1/2 and preserved RV function. Studies have shown that sildenafil improves exercise capacity and hemodynamic parameters and is available in a parenteral formulation. Riociguat, a newer drug that also targets the nitric oxide pathway, is contraindicated during pregnancy [4, 6, 13].

Prostacyclin analogs target the PGI_2 pathway. These agents are administered parenterally (epoprostenol), via inhalation (iloprost), or subcutaneously (treprostinil). Studies have demonstrated that epoprostenol improves symptoms and physical capacity and decreases mortality in nonpregnant patients with idiopathic PAH. Initiating therapy is decided by a cardiologist, with the primary goal of preserving RV function. Epoprostenol has a short half-life (3–5 min), and abrupt discontinuation can lead to a rebound effect. Treatment requires long-term tunneled venous access and should be administered with caution owing to the risk of septic complications. Inhaled iloprost has been successfully used during pregnancy; however, its requirement for multiple daily doses may be inconvenient for patients. Another concern with epoprostenol is increased risk of bleeding due to inhibition of platelet aggregation. There have been reports of wound hematomas, thrombocytopenia, and severe postpartum hemorrhage associated with epoprostenol use during pregnancy in patients with PAH. No cases of neuraxial hematoma during regional anesthesia have been reported [3, 16].

In addition to targeted therapy, antenatal care includes risk assessment of anticoagulation therapy. Idiopathic PAH is associated with an increased risk of thrombosis. Evidence indicates improved survival when such patients are treated with anticoagulants. Conversely, patients with Eisenmenger syndrome are at a higher risk of bleeding due to intrinsic deficiencies of vitamin K-dependent clotting factors and a predisposition to thrombocytopenia. Therefore, anticoagulant therapy in pregnant patients with PAH requires individualized risk assessment. Patients receiving warfarin or direct oral anticoagulants should be switched to low-molecular-weight heparin [19–21].

Decompensated right ventricular failure in patients with PAH results in fluid retention, increased central venous pressure, hepatic venous congestion, ascites, and peripheral edema. Diuretic therapy may be used carefully when needed to avoid adverse fetal effects. Furosemide is the first-line agent, whereas spironolactone is contraindicated in pregnancy owing to its teratogenicity. When diuretics are used, renal function and serum biochemistry should be closely monitored to detect hypokalemia and prerenal insufficiency [20, 21].

Iron deficiency is common in patients with PAH. Anemia should be corrected and monitored to optimize the oxygen-carrying capacity of blood [13, 20, 21].

Delivery

According to expert consensus, cesarean section is preferred for pregnant patients with PAH; however, supporting evidence is limited. The advantages of cesarean delivery over vaginal birth include avoidance of physiological stressors associated with labor, particularly pain-induced catecholamine release and the Valsalva maneuver. These stressors may be mitigated through epidural anesthesia and operative vaginal delivery. Several case series have reported successful vaginal births in patients with PAH. However, in primigravidas with severe PAH, the risk of maternal decompensation during prolonged labor induction should be considered. The mode of delivery should be individualized based on obstetric and perinatal indications, PAH severity, and patient preference. When vaginal delivery is planned, scheduled induction facilitates timely cessation of anticoagulation therapy, appropriate monitoring, neuraxial anesthesia, and timely cesarean section if warranted [14, 21, 22].

Several medications, diagnostic procedures, and therapeutic interventions are not readily available in delivery units, and transfer to the intensive care unit may be delayed in the event of sudden maternal or fetal deterioration. Delivery in a tertiary care center by a multidisciplinary team is optimal for these patients, ensuring prompt operative delivery or medical intervention, including ECMO if needed [7, 22].

The optimal timing of delivery is considered to be at 34 weeks of gestation; however, individual clinical scenarios may require a personalized approach. PAH during pregnancy is associated with a high risk of preterm birth and an increased incidence of neonatal complications. The timing of delivery should balance the maternal risk of clinical deterioration with the benefits of pregnancy prolongation for neonatal outcomes [22, 23].

Intrapartum hemodynamic goals include preventing increases in pulmonary vascular resistance and RV afterload while maintaining systemic vascular resistance. This requires preventing hypoxia, hypercapnia, acidosis, elevated airway pressures, and pain. Nonpharmacologic strategies should include supplemental oxygen

and careful fluid management to avoid volume overload. Furthermore, oxytocin should be administered in a concentrated solution to reduce the risk of fluid overload during labor induction [6, 23].

Neuraxial anesthesia is the recommended method for vaginal delivery and cesarean section in patients with PAH. Slowly titrated epidural analgesia initiated before labor induction minimizes hemodynamic instability, relieves pain, and allows a smooth transition to regional anesthesia for cesarean delivery if required. Alternative analgesic modalities, such as nitrous oxide and patient-controlled opioid analgesia, should be avoided owing to risk of increased circulating blood volume and potential worsening of hypoxia and hypercapnia [24, 25].

Adequate regional anesthesia for cesarean delivery requires a dermatomal block to the T5 level. Single-shot spinal anesthesia is contraindicated in patients with PAH because of the risk of rapid hemodynamic shifts, particularly vasodilation, which may impair RV perfusion. Epidural anesthesia allows for cautious titration but may not provide sensory blockade required for cesarean section. Combined spinal and epidural anesthesia is considered favorable because low-dose spinal anesthesia achieves a denser block without the risk of rapid hemodynamic instability [24, 25].

General anesthesia may be required in cases of cardiopulmonary decompensation or ongoing anticoagulation. However, it may result in impaired cardiac contractility, increased heart rate due to laryngoscopy, decreased preload, and increased PVR due to positive-pressure ventilation. General anesthesia further reduces functional residual capacity and causes atelectasis, thus worsening hypoxia and hypercapnia. Bedard et al. showed that pregnant patients with PAH who received general anesthesia were four times more likely to die compared with those who received regional anesthesia. Conversely, Bonnin et al. described a case series demonstrating favorable outcomes with general anesthesia, although the number of cases was small [26, 27].

Continuous ECG and pulse oximetry monitoring should be maintained throughout labor. Invasive blood pressure monitoring through intra-arterial catheter and central venous access is recommended. The use of pulmonary artery catheters (PACs) remains controversial owing to well-documented associated risks. There have been reports of uncomplicated PAC use, allowing for direct measurement of pulmonary pressures and therapeutic adjustment. However, placement of PACs may be challenging in patients with RV dilation or CHD, but can be employed in selected clinical cases [28].

The use of uterotonic agents in pregnant patients with PAH may affect PVR, decrease systemic vascular resistance, and induce tachycardia, potentially precipitating acute cardiovascular collapse. Large bolus doses of oxytocin should be avoided; oxytocin should be administered by slow intravenous infusion with continuous cardiovascular monitoring until adequate uterine tone is achieved. Carry et al. presented two cases of maternal death associated with bolus administration of oxytocin. Carboprost, a prostaglandin F2α analog, increases PVR and thus should be avoided. Ergometrine is also not recommended because of its hypertensive effect. Nonetheless, the use of uterotonics in pregnant patients with PAH should not be contraindicated in cases with a high risk of postpartum hemorrhage. Misoprostol is safe to use, although it is less effective in managing postpartum bleeding. The use of specific uterotonic agents should be determined ahead in the event of postpartum hemorrhage, with early consideration of hysterectomy [23, 29].

The primary goal of hemodynamic support is to minimize PAR and preserve RV function. Pulmonary vasodilators such as prostacyclin analogs should be continued during labor. Low-dose dobutamine may be administered for additional inotropic support. Adverse effects include peripheral vasodilation and tachyarrhythmias. Milrinone has inodilatory properties, but is more difficult to titrate. Its adverse effects include vasoplegia and renal insufficiency. Low-dose epinephrine improves RV contractility, but may increase myocardial oxygen demand and cause tachyarrhythmias at higher doses. Norepinephrine is used to preserve RV perfusion by counteracting the vasodilatory effects of neuraxial and inodilatory agents. At low doses, norepinephrine has minimal impact on pulmonary circulation and is associated with more favorable fetal outcomes than other vasopressors. Phenylephrine should be avoided for patients with PAH because it may worsen PVR. Vasopressin induces potent systemic vasoconstrictive effects with minimal influence on pulmonary circulation and has been successfully used postpartum in cases of clinical deterioration due to idiopathic PAH. However, it should be administered with caution before delivery owing to its potential uterotonic effect [30, 31].

There are no unified guidelines for ECMO use in pregnant patients with PAH. The decision to perform ECMO depends on right heart dysfunction severity and its functional status. ECMO should be considered in cases of acute decompensation and in heart–lung transplantation. In cases of clinical decompensation, venoarterial ECMO is most commonly used for ventricular failure. This may involve micropuncture cannulation and placement of ECMO on standby prior to attempted vaginal delivery, with ECMO ready for immediate initiation in the event of acute decompensation. However, the heparinization required for ECMO complicates neuraxial anesthesia use. Additional risks include thrombosis, hemorrhage, and lower limb ischemia. ECMO has been reported in six patients with PAH, none of whom survived beyond 3 months

postpartum. A later systematic review described a 50% survival rate among 28 patients with PAH. Clinical report studies describing ECMO use in this population are limited. Nonetheless, hospitalization in specialized cardiology centers with ECMO capability should be considered for such patients [31, 32].

An acute pulmonary hypertensive crisis possibly occurs in the immediate postpartum period. Clinical features may include chest pain, dyspnea, rales, oxygen desaturation, hypotension, or syncope. Right ventricular failure is the most probable differential diagnosis [26, 28].

Emergency management of acute pulmonary hypertensive crisis should include the following [31]:

1. Correction of precipitating factors such as hypoxia, hypercapnia, acidosis, elevated airway pressures, arrhythmias, and pain
2. Therapy with pulmonary vasodilators
3. RV support with dobutamine or milrinone
4. Maintenance of RV perfusion using norepinephrine or vasopressin
5. Reduction of RV preload with diuretics

A specific treatment plan for acute decompensated PAH (acute pulmonary hypertensive crisis) should be established early, with emergency medications and specialized equipment readily available prior to delivery [33].

The risk of complications in PAH is highest immediately after delivery, with the highest mortality occurring during the first month postpartum. Right ventricular failure remains the leading cause of death. Patients should be monitored in an intensive care unit for at least 24–48 h postpartum and may require continued RV support. However, because RV failure is the most common cause of death, other etiologies such as sepsis, thrombosis, and hemorrhage should also be considered. Patients with PAH are susceptible to thromboembolic complications in the postpartum period. Management includes oral anticoagulant therapy. Additionally, contraception counseling is critical, with attention to the contraindications for future pregnancy [32, 33].

CONCLUSION

PAH during pregnancy is rare, but is associated with a high risk of complications and mortality. However, recent data indicate improved survival in these patients. Revised diagnostic criteria for pulmonary hypertension and increasing life expectancy among women with comorbid conditions may lead to increased prevalence of PAH in pregnancy. However, patients with PAH are complex for management and delivery and require an individualized and multidisciplinary approach to achieve successful outcomes.

ADDITIONAL INFO

Authors' contribution. All authors made a significant contribution to the study and preparation of the article. E.V. Rudaeva, search and analytical work, writing the text, editing; V.G. Mozes, concept and design of the study, editing, reading and approval of the final version; V.V. Kashtalap, concept and design of the study; S.I. Elgina, editing, reading and approval of the final version.
Conflict of interest. The authors declare no conflict of interest.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Участие авторов. Все авторы внесли существенный вклад в проведение исследования и подготовку статьи. Е.В. Рудаева — поисково-аналитическая работа, написание текста, редактирование; В.Г. Мозес — концепция и дизайн исследования, редактирование, чтение и одобрение финальной версии; В.В. Кашталап — концепция и дизайн исследования; С.И. Елгина — редактирование, чтение и одобрение финальной версии.
Конфликт интересов. Авторы заявляют об отсутствии конфликта интересов.

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DOI: https://doi.org/10.17816/rmmar643161