Cardiovascular–obstetric state-of-the-art review: pulmonary hypertension in pregnancy

Joy Yi Shan Ong[1,*], MBChB, MRCP, Jeannie Jing Yi Yap[2,*], MBChB, MRCOG, Mahesh Choolani[2,3], FRCOG, PhD, Kian-Keong Poh[1], FRCP, FACC, Pradip Dashraath[2,†], MBBS, MRCOG, Ting-Ting Low[1,†], MBBS, MRCP

[1]Department of Cardiology, National University Heart Centre Singapore, [2]Department of Obstetrics and Gynaecology, National University Hospital, [3]Department of Obstetrics and Gynaecology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore
These authors are *co-first and †co-senior authors.

Abstract

Pulmonary hypertension in pregnancy has been associated with negative maternal and fetal outcomes over the past decades. With the emergence of novel treatment modalities, morbidity and mortality of women who have pulmonary hypertension in pregnancy have improved. In this review, we aim to explore the contemporary updates in the management of pre-capillary and post-capillary pulmonary hypertension in pregnancy.

Keywords: Adverse pregnancy outcomes, cardiac disease in pregnancy, maternal morbidity, maternal shock, pulmonary hypertension in pregnancy

INTRODUCTION

The incidence of pulmonary hypertension (PH) has been rising in recent years, with increased visibility shed in light of the European Society of Cardiology (ESC) and European Respiratory Society 2022 guidelines on aetiology-specific management of this previously elusive condition.[1] However, despite new risk stratification strategies and treatment recommendations, PH in pregnancy remains a hazardous condition with adverse maternal and fetal outcomes. There has not been a shift in formal World Health Organization (WHO) Pregnancy Risk Class IV recommendation against the continuation of pregnancy and discussion of termination.[2] In recent years, with careful patient selection, use of contemporary therapies and multidisciplinary management, reduction in maternal mortality and improved prognosis, from 38% in the late 1990s to 28% in 2010s and 12% in 2020s, have been observed.[3] In this review, we aim to delve into the latest understanding of management of precapillary and postcapillary PH in pregnancy, with particular attention to treatment advances in the last 5 years.

Haemodynamic definition and groups

Pulmonary hypertension comprises a heterogeneous group of conditions, with the shared haemodynamic definition of elevated pulmonary pressures. Currently, PH is defined as mean pulmonary arterial pressure (mPAP) >20 mmHg at rest. This measurement should be established by right heart catheterisation as a gold standard.[2,4] It is further classified haemodynamically into precapillary PH, postcapillary PH or combined pre- and postcapillary PH, depending on the pulmonary vascular resistance (PVR) and pulmonary capillary wedge pressure, as shown in Table 1. For the purpose of this review and ease of reference, precapillary PH is referred to as pulmonary arterial hypertension (PAH) and postcapillary PH as pulmonary venous hypertension (PVH). The intrinsic haemodynamic implications on heart disease in pregnancy and treatment nuances will be discussed comparatively [Figure 1].[1]

Pulmonary hypertension groups

Pulmonary hypertension conditions are subdivided into five WHO groups according to aetiology, pathophysiology and treatment trend [Figure 2]. The WHO PH groups are as follows: Group 1: PAH that may be idiopathic or hereditary, or associated with drugs, toxins, infections, connective tissue

Access this article online

Quick Response Code:

Website: https://journals.lww.com/SMJ

DOI: 10.4103/singaporemedj.SMJ-2024-198

Correspondence: A/Prof. Ting-Ting Low, Senior Consultant, Department of Cardiology, Level 9, NUHS Tower Block, 1E Kent Ridge Road, 119228, Singapore.
E-mail: ting_ting_low@nuhs.edu.sg

Received: 11 Sep 2024 **Accepted:** 04 Feb 2025 **Published:** 21 Mar 2025

How to cite this article: Ong JYS, Yap JJY, Choolani M, Poh KK, Dashraath P, Low TT. Cardiovascular–obstetric state-of-the-art review: pulmonary hypertension in pregnancy. Singapore Med J 2025;66:130-40.

Table 1. Haemodynamic classification of pulmonary hypertension (PH).

Parameter	Precapillary PH[a]	Postcapillary PH[b]	Combined pre- and postcapillary PH
Mean PAP (mmHg)	>20	>20	>20
PVR[c] (WU)	>2	≤2	>2
PCWP (mmHg)	≤15	>15	>15

[a]Pulmonary arterial hypertension. [b]Pulmonary venous hypertension. [c]New in the latest 2022 European Society of Cardiology and European Respiratory Society PH guidelines. PAP: pulmonary arterial pressure, PCWP: pulmonary capillary wedge pressure, PVR: pulmonary vascular resistance, WU: wood units

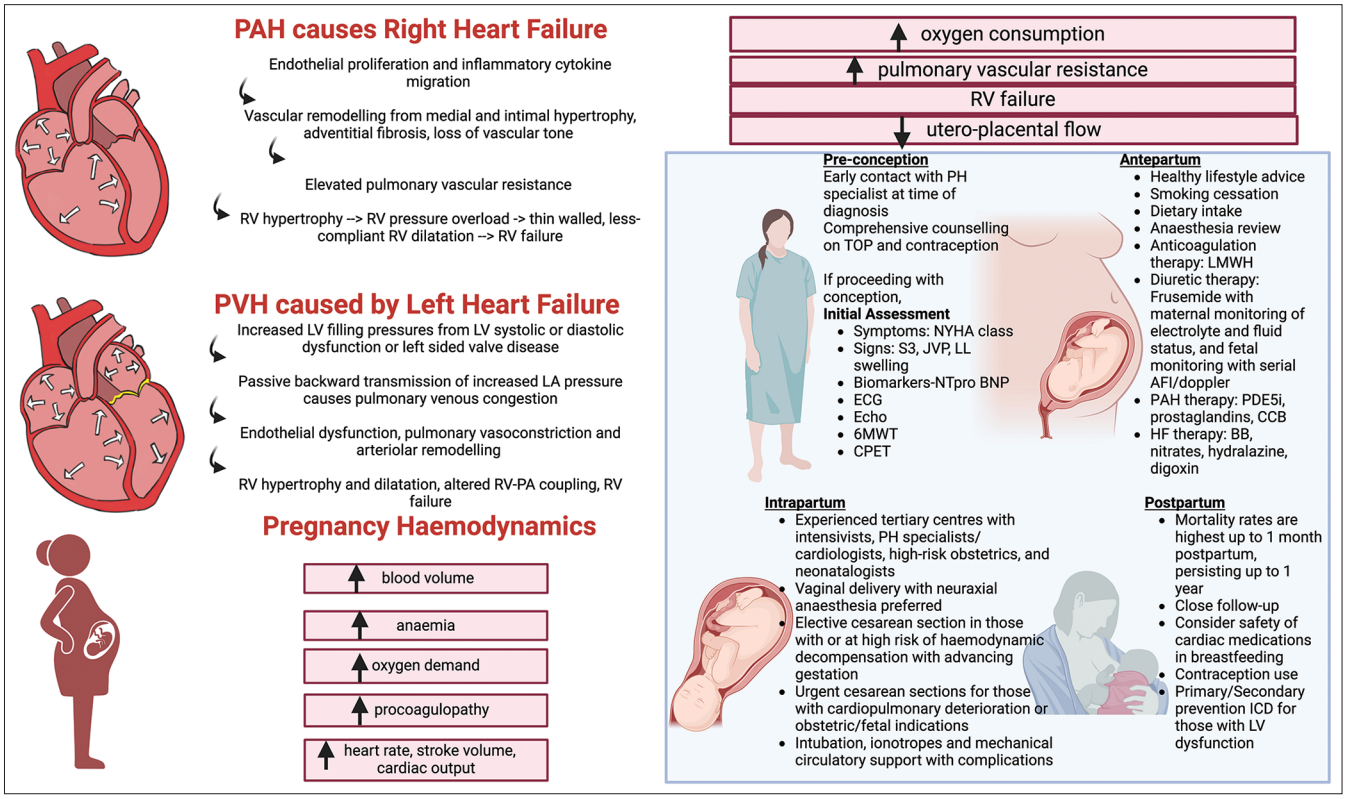

Figure 1: Central illustration for pulmonary hypertension (PH) in pregnancy. [Created with BioRender.com]. 6MWT: six minute walking test, AFL: atrial flutter, BB: beta-blockers, CCB: calcium channel blockers, CPET: cardiopulmonary exercise testing, ECG: electrocardiogram, HF: heart failure, ICD: implantable cardioverter-defibrillator, JVP: Jugular venous pressure, LA: left atrial, LL: lower limb, LMWH: low molecular weight heparin, LV: left ventricular, NTpro BNP: N-terminal pro-B-type natriuretic peptide, NYHA: New York Heart Association, PA: pulmonary artery, PAH: pulmonary arterial hypertension, PDE5i: phosphodiesterase 5 inhibitors, PVH: pulmonary venous hypertension, RV: right ventricular, TOP: termination of pregnancy

disease and congenital diseases; Group 2: PH secondary to left heart disease; Group 3: PH secondary to pulmonary disease; Group 4: PH due to chronic thromboembolic diseases; and Group 5: PH associated with multifactorial conditions or unclear mechanisms secondary to haematological, metabolic and systemic diseases.[1,5] In this review, the discussion will focus on mainly WHO Group 1 and Group 2 PH in pregnancy (being more prevalent), which will be referred to broadly as PAH and PVH, respectively.

INCIDENCE AND OUTCOMES

Pulmonary venous hypertension

The most common form of PH worldwide is PVH, accounting for 65%–85% of PH cases.[6] Encompassing mainly WHO Group 2 PH secondary to left heart disease, PVH stems from cardiomyopathy (regardless of whether left ventricular ejection fraction (LVEF) is reduced or preserved) and left-sided valvulopathy (usually severe aortic and mitral valve disease). The prevalence of PVH is reported to be around 50% in those with heart failure with preserved ejection fraction, 60%–70% in those with symptomatic severe mitral valve disease, and up to 50% in those with significant aortic stenosis.[6-9] Globally, heart failure incidence increased from 0.7% before 2010 to 10.9% up to 2018.[7]

Specific cardiomyopathies affecting women of reproductive age include ischaemic cardiomyopathy, familial dilated cardiomyopathies, hypertrophic cardiomyopathy, tachycardia-related cardiomyopathy, heart failure post-myocarditis or acute stressor event and even cancer therapy-related cardiac dysfunction. These

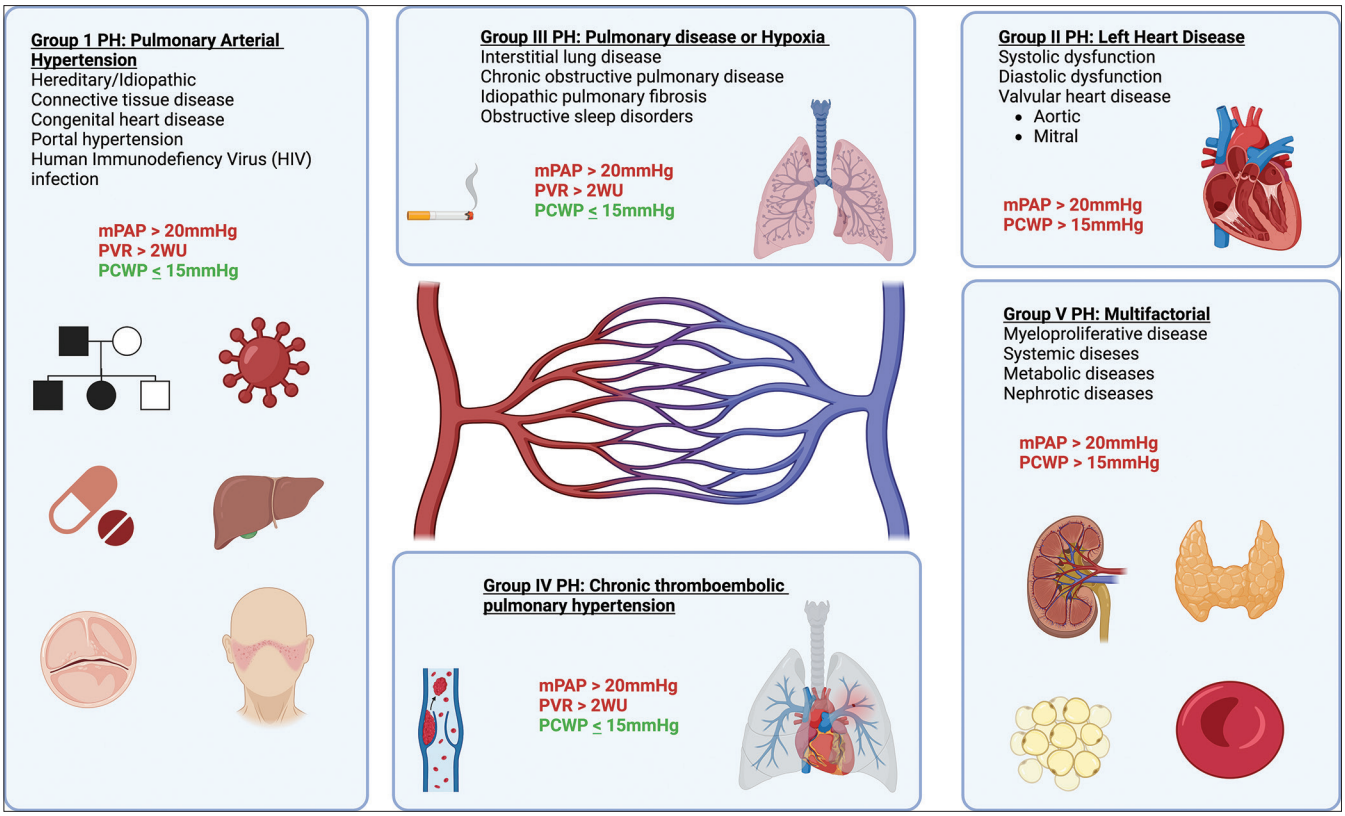

Figure 2: Diagram shows the classification of pulmonary hypertension (PH). [Created with BioRender.com]. PAP: pulmonary arterial pressure, PCWP: pulmonary capillary wedge pressure, PVR: pulmonary vascular resistance

conditions are more commonly encountered in pregnancy now, partly because of older maternal age in pregnancy and improved access to echocardiography.

Peripartum cardiomyopathy (PPCM) can be acquired *de novo* during the course of pregnancy. Peripartum cardiomyopathy is a diagnosis of exclusion, where approximately 13% of patients without pre-existing cardiac disease and with left ventricular systolic dysfunction <45% may present with PVH just before delivery up to 5 months postpartum.[10,11] About 25% of patients with PPCM go on to develop chronic heart failure.[12] Mortality data in the USA is reported to average 6%–10% in the first 6 months, while PPCM mortality data in Asia has been reported to average between 3% and 16% in 2017.[13]

With regards to left-sided valvular heart disease contributing to PVH, bicuspid aortic stenosis and rheumatic mitral stenosis (MS) are the usual suspects. The prevalence of congenital bicuspid aortic valvulopathy is about 1%–2%, and the condition is associated with premature aortic stenosis, regurgitation and dilated aortopathy.[14,15] Aortic stenosis typically leads to left ventricular hypertrophy, abnormal left ventricular relaxation and elevated left atrial and pulmonary pressures.[14] Pulmonary hypertension is present in 48%–75% of patients with significant aortic stenosis.[15,16] The incidence of bicuspid aortic valve in pregnancy is generally underreported in literature.[17] In women of childbearing age, MS is almost always rheumatic in origin.[18] Rheumatic heart disease is the most prevalent cardiac disease, as it affects >1% of pregnancies in developing countries, where rheumatic fever is rampant in 1 in 100,000, affecting patients in the third to fourth decades of life.[18-20] Up to 50% of patients with severe MS and 34% with moderate MS develop heart failure in pregnancy.[18-20] As a result of left ventricular inflow obstruction with subsequent elevations in left atrial pressure, PH and right ventricular (RV) dilatation, as well as its coexistence with atrial fibrillation (which further reduces diastolic filling time), MS is poorly tolerated in pregnancy.[19]

It was found that women with PVH have similar rates of major adverse cardiovascular events (MACE) to those with PAH. Due to the underlying heterogeneity in PVH, it is challenging to predict outcomes uniformly across all patients in the same group, regardless of left ventricular systolic function.[21] Factors associated with increased risk of MACE regardless of the WHO PH subgroup include RV systolic pressure (RVSP) ≥50 mmHg and pre-eclampsia.[22] Risk factors associated with admission for decompensated heart failure include hypertension and diabetes mellitus, which are more common in PVH patients.

Pulmonary arterial hypertension

Pulmonary arterial hypertension is much rarer than PVH. It is rapidly progressive if untreated or diagnosed late, culminating in fulminant RV failure. Registry data from Europe, North

America and Canada, and Korea between 2003 and 2020 reveal an incidence of around 1.5–32 cases per million patients and a prevalence of 12.4–268 cases per million patients with PAH.[23] Pulmonary arterial hypertension is also categorised as WHO Group 1 PH. Young women are predominantly affected; the underlying aetiologies are often idiopathic, hereditary or associated with connective tissue disease.[2]

The 1-, 2- and 3-year mortality rate for patients with PAH in the REVEAL registry in the USA was 10%, 19% and 25%, respectively.[24] Previously, total mortality reached beyond 56% on average in 2017–2018; with recent statistics reporting mortality of 9%–25% in 2021.[25] The registry of pregnancy and cardiac disease in the USA reports a mortality rate of up to 43% for PH in pregnancy, depending on the aetiology and severity of PH, while the CAR-PREG II study in Canada reports around 35.6% mortality regardless of the aetiology of PH.[24,26] Most times, women diagnosed with PAH are counselled strictly to avoid pregnancy due to previously reported high maternal mortality; furthermore, many PAH-specific drug therapies are also fetotoxic. The difficulty arises when contraceptive precautions are inadequate for those with pre-existing PAH or if PAH is diagnosed for the first time in pregnancy.

Significant maternal morbidity and mortality stems predominantly from RV failure, pulmonary hypertensive crisis, cardiac arrest and sudden death. The highest risks were observed in those with advanced pregnancies beyond 36 weeks of gestation and in the immediate week postpartum.[3] Severe right heart dysfunction, severe PH with mPAP >50 mmHg, systolic pulmonary artery pressure >70 mmHg, Eisenmenger syndrome and acute pulmonary hypertensive crisis or right heart failure are identified as the risk factors for mechanical circulatory support escalation at termination or delivery.[21]

PATHOPHYSIOLOGY LEADING TO RIGHT HEART FAILURE

Pulmonary venous hypertension typically due to left heart disease

Dysfunction of the left ventricle leads to increased left atrial pressure with resultant backward transmission into the pulmonary circulation. The increased hydrostatic pressure in the pulmonary vasculature results in pulmonary venous endothelial dysfunction and generation of pulmonary oedema. With time, prolonged elevation of pulmonary venous pressures leads to vascular remodelling with smooth muscle hypertrophy and hyperplasia in the pulmonary arterioles, resulting in thickening of vessel walls, narrowing of lumen and increased PVR. This eventually leads to RV dilation, initially to compensate for the increased afterload, and overtime with progression of the disease or if left untreated, it leads to decompensation and RV failure.[1,27]

Reduced cardiac output or forward failure, whether originating from left ventricular dysfunction first in the case of PVH or RV dysfunction first in the case of PAH, compromises uteroplacental perfusion. This leads to stunted growth of villi and placental ischaemic injury, which portend adverse fetal outcomes such as intrauterine growth restriction or small-for-gestation-age babies. Likewise, RV dysfunction and backward failure also cause raised systemic venous congestion and pressures, generate increased uteroplacental resistance and compromise uteroplacental perfusion.[28-30]

Pulmonary arterial hypertension typically spares left heart function

Cellular level alterations in the lung vasculature result in pulmonary vascular smooth muscle and endothelial tissue proliferation. There are also inflammatory cell migration and adventitial fibrosis mediated by signalling pathways.[28] With small, stiff pulmonary arterioles and reduced flow, the right ventricle first hypertrophies to compensate for increased PVR. Progressively, the right ventricle dilates with increased wall tension. Eventually, the loss of right ventricle and pulmonary artery coupling leads to decline in RV function and cardiac output. While the left heart function is typically spared in PAH, severe RV pressure overload can compromise left ventricular filling and resultant left ventricular cardiac output. This is because the two ventricles share a common wall, the ventricular septum, which allows for direct mechanical interaction via pressure equalisation and ventricular interdependence.[28-30]

PHYSIOLOGICAL CHANGES IN PREGNANCY AND DELIVERY

Supratherapeutic elevation in hormones — oestrogen, progesterone and human chorionic gonadotropin — and their metabolites in both PH and during pregnancy act to paradoxically aggravate pulmonary vasculature remodelling and decrease systemic vascular resistance.[29,30] Increase in heart rate and stroke volume from the elevated sympathetic tone leads to increased cardiac output. Coupled with an elevated preload by approximately 45% of plasma volume from the sixth to 32nd gestation week, there is a hyperdynamic system before delivery.[27,31,32] If RV function is inadequate to accommodate the increase in RV preload against an elevated PVR, RV dilatation will ensue with impaired RV contractility, subsequently compromising left ventricular preload and cardiac output.

Cardiac output reaches its peak during delivery and the immediate postpartum period.[32] There is an increase in vascular resistance with a dramatic decrease in oestrogen and progesterone after delivery of the placenta.[32] In the subsequent days following delivery, the increased preload to the heart remains from the relief of inferior vena cava obstruction, transfer of blood from the uterus to the systemic circulation, mobilisation of extracellular fluid and fluid administration at the time of delivery.[31,32] The risk of heart failure and mortality is the highest at the time of delivery and in the early postpartum stage.[33]

Table 2. Safety of pulmonary arterial hypertension medications in pregnancy and lactation.

Medications		Pregnancy	Lactation	Recommendations
Calcium channel blockers	Nifedipine Diltiazem			- Continue in pre-existing patients with PH - First choice for vasoreactivity-positive PH
PDE5i	Tadalafil Sildenafil			- Continue in pre-existing patients with PH - First choice for patients newly diagnosed with PH
Prostacyclin analogues	Iloprost (inhaled) Epoprostenol (IV)			- Continue in pre-existing patients with PH - Inhaled prostacyclin analogues are preferred add-on therapy to PDE5i in pregnancy - Use epoprostenol in decompensated PH
	Selexipag (oral) Treprostinil (oral)			
Endothelin receptor antagonists	Ambrisentan Bosentan Macitentan			- Switch to PDE5i for single therapy - Switch to inhaled or oral prostacyclin analogues for dual therapy cases if already on PDE5i - Potential teratogenicity
sGCS stimulators	Riociguat			- Switch to PDE5i - Potential teratogenicity
Nitric oxide				- Use in decompensated PH as rescue therapy

■ Considered safe ■ Contraindicated ■ Use with caution (limited data available) ■ Unknown (not recommended).
IV: intravenous, PDE5i: phosphodiesterase 5 inhibitors, PH: pulmonary hypertension, sGCS: soluble guanylate cyclase

MANAGEMENT OF PULMONARY HYPERTENSION DURING PREGNANCY

Preconception

During initial contact with the patients, any pre-existing cardiac condition causing PH needs to be optimally managed before the affected patients embark on pregnancy. The importance of preconception counselling by the primary cardiologist or PH specialist cannot be overemphasised. Women in the reproductive age group suffering from PAH or PVH should be clearly informed of pregnancy-related risks upon diagnosis of their heart condition. Traditionally, women with PAH are contraindicated from pregnancy as stipulated in current guidelines, and therapeutic abortion can be offered for an unplanned pregnancy, given the serious maternal mortality risks. For women with PVH from left-sided heart disease, strict contraception is advised until the underlying heart condition is well optimised. This may include recalibration or removal of some medications such as riociguat and endothelin receptor antagonists (ERA) to pregnancy-safe categories detailed in Table 2 for patients with PAH, while looking out for change in clinical status, valvular intervention or surgery, and arrhythmia management with or without ablation therapy or any other cardiomyopathy-specific treatment for patients with PVH.

Antepartum

Cardiology initial assessment

Regular follow-up care should be given at an experienced tertiary centre that has facilities with extracorporeal membrane oxygenation (ECMO) capability and a multidisciplinary team that includes maternal fetal medicine specialists, PH specialists, anaesthetists and neonatologists.[34] Initial cardiac assessment should consist of history taking, including functional class, examination to look for heart failure signs and cardiac investigations. A baseline electrocardiogram should be performed as an initial screening test for axis deviation, bundle branch block or chamber enlargement. Baseline transthoracic echocardiography is critical to document RV function, valvular regurgitation and the presence of PH.[28] Subsequent transthoracic echocardiograms may be repeated at regular intervals every trimester, or more frequently, depending on the underlying aetiology of PH.[2] Brain natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NTproBNP) levels could rule out PVH in view of the high negative predictive value.[35] The suggested upper reference limit is BNP 50 pg/mL with no inter-trimester differences, and NT-proBNP 200 pg/mL in the first and second trimesters and 150 pg/mL in the third trimester and postpartum period. BNP ≤100 pg/mL and NT-proBNP <128 pg/mL had a negative predictive value of 100% for identifying events during pregnancy.[35,36] Risk scores such as Cardiac Disease in Pregnancy Study, Zwangerschap bij Aangeboren HARtAfwijking [Pregnancy in Women With Congenital Heart Disease] and modified WHO are validated tools to calculate maternal cardiac risk complications from general parameters during the baseline visit.[26]

Obstetrics initial antenatal visit

The initial antenatal visit includes a detailed maternal assessment, obtaining a detailed medical history, and reviewing current symptoms and physical findings (both cardiac and obstetric), in addition to confirming the viability of an intrauterine pregnancy. Regular antenatal visits should be conducted with three-weekly, two-weekly and weekly follow-ups during the first, second and third trimesters, respectively. There should be regular monitoring of the maternal vital signs, symptoms, weight, biomarkers such as BNP and serial echocardiography for continued assessment of the ventricular function and estimation of pulmonary artery pressures with the cardiologist. Serial growth scans are

Table 3. Safety of heart failure medications in pregnancy and lactation.

Medications		Pregnancy	Lactation	Recommendations
Loop diuretics	Furosemide Bumetanide Metolazone			- Judicious use in pregnancy, limited to patients with clinical signs of congestion (can result in oligohydramnios and increase the risk of electrolyte imbalance in fetus) - Can suppress lactation at higher doses
Hydralazine				
Nitrates	Nitroglycerin			- Potential hypotension (crosses placenta)
	Nitroprusside			- Nitroglycerin is preferred over nitroprusside due to the toxic fetal cyanide levels with the latter
Beta-blockers	Metoprolol Bisoprolol Labetalol			- Metoprolol and bisoprolol are preferred - Continued in patients on existing beta-blocker therapy
	Carvedilol			
	Atenolol			- Atenolol is contraindicated in pregnancy as it has been associated with birth defects and IUGR. It is also transferred to breast milk in low levels.
Digoxin				- Used in women with persistent heart failure symptoms despite diuretics and vasodilator therapy - Drug monitoring is suggested (digoxin intoxication is associated with fetal loss)
Calcium channel blockers	Nifedipine			
	Verapamil Diltiazem			
	Amlodipine			
Angiotensin-converting enzyme inhibitors	Captopril Enalapril			- Teratogenic — associated with oligohydramnios, fetal renal and cardiac abnormalities - Low levels are excreted into breastmilk; monitor fetal weight every 4 weeks
Angiotensin receptor blockers **ARNI**				- Teratogenic — associated with oligohydramnios, fetal renal and cardiac abnormalities
Aldosterone antagonists	Spironolactone			- Spironolactone has been associated with feminisation (anti-androgenic effects)

Considered safe Contraindicated Use with caution (limited data available) Unknown (not recommended).
ARNI: angiotensin receptor neprilysin inhibitor, IUGR: intrauterine growth restriction

arranged at 28, 32 and 36 weeks of gestation for fetal growth monitoring in view of the risk of fetal growth restriction. Women with PH are at an increased risk of thromboembolic events. Therefore, signs and symptoms, such as asymmetrical redness, warmth and tenderness in the limbs, should be communicated to patients. Additionally, this risk should be regularly assessed during each visit. A referral to an anaesthetist in the third trimester should be made. General advice should also be given to patients, such as lying in a lateral decubitus position to prevent caval impediment, judicious fluid and salt limitation, diuretic compliance and supplementary oxygen utilisation as required. If the patient is on regular diuretics, there should also be regular monitoring of electrolytes and fluid status to allow titration in the doses accordingly. Fetal monitoring should also be in place with serial amniotic fluid and Doppler monitoring in view of the risk of oligohydramnios from fluid shifts.

Medical therapy

Pulmonary venous hypertension

Strict fluid management is important to avoid both the extremes of fluid overload and over-diuresis. Fluid restriction, if any, should be individualised, taking into account the patient's clinical symptoms, and guided by the cardiac investigation findings. Medications for PAH should be avoided in this group of patients with PVH in view of the propensity to exacerbate fluid overload.[1] Management of heart failure with beta-blockers and diuretics should be continued to maintain maternal cardiovascular stability.[37] The use of nitrates, hydralazine and digoxin is also generally safe with pregnancy and during lactation.[37] Beta-1-selective beta-blockers such as metoprolol and bisoprolol are preferred, as they are less likely to affect uterine contraction and peripheral vasodilation, and they have been associated with lower rates of fetal growth restriction. However, non-selective beta-blockers such as atenolol have been associated with higher rates of fetal growth restriction, and are therefore generally avoided in pregnancy. Medications such as angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs) and mineralocorticoid receptor antagonists, and ivabradine should be discontinued in view of the potential risks to the fetus.[38] Safety of medications used in patients with heart failure is summarised in Table 3.

Anticoagulation for prophylaxis against intracardiac thrombus formation is recommended by the American Heart Association and European Society of Cardiology guidelines[39,40] when LVEF is <30% and <35%, respectively.[40] This should be administered from late pregnancy until 6–8 weeks postpartum, as this postpartum period is also associated with increased

risk for left ventricular thrombus formation and systemic thromboembolism. Low-molecular-weight heparin is generally the drug of choice. It is safe to start this antepartum, but should be omitted 48 hours before planned delivery or switched to unfractionated heparin, especially if there is consideration for neuroaxial anaesthesia.[38] Oral anticoagulation drugs such as warfarin and direct oral anticoagulants are generally not deemed safe for pregnancy.[38,41-43] Iron deficiency has an independent adverse outcome on cardiac function and maternal health and is common in patients with heart failure. Hence, oral iron supplementation should be in place.

Pulmonary arterial hypertension

Termination of pregnancy (TOP) has been advocated in standard guidelines for PAH, but there is a paucity of evidence-based data for the recommended treatment of PAH during pregnancy. Table 2 details the PAH medications that are safe for use during pregnancy. There are five main classes of medication therapy in treating PAH — prostaglandins, phosphodiesterase-5 (PDE5) inhibitors (PDE5i), ERA, soluble guanylate cyclase (sGCS) stimulators and calcium channel blockers (CCBs) — for those with vasoactive reactivity. Generally, patients can be continued on PDE5, prostaglandins and CCBs if they were on them previously.[44-46] Category X drugs, ERA and sGCS, should be discontinued in pregnancy.[47] Additionally, retrospective registry data and real-world experience have shown that oral selexipag is associated with fewer inpatient hospitalisations and outpatient presentations than inhaled iloprost or parenteral prostacyclin analogues.[48]

Furosemide is the recommended diuretic in pregnancy, with spironolactone falling in pregnancy category D. Anticoagulation with once-daily Clexane may be considered as prophylaxis against venous thromboembolism, as pulmonary embolism is very poorly tolerated in patients with PAH. Thus, PAH-specific therapy should be optimised.[29]

Complications

Pre-emptive planning for timing and mode of delivery at an expert centre should be undertaken. Unstable haemodynamics should prompt TOP if diagnosed before fetal viability. If the condition is diagnosed beyond fetal viability (24 weeks), a balance between the effects of fetal prematurity and fetal well-being should be weighed against that of the mother, aiming for an elective caesarean section between 34 to 36 weeks of gestation.[29,37] Early admission to a dedicated intensive care unit (ICU) with combined care by PH specialists, obstetricians and cardiac intensivists is paramount in mitigating maternal and fetal risks. This should be a pre-emptive action taken in response to the patient requiring caesarean section or facing clinical deterioration. A multidisciplinary huddle of the abovementioned specialists, along with anaesthetists, neonatologists and other relevant physicians caring for inter-related conditions, should be organised regularly to make contingency plans for complications and rapid delivery or TOP.

Pure right ventricular failure from pulmonary arterial hypertension

In the event of ventricular failure, treatment is typically supportive and involves prevention of further hypotensive and hypoxic insults. Patients with PAH may need triple PAH-specific therapy with pulmonary artery catheter insertion for continuous monitoring of right heart haemodynamics, together with titration of vasopressors if needed. The ideal vasopressors for use in acute RV failure would be agents that increase systemic arterial pressure and RV contractility without raising PVR, and this may sometimes involve a combination of milrinone, dopamine and/or norepinephrine.

Oxygenation is usually given maximally through high-flow masks to prevent hypoxic pulmonary vasoconstriction. Mechanical ventilation for hypoxaemia is generally discouraged in PAH patients, as intubation and positive pressure ventilation often exacerbate the ailing right ventricle and can lead to RV arrest. The use of mechanical circulatory system support such as ECMO should be considered and planned for as standby to prevent pulmonary circulatory collapse.[29,49,50]

Left ventricular failure with pulmonary venous hypertension and cardiogenic shock

In the event of acute left heart failure, afterload reduction may be achieved with intravenous vasodilators such as nitroglycerin.[37] Ionotropic boost may be provided by levosimendan and milrinone.[37] The use of dobutamine was linked to worse outcomes in some studies.[50] In patients with deteriorating haemodynamics in spite of chemical ionotropy, mechanical circulatory support may need to be considered promptly to support left ventricular failure. There are temporary options like intra-aortic balloon pump, percutaneous ventricular assist device and veno-arterial ECMO, or left ventricular assist devices as a bridge to transplant or as a destination therapy.[37]

Peripartum

Delivery mode and timing

Delivery should be planned in experienced hospitals with direct access to high-risk intensive care and monitoring locale and with provision of care by dedicated PH specialists, cardiologists, cardiothoracic surgeons, cardiac anaesthesiologists, critical care physicians, maternal fetal medicine specialists, neonatologists and nursing support. Regional perinatal healthcare centres (level IV) are the recommended centres for women with PH to deliver, as identified by the American College of Obstetricians and Gynecologists and the Society for Maternal Fetal Medicine classification system for levels of maternal care.[29]

Timing of delivery is individualised, with consideration of the following factors: gestational age, maternal assessment (which includes the severity of PH and its response to treatment), any maternal or antenatal complications, and fetal assessment. It is

Table 4. Safety of drugs commonly used in intrapartum and postpartum periods in cardiac patients.

Drug	Safety reports
Atosiban	- No reported serious cardiac side effects
Carboprost (prostaglandin F2α)	- Contraindicated in patients with myocardial ischaemia
Dinoprostone (prostaglandin E)	- Safe for use in induction - Contraindicated in patients with myocardial ischaemia
Ergometrine	- Poorest cardiac profile: causes coronary, peripheral and pulmonary vasoconstriction - Avoided in patients with hypertension, pre-eclampsia or aortic root disorders
Magnesium sulfate	- No known serious cardiac side effects
Misoprostol (prostaglandin E1)	- Safe for use in induction and prophylaxis of postpartum haemorrhage - Can decrease systemic vascular resistance and precipitate arrythmias - Contraindicated in patients with myocardial ischaemia
Oxytocin	- Can be given as slow infusion (12 mU/min for 4 h) - May cause hypotension, decrease in cardiac contractility and bradycardia - Avoid in patients where vasodilation is poorly tolerated
Terbutaline (β2 agonist)	- Can cause arrhythmias, pulmonary oedema and myocardial ischaemia
Tranexamic acid	- Generally safe to use - Possible association with acute myocardial infarction (limited data)

important to ensure careful coordination between the obstetric and cardiac teams in planning for the optimal timing and mode of delivery that would minimise risks to both the mother and baby. Delivery should be considered ideally after 32 weeks of gestation, when fetal survival without major disability is expected, or earlier if there are significant risks to the life or long-term health of the mother with continuation of pregnancy, suboptimal response to medical therapy or fetal indications.

Vaginal delivery with epidural anaesthesia is the preferred mode of delivery due to lower risks of blood loss, infection and venous thromboembolism as compared to caesarean deliveries, which were favoured in the past for quicker and more controlled delivery duration.[51] However, caesarean delivery may be required for obstetric or maternal indications such as cardiopulmonary deterioration.[27]At present, ESC guidelines recommend caesarean delivery for patients with heart failure, although vaginal delivery may sometimes be possible.[27] Mortality outcomes in women with successful vaginal deliveries were comparable to those in women who had planned caesarean deliveries (5% vs. 9%–10%),[34] although the mortality increases to 33% when an intrapartum conversion to emergency caesarean section is required.[52]

Care of the patient in labour involves routine monitoring of the maternal vitals (blood pressure, heart rate, oxygen saturations and respiratory rate), strict monitoring of fluid input/output and continuous fetal monitoring with cardiotocography.[21]

Anaesthetic considerations

There should be a focus on optimising inhaled and intravenous pulmonary vasodilator therapy peridelivery to accommodate the increased preload.[21] Adjunctive use of diuretics and inotropes may also stabilise the patient's haemodynamics and support RV function, although placental delivery would ultimately decrease oxygenation demand, cardiac output and plasma volume.[21] Haemodynamics may be guided with placement of a pulmonary artery catheter in centres with experience;[21,53] if not, mixed venous oxygenation and central venous pressure may be utilised as surrogates of haemodynamic measurement.[37]

Sufficient neuraxial anaesthesia via epidural, dural or combined spinal epidural techniques to downregulate catecholamine release is recommended in those undergoing vaginal delivery.[54] For those undergoing caesarean delivery, neuraxial anaesthesia with combined spinal epidural is the preferred technique, as it allows for careful titration of analgesia to combat haemodynamic fluctuations.[21]

Labour medications

Cautious use of uterotonics is advised [Table 4]. It is safe to use oxytocin and misoprostol, as they have minimal effect on the pulmonary vasculature and pulmonary artery pressures; however, they should be avoided in patients with myocardial ischaemia.[21,55] Oxytocin is the most commonly used uterotonic and can be administered via a slow intravenous infusion (10 units of oxytocin diluted in 500 mL of normal saline, infused at 36 mL/h over 4 hours), with careful attention to avoid bolus injections. This approach contrasts with administering a 10-unit intravenous bolus in an otherwise healthy patient during the third stage of labour.[56] Other uterotonics such as carboprost, which may cause smooth muscle contraction and precipitate bronchospasm, and ergometrine, which can cause coronary, peripheral and pulmonary vasoconstriction, should be avoided.[21] Early recognition and escalation to surgical treatment are important to manage postpartum haemorrhage.

Surgical considerations

Surgeons are discouraged from externalising the uterus, as this may predispose to micro air embolisms that form within the venous sinuses above the level of the right atrium.[21,29] Concurrent tubal ligation for contraception should be considered for women undergoing caesarean section, given the increased risks of morbidity and mortality associated with the condition.[21,29]

Postpartum

Close monitoring and anticipatory management of the patient are warranted in the postpartum period, as maternal cardiovascular changes can persist or worsen. Postpartum ICU admission for close haemodynamic and respiratory monitoring is common, along with generous prescription of diuresis with judicious weaning of intravenous inotropes and

pulmonary vasodilators. Regular bowel regimen should be prescribed to prevent the Valsalva manoeuvre with resultant haemodynamic shifts.[21]

In patients with PVH, the risk of fluid overload and mortality is highest in the postpartum period, given the haemodynamic shifts during delivery. Hence, close monitoring for fluid overload is essential in the first 72 h post-delivery.[37] Signs and symptoms such as orthopnoea, cough and raised jugular venous distension are highly suggestive of heart failure. Postpartum management should include continuation of peripartum heart failure therapeutic drugs.[38] In patients with PAH, the highest risk for maternal demise was 0–4 days postpartum and most maternal deaths occurred within 2 weeks postpartum.[3,27] This underscores the importance of vigilant management in ICU postpartum for a longer-than-usual duration and even consideration of early escalation of medical therapy post-delivery.

Thromboprophylaxis should be considered due to the hypercoagulable state of pregnancy that continues into its postpartum period. Heart failure is an intermediate risk factor of venous thromboembolism, and it is recommended to have at least 10 days of prophylactic anticoagulation postnatally.[57]

Post-discharge

Close postpartum follow-up care is necessary in women with PH. Mortality rate is highest during the first 3 weeks to 1 month, but persists at 6 months and up to at least 1 year. In addition, after delivery, PH medication options expand, and medication regimens should be optimised as soon as possible. Contraception options should be discussed.[21]

Contraception

Contraception recommendations stand on the avoidance of oestrogen-containing contraceptives that are prothrombotic and associated with increased cardiovascular risks in patients with PH. Progesterone-only contraception and non-hormonal contraception, which are safer options, are generally advised. When considering intrauterine devices, the hormonal (levonorgestrel-releasing) intrauterine system is favoured to copper intrauterine contraceptive device due to the reduction in menstrual blood flow, and if chosen, should be implanted in an experienced centre due to risks of stimulating a vasovagal syncope in this high-risk subset at the time of implantation. Permanent sterilisation in the form of tubal ligation or vasectomy in the male partner may be considered. Barrier methods such as condoms and diaphragms are non-hormonal options and do not affect the cardiovascular health; however, they have a higher failure rate compared to the above contraceptive options. Emergency contraception may be achieved using the abovementioned techniques; however, patients on bosentan are advised to practise additional contraceptive methods due to drug–drug interactions. In general, the selection of contraception should prioritise patient safety and preference, with minimisation of cardiovascular risks.[29,58]

Breastfeeding

Pulmonary arterial hypertension therapies such as CCBs and PDE5i are considered safe in breastfeeding; ERAs are contraindicated, while sGCS and prostacyclin analogues confer unknown effects.[31] Most heart failure therapies are safe in breastfeeding.[37] Low levels of ACE inhibitors are found to be excreted into breastmilk; hence, monitoring of the baby's weight every 4 weeks is recommended.[55] Currently, there is no available data on the safety of ARB or angiotensin receptor neprilysin inhibitor while breastfeeding.[38] Breastfeeding is tolerated in most patients with mild heart failure and should not be discouraged. Necessary medical treatment should not be withheld due to the patient's desire to breastfeed.[37]

Implantable cardioverter defibrillator therapy

Guidelines recommend the use of implantable cardioverter defibrillators for primary prevention in patients with LVEF <35% and symptomatic heart failure despite optimal pharmacotherapy, or for secondary prevention in those with documented ventricular arrhythmias.[1,38]

CONCLUSION

Pulmonary hypertension includes a heterogeneous group of conditions that is increasingly well defined in literature. With better access to diagnostics, early contact with healthcare providers and prompt commencement of effective therapeutics, mortality associated with PH in pregnancy has improved significantly over the past decade. Close monitoring, longitudinal follow-up and anticipatory management with an expert multidisciplinary team are required for continued improvement in morbidity and mortality outcomes in this treatable group of conditions.[59]

Financial support and sponsorship

Nil.

Conflicts of interest

Choolani M and Poh KK are members of the SMJ Editorial Board and were thus not involved in the peer review and publication decisions of this article.

REFERENCES

1. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, *et al*. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Heart J 2022;43:3618-3731. Erratum in: Eur Heart J 2023;44:1312.
2. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, Blomström-Lundqvist C, Cífková R, De Bonis M, *et al*. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J 2018;39:3165-241.
3. Low TT, Guron N, Ducas R, Yamamura K, Charla P, Granton J, *et al*. Pulmonary arterial hypertension in pregnancy-a systematic review of outcomes in the modern era. Pulm Circ 2021;11:20458940211013671.
4. Galiè N, McLaughlin VV, Rubin LJ, Simonneau G. An overview of the 6th World Symposium on Pulmonary Hypertension. Eur Respir J 2019;53:1802148.
5. Simonneau G, Robbins IM, Beghetti M, Channick RN, Delcroix M, Denton CP, *et al*. Updated clinical classification of pulmonary hypertension. J Am Coll Cardiol 2009;54 (1 Suppl):S43-54.

6. Rosenkranz S, Gibbs JS, Wachter R, De Marco T, Vonk-Noordegraaf A, Vachiery JL. Left ventricular heart failure and pulmonary hypertension. Eur Heart J 2016;37:942-54.
7. Bright RA, Lima FV, Avila C, Butler J, Stergiopoulos K. Maternal heart failure. J Am Heart Assoc 2021;10:e021019.
8. Tichelbacker T, Dumitrescu D, Gerhardt F, Stern D, Wissmuller M, Adam M, *et al*. Pulmonary hypertension and valvular heart disease. Herz 2019;44:491-501.
9. Weber L, Rickli H, Haager PK, Joerg L, Weilenmann D, Brenner R, *et al*. Haemodynamic mechanisms and long-term prognostic impact of pulmonary hypertension in patients with severe aortic stenosis undergoing valve replacement. Eur J Heart Fail 2019;21:172-81.
10. Sliwa K, Hilfiker-Kleiner D, Petrie MC, Mebazaa A, Pieske B, Buchmann E, *et al*. Current state of knowledge on aetiology, diagnosis, management, and therapy of peripartum cardiomyopathy: A position statement from the Heart Failure Association of the European Society of Cardiology Working Group on peripartum cardiomyopathy. Eur J Heart Fail 2010;12:767-78.
11. Pearson GD, Veille JC, Rahimtoola S, Hsia J, Oakley CM, Hosenpud JD, *et al*. Peripartum cardiomyopathy: National Heart, Lung, and Blood Institute and Office of Rare Diseases (National Institutes of Health) workshop recommendations and review. JAMA 2000;283:1183-8.
12. Yaméogo NV, Samadoulougou AK, Kagambèga LJ, Kologo KJ, Millogo GRC, Thiam A, *et al*. Maternal and fetal prognosis of subsequent pregnancy in black African women with peripartum cardiomyopathy. BMC Cardiovasc Disord 2018;18:119.
13. Wu VC, Chen TH, Yeh JK, Wu M, Lu CH, Chen SW, *et al*. Clinical outcomes of peripartum cardiomyopathy: A 15-year nationwide population-based study in Asia. Medicine (Baltimore) 2017;96:e8374.
14. Kiefer TL, Bashore TM. Pulmonary hypertension related to left-sided cardiac pathology. Pulm Med 2011;2011:381787.
15. Boxhammer E, Berezin AE, Paar V, Bacher N, Topf A, Pavlov S, *et al*. Severe aortic valve stenosis and pulmonary hypertension: A systematic review of non-invasive ways of risk stratification, especially in patients undergoing transcatheter aortic valve replacement. J Pers Med 2022;12:603.
16. Youssef GS. Aortic Valve Diseases in Pregnancy. E-Journal of Cardiology Practice 2020;18. Available from: https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-18/aortic-valve-diseases-in-pregnancy.
17. Herzig MS, McIlvaine S, Feinberg L, Spiel MH, Carroll BJ. Outcomes of bicuspid aortic valve in pregnancy. Am J Cardiol 2024;221:74-6.
18. Youssef GS. Mitral stenosis in pregnant patients. E-journal of Cardiology Practice 2018;16. Available from: https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-16/Mitral-stenosis-in-pregnant-patients.
19. van Hagen IM, Thorne SA, Taha N, Youssef G, Elnagar A, Gabriel H, *et al*. Pregnancy outcomes in women with rheumatic mitral valve disease: Results from the registry of pregnancy and cardiac disease. Circulation 2018;137:806-16.
20. French KA, Poppas A. Rheumatic heart disease in pregnancy: Global challenges and clear opportunities. Circulation 2018;137:817-9.
21. McNeil A, Chen J, Meng ML. Pulmonary hypertension in pregnancy-the Anesthesiologist's perspective. Int J Cardiol Congenital Heart Disease 2021;5(Suppl 1):100234. doi: 10.1016/j.ijcchd.2021.100234.
22. Marshall WH, Gee S, Lim W, Lastinger LT, Cackovic M, Benza RL, *et al*. Maternal and fetal outcomes in pregnant women with pulmonary hypertension: The impact of left heart disease. Int J Cardiol Congenit Heart Dis 2022;8:100354.
23. Leber L, Beaudet A, Muller A. Epidemiology of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension: Identification of the most accurate estimates from a systematic literature review. Pulm Circ 2021;11:2045894020977300.
24. Chang KY, Duval S, Badesch DB, Bull TM, Chakinala MM, De Marco T, *et al*. Mortality in pulmonary arterial hypertension in the modern era: Early insights from the pulmonary hypertension association registry. J Am Heart Assoc 2022;11:e024969.
25. Krishnan S, Fricke EM, Cordoba M, Chalifoux LA, Girgis RE. Pulmonary hypertension complicating pregnancy. Curr Pulmonol Rep 2021;10:71-83.
26. Silversides CK, Grewal J, Mason J, Sermer M, Kiess M, Rychel V, *et al*. Pregnancy Outcomes in Women With Heart Disease: The CARPREG II Study. J Am Coll Cardiol 2018;71:2419-30.
27. Low TT, Granton J. Pregnant with pulmonary arterial hypertension-Can we handle the pressure? Int J Cardiol 2021;328:180-1.
28. Ballard W 3rd, Dixon B, McEvoy CA, Verma AK. Pulmonary arterial hypertension in pregnancy. Cardiol Clin 2021;39:109-18.
29. Anjum H, Surani S. Pulmonary hypertension in pregnancy: A review. Medicina (Kaunas) 2021;57:259.
30. Vaidy A, Vaidya A. Pulmonary arterial hypertension in pregnancy. Curr Opin Cardiol 2023;38:250-6.
31. Low TT, Silversides C. Pregnancy management in patients with pulmonary arterial hypertension. In: Sharma G, Scott NS, Davis MB, Economy KE, eds. Contemporary Topics in Cardio-Obstetrics. Humana Cham 2023:395-405.
32. Barańska-Pawełczak K, Wojciechowska C, Jacheć W. Pregnancy in patients with pulmonary arterial hypertension in light of new ESC guidelines on pulmonary hypertension. Int J Environ Res Public Health 2023;20:4625.
33. Muller BA, Diab KA. Pulmonary hypertension in pregnancy and its effects on the fetus. Semin Fetal Neonatal Med 2022;27:101348.
34. Kiely D, Condliffe R, Webster V, Mills G, Wrench I, Gandhi S, *et al*. Improved survival in pregnancy and pulmonary hypertension using a multiprofessional approach. BJOG 2010;117:565-74.
35. Sarma AA, Aggarwal NR, Briller JE, Davis M, Economy KE, Hameed AB, *et al*. The utilization and interpretation of cardiac biomarkers during pregnancy: JACC: Advances expert panel. JACC Adv 2022;1:100064.
36. Tanous D, Siu SC, Mason J, Greutmann M, Wald RM, Parker JD, *et al*. B-type natriuretic peptide in pregnant women with heart disease. J Am Coll Cardiol 2010;56:1247-53.
37. Davis MB, Arany Z, McNamara DM, Goland S, Elkayam U. Peripartum cardiomyopathy: JACC state-of-the-art review. J Am Coll Cardiol 2020;75:207-21.
38. Park K, Bairey Merz CN, Bello NA, Davis M, Duvernoy C, Elgendy IY, *et al*. Management of women with acquired cardiovascular disease from pre-conception through pregnancy and postpartum: JACC focus seminar 3/5. J Am Coll Cardiol 2021;77:1799-812.
39. Bozkurt B, Colvin M, Cook J, Cooper LT, Deswal A, Fonarow GC, *et al*. Current diagnostic and treatment strategies for specific dilated cardiomyopathies: A scientific statement from the American Heart Association. Circulation 2016;134:e579-646.
40. Bauersachs J, Arrigo M, Hilfiker-Kleiner D, Veltmann C, Coats AJ, Crespo-Leiro MG, *et al*. Current management of patients with severe acute peripartum cardiomyopathy: Practical guidance from the Heart Failure Association of the European Society of Cardiology Study Group on peripartum cardiomyopathy. Eur J Heart Fail 2016;18:1096-105.
41. European Society of Gynecology (ESG); Association for European Paediatric Cardiology (AEPC); German Society for Gender Medicine (DGesGM); Regitz-Zagrosek V, Blomstrom Lundqvist C, Borghi C, *et al*. ESC Guidelines on the management of cardiovascular diseases during pregnancy: The Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). Eur Heart J 2011;32:3147-97.
42. McLaughlin VV, Archer SL, Badesch DB, Barst RJ, Farber HW, Lindner JR, *et al*. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. J Am Coll Cardiol 2009;53:1573-619.
43. Galie N, Torbicki A, Barst R, Dartevelle P, Haworth S, Higenbottam T, *et al*. Guidelines on diagnosis and treatment of pulmonary arterial hypertension. The Task Force on Diagnosis and Treatment of Pulmonary Arterial Hypertension of the European Society of Cardiology. Eur Heart J 2004;25:2243-78.
44. Duarte AG, Thomas S, Safdar Z, Torres F, Pacheco LD, Feldman J, *et al*. Management of pulmonary arterial hypertension during pregnancy: A retrospective, multicenter experience. Chest 2013;143:1330-6.
45. Brittain EL, Pugh ME, Wheeler LA, Robbins IM, Loyd JE,

Newman JH, *et al*. Prostanoids but not oral therapies improve right ventricular function in pulmonary arterial hypertension. JACC Heart Fail 2013;1:300-7.
46. Sitbon O, Humbert M, Jaïs X, Ioos V, Hamid AM, Provencher S, *et al*. Long-term response to calcium channel blockers in idiopathic pulmonary arterial hypertension. Circulation 2005;111:3105-11.
47. Rosengarten D, Blieden LC, Kramer MR. Pregnancy outcomes in pulmonary arterial hypertension in the modern management era. Eur Respir J 2012;40:1304-5.
48. Song C, Kunovszki P, Beaudet A. Comparison of healthcare encounters and drug persistence in patients with pulmonary arterial hypertension receiving oral selexipag, inhaled iloprost, or parenteral treprostinil: A retrospective database analysis. J Health Econ Outcomes Res 2022;9:151-60.
49. Gayat E, Mebazaa A. Pulmonary hypertension in critical care. Curr Opin Crit Care 2011;17:439-48.
50. Mishra A, Kumar B, Dutta V, Arya VK, Mishra AK. Comparative effect of levosimendan and milrinone in cardiac surgery patients with pulmonary hypertension and left ventricular dysfunction. J Cardiothorac Vasc Anesth 2016;30:639-46.
51. Hemnes AR, Kiely DG, Cockrill BA, Safdar Z, Wilson VJ, Al Hazmi M, *et al*. Statement on pregnancy in pulmonary hypertension from the pulmonary vascular research institute. Pulm Circ 2015;5:435-65.
52. Meng L, Landau R, Viktorsdottir O, Banayan J, Grant T, Bateman B, *et al*. Pulmonary hypertension in pregnancy: A report of 49 cases at four tertiary north American sites. Obstet Gynecol 2017;129:511-20.
53. Sliwa K, van Hagen IM, Budts W, Swan L, Sinagra G, Caruana M, *et al*. Pulmonary hypertension and pregnancy outcomes: Data from the Registry Of Pregnancy and Cardiac Disease (ROPAC) of the European Society of Cardiology. Eur J Heart Fail 2016;18:1119-28.
54. Meng ML, Arendt KW. Obstetric anesthesia and heart disease: Practical clinical considerations. Anesthesiology 2021;135:164-83.
55. Afari H, Sheehan M, Reza N. Contemporary management of cardiomyopathy and heart failure in pregnancy. Cardiol Ther 2024;13:17-37.
56. Cauldwell M, Steer PJ, Swan L, Uebing A, Gatzoulis MA, Johnson MR. The management of the third stage of labour in women with heart disease. Heart 2017;103:945-51.
57. Al-Sabbak, Muhsin. Reducing the Risk of Venous Thromboembolism during Pregnancy and the Puerperium. Green-top Guideline No. 37a. 2017.
58. Cleland K, Zhu H, Goldstuck N, Cheng L, Trussell J. The efficacy of intrauterine devices for emergency contraception: A systematic review of 35 years of experience. Hum Reprod 2012;27:1994-2000.
59. Ong JYS, Yap JJY, Dashraath P, Low TT, Choolani M, Poh KK. Pulmonary hypertension in pregnancy: two sides to a coin. Singapore Med J 2025;66:168-72.