Journal of Cardiothoracic Surgery

RESEARCH

Open Access

Clinical outcomes of pregnancy in patients with pulmonary hypertension: A single center observational study

Jianrong Pan[2†], Qingsong Wu[1†], Shixin Chen[3], Huilan Wang[2] and Qimin Wang[1*]

Abstract

Background Pulmonary hypertension (PH) is associated with right ventricular failure in pregnant women and increases maternal morbidity and mortality during parturition and postpartum periods. According to current guidelines, pregnancy is contraindicated in women with PH. However, in recent decades, favorable outcomes have been observed in cases where the disease is well controlled. However, several questions remain unanswered regarding this issue.

Objective This study aimed to investigate the medium-term outcomes of pregnancy in women with PH and to identify predictors for poor pregnancy outcomes in this population.

Methods A retrospective review of the medical records at our hospital was conducted to identify pregnant women with PH between July 2017 and December 2021. We collected data on maternal age, gravidity, parity, PH category, New York Heart Association Function class, N-terminal-pro Brain natriuretic peptide (NT-ProBNP) levels, mode of delivery, type of anesthesia, use of advanced therapy, and fetal outcomes. Based on the severity of PH, patients were categorized into three groups: group A systolic pulmonary arterial pressure (SPAP) 40–50 mmHg, group B 50–70 mmHg, and group C SPAP ≥ 70 mmHg.

Results The study included 78 individuals in group A, 22 in group B, and 18 in group C. Of the 118 individuals, 80 were classified as having pulmonary arterial hypertension (PAH), including congenital heart disease-associated PAH, idiopathic PAH, and other PAH subtypes, while 38 were classified as having PH associated with left heart disease (PH-LHD). The mortality rate was higher in the PAH category (6.3%, 5/80) than in the PH-LHD category (2.6%, 1/38). The NT-proBNP value was highest in group C (1723.5 ± 738.0pg/ml), compared with group B (196.6 ± 79.6 pg/ml) and group A (128.7 ± 54.3 pg/ml). Overall maternal mortality was 5.1% (6/118), with significantly higher mortality rates observed in group C (27.8%, 5/18) compared to group B (4.6%, 1/22), and no deaths in group A. Compared to groups A and B, gestational duration was shorter (median 26 weeks), and abortion rates were higher (38.9%, 7/18) in group C. Cesarean section rates were high across all three groups. The overall maternal mortality rate was 5.1% (6/118). Of

†Jianrong Pan and Qingsong Wu are contributed equally to this study and share first authorship.

*Correspondence:
Qimin Wang
wangqm98@163.com

Full list of author information is available at the end of the article

them, five individuals were in group C, only one woman had moderate PH with perinatal cardiomyopathy and a lower LVEF of 15%. There was no maternal mortality in Group A with mild PH. All maternal deaths occurred postpartum. Excluding 17 cases of miscarriage (gestation less than 28 weeks), the overall offspring mortality rate was 4.0% (4/101), with one fetal mortality in group B, three fetal deaths in group C, and no fetal mortality observed in group A.

Conclusion Severe PH and high NT-proBNP levels are strongly correlated with increased maternal mortality rates in pregnant women. Conception should be contraindicated in cases of severe PAH with elevated NT-proBNP levels. In situations where unplanned pregnancy occurs in severe PAH patients with decompensated heart function, early pregnancy termination and multidisciplinary management are crucial to ensure maternal safety. However, pregnancy should be considered individually in women with moderate and mild PH and preserved right heart function.

Keywords Pulmonary arterial hypertension, Pregnancy, Pregnancy outcomes, Fetal outcomes, Pulmonary hypertension

Introduction

Pulmonary hypertension (PH) is rare. Severe PH is characterized by pulmonary vascular bed remodeling. The incidence rate of PH is approximately 1% in the global population [1]. Several underlying conditions can lead to these disorders. Severe PH increases pulmonary vascular bed resistance, resulting in right-sided heart failure, reducing the patient's life expectancy [2]. According to the 2022 the European Society of Cardiology/the European Respiratory Society Guidelines for the diagnosis and treatment of PH, pregnancy in women with pulmonary arterial hypertension (PAH) and other forms of severe PH has been historically associated with maternal mortality rates of up to 56% and neonatal mortality rates of up to 13%. With improved treatment of PAH and new approaches to managing women during pregnancy and the peri-partum period, maternal mortality has declined but remains high, ranging 11–25%. For these reasons, previous European Society of Cardiology/the European Respiratory Society Guidelines for the diagnosis and treatment of PH have recommended that patients with PAH should avoid pregnancy [3, 4].

Pregnancy causes an increase in blood volume of approximately 50% and a reduction in systemic vascular resistance [5]. Therefore, during parturition, cardiac output increases by 50%. However, in pregnant patients with PH, the ability of the pulmonary vascular bed to withstand the elevated blood volume is limited, and pulmonary arterial pressure tends to increase linearly with cardiac output resulting in the failure of right heart function [5, 6]. Therefore, pregnant women with PH are associated with an increased risk of maternal and fetal morbidity [7–9]. Traditionally, contraception is advised in women with PH [10, 11]. However, in recent years, a better understanding of the pathophysiology of PH, advanced drug therapy, and availability of multidisciplinary care teams, increasing reports of young women with well-controlled PH have shown favorable pregnancy outcomes [12–14]. Due to the absence of large-scale prospective studies, many questions remain unanswered [9]. This study aimed to analyze midterm pregnancy outcomes in women with PH and identify the risk factors associated with maternal mortality in a single tertiary center in China.

Methods

Patients

Approval to perform a retrospective review of the obstetric, maternal, and neonatal outcomes among pregnant women with pulmonary hypertension was obtained from the review board of the Union Hospital of Fujian Medical University. We analyzed 118 case records of pregnant women with PH from July 2017 to December 2021 in our hospital. The inclusion criterion was systolic pulmonary arterial blood pressure (PABP) > 40 mmHg as measured by right heart catheterization. However, few patients underwent right-sided heart catheterization before pregnancy. Throughout pregnancy, PABP was monitored using echocardiography. In this study, PH was divided into mild PH (40–50 mmHg), moderate PH (50–70 mmHg) and severe PH (≥ 70 mmHg). Baseline data of all pregnant women were collected including age, gravida parity, the underlying heart lesion, New York Heart Association (NYHA) functional class, N-terminal pro-brain natriuretic peptide (NT-proBNP) levels, mode of delivery, time of delivery, gestational age (weeks), type of anesthesia, postpartum complications, fetal outcomes, use of anticoagulation, and advanced therapy (such as nitric oxide, prostacyclin analogs, bosentan, or sildenafil) were recorded in all cases.

Patients were classified into three groups, A, B, and C, according to the severity of PH, to identify whether the severity of PH affects the morbidity and mortality of pregnant women. According to the etiology, PH is classified into five clinical subgroups (Supplementary Table 1) [3]: ① pulmonary arterial hypertension (PAH) including idiopathic PH (IPAH), PH associated with congenital heart disease (PAH-CHD), ② PH associated with left heart disease (PH-LHD), ③ PH associated with lung diseases and/or hypoxia, ④ PH associated with pulmonary

artery obstructions, ⑤ PH with unclear and/or multifactorial mechanisms [3, 4].

Statistical analysis

The patients' baseline characteristics, peripartum management, and pregnancy outcomes are presented for each group. Numerical values are presented as medians (ranges) and categorical variables as numbers (percentages) per group. Categorical data were compared using the X^2 test with Yates correction for small sample sizes. Fisher's exact test was used for groups with fewer than five cases. Univariate logistic regression was used to identify predictors of maternal mortality between demographic and clinical variables, including the model of delivery, model of anesthesia, and severity and categories of PH. Statistical significance was set at $P<0.05$. All analyses were performed using SPSS (version 26.0. SPPS Inc.)

Results

Demographic characteristics

There were a total of 118 women with 78 (66.1%) in group A with mild PH, 22 (18.6%) in group B with moderate PH, and 18 (15.3%) in group C with severe PH. All patients were diagnosed using transthoracic echocardiography, and 12 underwent right heart catheterization. There was no difference in age among the three groups ($P>0.05$) (Table 1).

Obstetric characteristics

Of 118 cases, 40 (33.9%) involved nulliparous individuals, 63 cases (53.4%) were second-time deliveries, 10 (8.5%) were third-time deliveries, and five cases (4.2%) were fourth-time deliveries. There were 12 (10.1%) patients diagnosed with PH before pregnancy. Most pregnancies were unplanned. NYHA class differed among the three groups. In group A, 74 (94.8%) patients had good heart

Table 1 Baseline characteristics, management, and outcomes of pregnant women

	Group A (*N* = 78)	Group B (*N* = 22)	Group C (*N* = 18)	*P* Value
Age, years	28.4 ± 11.0	28.6 ± 9.7	27.5 ± 10.0	0.805
Nulliparous, n (%)	32 (41.0)	6 (27.3)	2 (11.1)	0.041
Diagnosis made				
Before pregnancy, n (%)	15 (19.2)	5 (22.7)	3 (16.7)	0.886
During pregnancy, n (%)	63 (80.8)	17 (77.3)	15 (83.3)	0.886
NYHA class				
I, n (%)	68 (87.2)	12 (54.5)	0 (0.0)	< 0.001
II, n (%)	8 (10.3)	7 (31.8)	8 (44.4)	0.001
III, n (%)	2 (2.6)	2 (9.1)	6 (33.3)	< 0.001
IV, n (%)	0 (0.0)	1 (4.5)	4 (22.2)	< 0.001
Systolic PABP, mmHg	45.3 ± 8.4	59.8 ± 12.2	87.6 ± 13.7	< 0.001
NT-proBNP, pg/ml	128.7 ± 54.3	196.6 ± 79.6	1723.5 ± 738.0	< 0.001
LVEF, %	65.4 ± 5.7	64.2 ± 14.8	61.9 ± 18.3	0.459
Management				
Anticoagulation, n (%)	0 (0.0)	5 (22.7)	7 (38.9)	< 0.001
Diuretic, n (%)	0 (0.0)	4 (18.2)	9 (50.0)	< 0.001
Advanced drug, n (%)	0 (0.0)	3 (13.6)	7 (38.9)	< 0.001
Pregnant Duration				
Q ≤ 20 weeks, n (%)	7 (8.9)	2 (9.1)	7 (38.9)	0.035
20 < Q ≤ 30 weeks, n (%)	2 (2.6)	1 (4.6)	3 (16.7)	0.049
30 < Q ≤ 35 weeks, n (%)	6 (7.7)	7 (31.8)	3 (16.7)	0.013
Q > 35 weeks, n (%)	63 (80.8)	12 (54.5)	5 (27.8)	< 0.001
Delivery model				
Cesarean section, n (%)	45 (63.4)	19 (95.0)	10 (90.9)	0.039
Vaginal delivery, n (%)	26 (36.6)	1 (5.0)	1 (10.1)	0.003
Anesthesia				
No, n (%)	26 (33.3)	1 (22.7)	1 (5.56)	0.003
Epidural anesthesia, n (%)	43 (51.3)	12 (50.0)	10 (55.6)	0.999
General anesthesia, n (%)	19 (24.4)	9 (40.9)	7 (38.9)	0.210
Maternal death, n (%)	0 (0.00)	1 (4.55)	5 (27.8)	< 0.001

PABP = pulmonary arterial blood pressure,

NYHA = New York Heart Association,

NT-proBNP = N-terminal pro-brain natriuretic peptide,

LVEF = Left ventricular ejection fraction

function (NYHA class I–II), and only two individuals were NYHA class III. However, in group C, 10 patients were NYHA class III, and five patients were NYHA class IV. The value of NT-ProBNP was 128.7 ± 54.3 pg/ml in group A, 196.6 ± 79.6 pg/ml in group B, and 1723.5 ± 738.0 pg/ml in group C. The LVEF value was low in group C, but the difference was not statistically significant.

The gestation duration was significantly different among the three groups. The overall average gestation duration was 32 ± 8.1 weeks (7 weeks to 39 weeks). Of the 118 cases, 80 were classified as PAH including congenital heart disease-associated PAH, idiopathic PAH, and other PAH subtypes, while 38 cases were classified as left-sided heart disease-associated PH. The mortality rate was higher in the PAH category (6.3%, 5/80) compared to PH-LHD (2.6%, 1/38). Gestational duration (range, 7–38 weeks) was shorter in group C. Overall, 16 patients had a gestational duration < 20 weeks because of therapeutic abortion due to uncontrolled PH, primary heart disease, and fetal abnormalities. The abortion rates were 38.9% (7/18), 9.1% (2/22), and 9.0% (7/78) in groups C, B, and A, respectively. The rates of gestational duration > 35 weeks were 80.8%, 54.0%, and 27.8% in groups A, B, and C, respectively which indicated that severe PH was associated with shorter gestational duration and a high rate of unsuccessful pregnancies. Overall, 74 women (72.5%,74/102) underwent cesarean section, which was high in all three groups, Among them, 63.4% (45/71) were in group A, 95.0% (19/20) in group B and 90.9% (10/11) in group C. While 28 (27.5%) underwent vaginal delivery. Epidurals and/or spinal blocks were performed in 65 (55.1%) patients and 35 (29.7%) patients were administered general anesthesia. Epidurals and/or spinal blocks were performed in 65 (55.1%) patients, primarily for cesarean sections and some vaginal deliveries, while 35 (29.7%) patients received general anesthesia, mainly in emergency situations or when regional anesthesia was contraindicated. The remaining 18 (15.2%) patients did not receive anesthesia, as they underwent spontaneous vaginal delivery (1.7%) or pregnancy termination(13.5%). There was no significant difference in the selection of anesthesia methods (epidural vs. general anesthesia) among the three groups ($P > 0.05$).

Management of PH

A total of 106 (89.3%) pregnant women were unaware of the presence of PH before pregnancy. Diuretics were used in 13 (10.1%) patients whose heart function was higher than NYHA class III. Anticoagulants were administrated to eight (6.8%) patients. There were ten (8.5%) patients who took pulmonary vascular-targeted medication during pregnancy or postpartum, of whom eight were taking endothelin-receptor antagonists and two were taking a phosphodiesterase type 5 inhibitor, A prostaglandin I.

The distribution of PH etiology

With regard to PH etiology, 80 (67.8%) cases were PAH, and 38 (32.2%) were PH-LHD. Of the 80 PAH cases, 57 (48.3%) were PAH-CHD, 11 (9.3%) were IPAH, and 12 (10.2%) were OPAH. There was no statistically significant difference in the distribution of PH etiologies among the three groups. However, the maternal mortality rate between the PH subgroups was significantly different with 6.1% (5/80) for PAH and 2.6% (1/38) for PH-LHD. Among the 57 cases of PAH-CHD, there were three fatal cases of Eisenmenger syndrome (Table 2).

Maternal outcomes

Maternal mortality

Six maternal deaths occurred, corresponding to a 5.1% mortality rate. Of them, five were in group C with severe PH, only one patient with moderate PH and perinatal cardiomyopathy with a low LVEF of 15%, whose pregnancy was terminated at 10 weeks gestation. There were no maternal mortalities in group A with mild PH, five patients died postpartum, and one patient died due to cardiac arrest during cesarean section under general anesthesia. We believe this was likely caused by right heart failure and hemodynamic instability induced by severe PH. Among the six deaths, three were due to Eisenmenger syndrome PAH-CHD, one was IPAH, one was PH-LHD, one was perinatal cardiomyopathy, and the other was OPAH with hyperthyroidism. The NT-proBNP level was > 1000 pg/ml in patients who died. NYHA class grade was > III. There were two patients with normal LVEF and three patients with low LVEF. Gestation was short, resulting from early termination due to maternal worsening of heart function and increasing PH. There was only one case of neonatal survival, whose gestation was 29 weeks (Table 3).

Follow up data

A total of 112 discharged patients with PH were followed up for a period of 6 months to 1 year. Patients in group A were followed up for six months, while those in the other two groups were followed up for one year. During the follow-up period, 13 patients underwent heart surgery for atrial septal defect correction, and five PAH patients in group C received medication to reduce PH and anticoagulation. No patient died during the follow-up period.

Fetal outcomes

After excluding 17 abortions, 101 children were born. There were four fetal mortalities, and the total offspring mortality rate was 4.0% (4/101). The overall fetal survival rate was 96.0% (97/101), which was lower in group C

Table 2 Etiology distribution of diseases in patients with pulmonary hypertension

Etiology of lesion	Mild PAH *N* = 78	Moderate PAH *N* = 22	Severe PAH *N* = 18
IPAH, n (%)	7 (9.0)	2 (9.1)	2 (11.1)
PAH-CHD, n (%)	37 (47.4)	10 (45.5)	10 (45.5)
Atrial septal defect, n (%)	24 (30.8)	6 (27.3)	4 (22.2)
Ventricle septal defect, n (%)	12 (15.4)	2 (9.1)	4 (22.2)
Patent ductus arteriosus, n (%)	4 (5.1)	2 (9.1)	2 (11.1)
Endocardial cushion defect, n (%)	2 (2.6)	1 (4.5)	0 (0.0)
Total anomalous pulmonary venous connection, n (%)	1 (1.3)	0 (0.0)	0 (0.0)
OPAH	8 (10.3)	3 (13.6)	1 (5.6)
Systemic lupus erythematosus, n (%)	2 (2.6)	1 (4.5)	0 (0.0)
Mixed collective tissue diseases, n (%)	3 (3.8)	0 (0.0)	0 (0.0)
Hyperthyroidism, n (%)	4 (5.1)	1 (4.5)	1 (5.6)
PH-LHD	26 (33.3)	7 (31.8)	5 (22.7)
Mitral valve insufficient/stenosis, n (%)	18 (23.1)	5 (22.7)	5 (22.7)
Aortic valve insufficient/stenosis, n (%)	5 (6.4)	1 (4.5)	1 (5.6)
Hypertrophy obstruction myocardiopathy, n (%)	2 (2.6)	0 (0.0)	0 (0.0)
Perinatal cardiomyopathy, n (%)	1 (1.3)	1 (4.5)	1 (5.6)
Total, n (%)	78 (100)	22 (100)	18 (100)

PAH = pulmonary arterial hypertension,

IPAH = idiopathic pulmonary arterial hypertension,

PAH-CHD = pulmonary hypertension associated with congenital heart disease,

OPAH = other reason pulmonary arterial hypertension,

PH-LHD = pulmonary hypertension associated with left heart disease

Table 3 Characteristics of maternal mortalities

Characters	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age years	27	38	40	30	23	25
Parity	G4P1	G6P3	G5P1	G2P1	G2P1	G1P0
Etiology of disease	PAH-CHD (atrial septal defect)	OPAH	IPAH	PH-CHD (atrial septal defect)	PH-LHD	PAH-CHD (Ventricle septal defect, Patent ductus arterial)
Eisenmenger' syndrome	Yes	No	No	Yes	No	Yes
Complication	hepatitis	Gestational diabetic melius, Hyperthyroidism	Hydronephrosis, pneumonia	Pulmonary thrombosis	Cardiomyopathy	Pneumonia
NYHA class	IV	IV	IV	IV	IV	IV
S-PABP, mmHg	116	83	167	193	81	130
NT-proBNP, pg/mL	4367	1275	3992	4357	2233	1071
LVEF, %	67	40	57	36	25	52
G. week of diagnose PH	28^{+4}	27^{+4}	12^{+4}	7^{+2}	10^{+2}	22^{+2}
Termination of G. weeks	29^{+2}	28^{+4}	19^{+3}	8^{+1}	10^{+3}	29
Delivery model	Caesarean section	Caesarean section	Abortion	Abortion	Abortion	Caesarean section
Anesthesia model	Epidural	Epidural	General	Epidural	Epidural	General
Timing death	during Delivery	9d Post Delivery	6d Post Delivery	2d Post Delivery	30d Post Delivery	21d post Delivery
Advance therapy	NO	Sildenafil	Bosten	Bosten	NO	Prostaglandin E and Sildenafil
Death reason	Cardiac arrest	Cardiac arrest, Multiple organ failure	Cardiac arrest	Hypoxia	Cardiac shock	Fungal Sepsis
Fetal destiny	Died	Died	Miscarriage	Miscarriage	Miscarriage	survival

PH = pulmonary hypertension, IPAH = idiopathic pulmonary arterial hypertension, PAH-CHD = pulmonary hypertension associated with congenital heart disease, OPAH = other reason pulmonary arterial hypertension, PH-LHD = pulmonary hypertension associated with left heart disease, NYHA = New York heart association, NT-proBNP = N-terminal pro-brain natriuretic peptide, LVEF = Left ventricular ejection fraction, G. week = Gestational week

Table 4 Fetal and neonatal outcomes

Fetal complication	Group A (*N* = 78)	Group B (*N* = 22)	Group C (*N* = 18)	*P* value
Body weight (g)	3027.6 ± 563.3	2688.8 ± 354.4	1953.2 ± 368.0	< 0.001
Premature delivery < 37 weeks, n (%)	18 (23.1)	11 (50.0)	7 (38.9)	0.037
Miscarriage < 28 weeks, n (%)	7 (9.0)	2 (9.1)	7 (38.9)	0.006
Fetus mortality ≥ 28 weeks, n (%)	0	1 (4.5)	3 (16.7)	0.002

(72.7%, 8/11) than in group B (95.0%, 19/20). There was no fetal mortality in group A. Of the 17 miscarriages, 13 were therapeutic abortion and three cases were spontaneous abortions. Of the four fetal deaths, two died of multiple malformations, two were stillborn, and one had a lung hemorrhage with a low body weight. Three offspring were born with congenital heart disease, one neonatal with patent ductus arteriosus, and two with atrial septal defect, and all were doing well at the 6-month follow-up (Table 4).

Discussion

Previous studies showed that pregnant patients with severe PH had maternal mortality rates as high as 30–56% [15,16]. Even after the introduction of pulmonary vascular-targeted medications, maternal mortality remains high [9, 17, 18]. However, there has been a decreasing trend in maternal mortality, as low as 2.5–5.6%, over the past several years [19–21], which results from a more precise understanding of the pathophysiological hemodynamic changes in pregnancy with PH and advanced peripartum management, especially in the multidisciplinary cardio-obstetrics care team.

Karen et al. [22] reported a 3.3% maternal mortality rate among 151 cases of pregnant women with PH from several European hospitals in the Registry On Pregnancy and Cardiac disease. Our study showed that, among 118 pregnant women with PH, the overall maternal mortality rate was 5.1% (6/118). Indeed, progress in the outcome of pregnancies of women with PH has been made over the past decades, not only in Europe but also in China, a developing country [20, 23]. Our hospital is the largest general tertiary hospital with the largest cardiovascular center in Fujian province. Many pregnant women with cardiovascular disease were transferred to our hospital, and it was necessary to set up a multidisciplinary care team to deal with PH in pregnant women. Based on recorded data, there were four mortality cases before Feb 2019 and maternal mortality decreased after implementation of multidisciplinary care, which was critical in the management of pulmonary artery hypertension-complicated pregnancies and deliveries [13]. For management of PH patients during pregnancy, ① Patients with PH during pregnancy require close monitoring, with follow-up frequency including echocardiography and NT-proBNP testing every 2 months. ② Recommended examinations include NT-proBNP testing, echocardiography, 6-minute walk test, and fetal ultrasound (if necessary). ③ A multidisciplinary team approach is recommended, involving regular consultations with community physicians, gynecologists, obstetricians, pharmacists, cardiologists, cardiac surgeons, and anesthesiologists, with meetings held once a month. We recommend that the multidisciplinary team includes gynecologists, obstetricians, cardiologists, cardiac surgeons, anesthesiologists, intensive care union physicians, neonatologists and Nursing staff.

Earlier pregnancy termination may have been associated with the low maternal mortality in our study. Selection of the timing of termination of pregnancy is a very important issue in dealing with pregnancy in women with PH [26, 27], the timing of termination depends not only on the severity of pulmonary artery pressure but also on heart function, hemodynamic state, NT-proBNP, and fetal maturity. Only 23 patients were diagnosed with PH before pregnancy. For women with unplanned pregnancy and well-controlled PH, close follow-up is recommended throughout the pregnancy. For women with PAH, if the hemodynamic status is stable, right heart function is preserved, left ventricle ejection fraction is good, NT-proBNP is normal, fetal maturity should be considered, and birth can be postponed to 37 weeks. In this study, mature delivery occurred in 49 cases (62.8%) in group A, nine cases (40.9%) in group B, and four cases (22.2%) in group C. When pregnant women show worsened heart function (NYHA class IV grade), NT-proBNP levels increased to more than 1000Pg/ml, and impaired right heart function, termination of the pregnancy should be considered for the safety of the mother. In this study, 38 pregnancies (32.2%) were terminated before 35 weeks of gestation. 16 of these terminations occurred before 20 weeks, six between 20 and 30 weeks, and 16 between 30 and 34 weeks. The abortion rates were very high in group C (38.9% [7/18]), followed by 9.1% (2/22) in group B, and 9.0% (7/78) in group A.

Vaginal delivery reportedly improves mortality rates in pregnant women with PAH [27]. However, given that vaginal delivery has the potential risk of pain that can increase catecholamine release and cause hypoxia and acidosis, resulting in worsening pulmonary vasculature and right ventricle function. Although neuraxial anesthesia can effectively manage pain during vaginal delivery, some patients in our study did not receive epidural anesthesia due to emergency situations. Therefore, cesarean section was preferred to shorten the birth process

and better control hemodynamics and avoid the liability of labor. Therefore, cesarean section is recommended in pregnant women with severe PH, according to current guidelines [2]. In our study, cesarean section was the first choice of delivery method in groups B and C. The cesarean section rates were 90.9% and 75% in Group B, respectively. Only two patients had successful vaginal deliveries in groups B and C; these two patients were multipara. However, 26 patients in group A delivered vaginally.

Although the study showed favorable outcomes of pregnancy with mild and moderate PH overall, the mortality rate was still high in women with severe PH. It was 27.7% (5/18) in group C, these five patients had very severe PH, and the systolic PABP value was >100 mmHg. The high mortality rate in group C indicated that the severity of pulmonary disease (>100 mmHg) was a strong predictive risk factor in pregnant women with PH. It was reported that women with PAH had a higher mortality rate than those with PH-LHD [22, 24]. This was confirmed in our study, of the six maternal deaths five were PAH patients with a mortality rate of 6.1%(5/80). A single death occurred in an PH-LHD patient resulting in a mortality rate of 2.6% (1/38) for this etiology. Among the 57 patients with PAH-CHD, three deaths were in patients with Eisenmenger syndrome. PAH, particularly Eisenmenger syndrome, is a risk factor for maternal mortality in pregnant women with PH.

The NT-proBNP value was critical for risk stratification in the assessment of PH [3, 25], 1100.0 pg/ml is the cut-off level for the highest risk level of the four-class stratum model. In this study, the NT-proBNP value (1723.5 ± 738.0 pg/ml) was very high in group C, compared with 196.6 ± 79.6 pg/ml in group B, and 128.7 ± 54.3 pg/ml in group A. Among the six patients who died, four had elevated levels of NT-proBNP (>2000.0 pg/ml) and the remaining two patients had levels >1000.0 pg/ml. This indicates that elevated NT-proBNP levels are associated with a high risk of mortality in women during pregnancy.

The model of anesthesia is considered an impact factor for maternal death [7, 24]. Spinal anesthesia can prevent significant changes in hemodynamics. In our study, epidural or spinal anesthesia was most likely to be performed during cesarean sections and abortions in all groups. Overall, 55 (46.6%) patients underwent spinal or epidural anesthesia, and 32 (27.1%) underwent general anesthesia. Of the six deaths, three were treated with epidural anesthesia, and the other three patients underwent general anesthesia. The selection of the anesthesia model had little effect on maternal mortality in pregnant women.

Among pregnant patients with PH who die after delivery, most have severe PH rather than mild or moderate PH [22, 26, 28], and postpartum care and management are important issues for patients with severe PH. After delivery, an immediate fluid shift can increase the preload of the right ventricle and lead to high pulmonary venous pressure, which is more likely to result in congestive heart failure [28]. Therefore, diuretic therapy for a net negative fluid balance in severe postpartum PH is required. Patients were monitored for several days until their hemodynamics stabilized and NT-proBNP levels decreased. Twelve patients were transferred to the intensive care unit postpartum. Of the six cases of maternal death, one patient experienced cardiac arrest during the operation and died, while the other five died postpartum. This is similar to that reported in the literature [8, 18, 22]. The timings of death are presented in Table 3. The causes of death were cardiac arrest in three cases, cardiac shock in one case, severe hypoxia in one case and infection (fungal sepsis) in one case respectively. Management included hemodynamic monitoring, diuretic therapy, positive inotropic treatment, PH-targeted advanced drugs, and respiratory function support. However, for PAH patients with Eisenmenger's syndrome, severe PH is difficult to reverse using advanced targeted drugs and more likely to result in severe hypoxia and circulatory collapse. Extracorporeal membrane oxygenation and lung transplantation are the only available options.

Fetal outcomes differed among the three groups. The neonatal body weight in group A was normal while it was the lowest in group C. The miscarriage rates were high in groups C and B. It is still challenging to deal with neonates whose gestational age is less than 29 weeks, and there were 4 fetal deaths. Jha et al. demonstrated that the risk of adverse fetal outcomes is significantly increased in pregnancy with PH. Ladouceur et al. reported that patients with congenital heart disease-associated PH have poorer fetal outcomes [9, 21].

Based on the study data, the midterm maternal outcomes of pregnancy in women with mild and moderate PH were satisfactory, and some pregnant women with severe PH (well-controlled disease) also achieved favorable outcomes with the implementation of a multidisciplinary care plan and improvement of perinatal management. However, maternal mortality in patients with severe PAH remains high [25, 28, 29]. Therefore, the predictive risk factors for maternal mortality include high severity of PH, NT-proBNP level, state of heart function, and the etiology of PH. For young women with PH who want to become pregnant, it is crucial to consult obstetric and cardiac doctors and make risk assessments. The factors considered include the severity of PH, etiology of PH, state of right ventricle function, LVEF, and NT-proBNP level. For those unplanned pregnancies in women with moderate and severe PH, close perinatal monitoring and care must be conducted PH. Once heart function worsens and NT-proBNP levels greatly increase

after diuretic and advanced medicine therapy, early termination of pregnancy is indicated.

This study has several limitations. First, most cases of PH were diagnosed by echocardiography rather than a right heart catheter, which is invasive and unfeasible for pregnancy; therefore, data interpretation should be considered. Second, most PAH maternal deaths occurred postpartum [2]. In our study, the postpartum follow-up was only 6 months to 1 year, and the incidence of late mortality and long-term complications may be underestimated [1]. Third, NYHA was used for assessment of heart function, 6-minute walking distance was used only in a few cases, and heart function identification was objectively less exact. In addition, this study was a single-center retrospective study with a small sample size and limited extrapolation of results. Considering these factors, our conclusion is limited; therefore, further studies are needed to settle debated issues concerning pregnancy in women with PH.

Conclusion

Severe PH and high NT-proBNP levels are strongly correlated with increased maternal mortality rates in pregnant women. Conception should be contraindicated in cases of severe PAH with elevated NT-proBNP levels. In situations where unplanned pregnancy occurs in severe PAH patients with decompensated heart function, early pregnancy termination and multidisciplinary management are crucial to ensure maternal safety. However, pregnancy should be considered individually in women with moderate and mild PH and preserved right heart function.

Abbreviations

CHD	Congenital heart disease
IPAH	Idiopathic pulmonary arterial hypertension
LHD	Left heart disease
LVEF	Left ventricular ejection fraction
NT-proBNP	N-terminal pro-brain natriuretic peptide
OPAH	Other reason pulmonary arterial hypertension
PH	Pulmonary hypertension
PAH	Pulmonary arterial hypertension
PAH-CHD	Pulmonary hypertension associated with congenital heart disease
PAP	Pulmonary arterial pressure
RHC	Right heart catheterization
SPAP	Systolic pulmonary arterial pressure

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13019-025-03435-5.

Supplementary Material 1

Acknowledgements

We would like to thank Editage (www.editage.cn) for English language editing.

Author contributions

Qimin Wang designed the study and submitted the manuscript. Jianrong Pan and Qingsong Wu prepared the first draft of the manuscript and made the literature review. Jianrong Pan and Qingsong Wu are contributed equally to this study and share first authorship. Qimin Wang made substantial changes in the manuscript. Shixin Chen and Huilan Wang collected and analyzed data together. All authors read and approved the final manuscript.

Funding

This work was funded by the Key Laboratory of Cardio-Thoracic Surgery (Fujian Medical University), Fujian Province University (No.2019-067) and the Fujian Provincial Natural Science Foundation of China (2024J01627).

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was complied with the principles of the Declaration of Helsinki and approved by Union Hospital Fujian Medical University of the institutional review board (No.XH2023-069). Informed consent was waived in accordance with institutional policy for retrospective studies.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Cardiovascular Surgery, Union Hospital, Fujian Medical University, Xinquan Road 29, 350001 Fuzhou, Fujian, P. R. China
[2]Department of gynaecology and obstetrics, Union Hospital, Fujian Medical University, Fuzhou, Fujian, P. R. China
[3]Fujian Medical University, Fuzhou, Fujian, P. R. China

Received: 5 November 2024 / Accepted: 6 April 2025
Published online: 16 April 2025

References

1. Galiè N, Humbert M, Vachiery JL, Gibbs S, Lang I, Torbicki A, ESC Scientific Document Group. 2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension: the joint task force for the diagnosis and treatment of pulmonary hypertension of the European society of cardiology (ESC) and the European respiratory society (ERS): endorsed by: association for European paediatric and congenital cardiology (AEPC), international society for heart and lung transplantation (ISHLT). Eur Heart J. 2016;37(1):67–119.
2. Coursen J, Simpson CE, Mukherjee M, Vaught AJ, Kutty S, Al-Talib TK, et al. Pregnancy considerations in the multidisciplinary care of patients with pulmonary arterial hypertension. J Cardiovasc Dev Dis. 2022;9(8):260.
3. Hoeper MM, Pausch C, Olsson KM, Huscher D, Pittrow D, Grünig E, et al. COMPERA 2.0: a refined four-stratum risk assessment model for pulmonary arterial hypertension. Eur Respir J. 2022;60(1):2102311.
4. Vonk Noordegraaf A, Chin KM, Haddad F, Hassoun PM, Hemnes AR, Hopkins SR, et al. Pathophysiology of the right ventricle and of the pulmonary circulation in pulmonary hypertension: an update. Eur Respir J. 2019;53(1):1801900.
5. 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(3):435–65.
6. Galiè N, Channick RN, Frantz RP, Grünig E, Jing ZC, Moiseeva O, et al. Risk stratification and medical therapy of pulmonary arterial hypertension. Eur Respir J. 2019;53(1):1801889.
7. Maligireddy A, Jabri A, Zghouzi M, Rojulpote C, VanAken G, Janga C, et al. Maternal and fetal outcomes in pulmonary hypertension during pregnancy: A contemporary nationwide analysis. Am J Cardiol. 2024;221:113–9.
8. Duarte AG, Thomas S, Safdar Z, Torres F, Pacheco LD, Feldman J, deBoisblanc B. Management of pulmonary arterial hypertension during pregnancy: a retrospective, multicenter experience. Chest. 2013;143(5):1330–6.
9. Jha N, Jha AK, Mishra SK, Sagili H. Pulmonary hypertension and pregnancy outcomes: systematic review and Meta-analysis. Eur J Obstet Gynecol Reprod Biol. 2020;253:108–16.

10. Kamp JC, von Kaisenberg C, Greve S, Winter L, Park DH, Fuge J, Kühn C, Hoeper MM, Olsson KM. Pregnancy in pulmonary arterial hypertension: midterm outcomes of mothers and offspring. J Heart Lung Transpl. 2021;40(3):229–33.
11. European Society of Gynecology (ESG); Association for European Paediatric Cardiology (AEPC); German Society for Gender Medicine (DGesGM); Regitz-Zagrosek, Blomstrom Lundqvist V, Borghi C, Cifkova C, Ferreira R, Foidart R et al. JM,. ESC Committee for Practice Guidelines. 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(24):3147-97.
12. Zhou Q, Peng P, Liu X, Liu J, Gao J, Chen W. Evaluation of maternal and fetal outcomes in pregnancy complicated with pulmonary arterial hypertension. Ann Palliat Med. 2021;10(2):1404–10.
13. Shu T, Feng P, Liu X, Wen L, Chen H, Chen Y, et al. Multidisciplinary team managements and clinical outcomes in patients with pulmonary arterial hypertension during the perinatal period. Front Cardiovasc Med. 2021;8:795765.
14. Corbach N, Berlier C, Lichtblau M, Schwarz EI, Gautschi F, Groth A, et al. Favorable pregnancy outcomes in women with Well-Controlled pulmonary arterial hypertension. Front Med (Lausanne). 2021;8:689764.
15. Weiss BM, Zemp L, Seifert B, Hess OM. Outcome of pulmonary vascular disease in pregnancy: a systematic overview from 1978 through 1996. J Am Coll Cardiol. 1998;31(7):1650–7.
16. Yentis SM, Steer PJ, Plaat F. Eisenmenger's syndrome in pregnancy: maternal and fetal mortality in the 1990s. Br J Obstet Gynaecol. 1998;105(8):921–2.
17. Ma L, Liu W, Huang Y. Perioperative management for parturients with pulmonary hypertension: experience with 30 consecutive cases. Front Med. 2012;6(3):307–10.
18. Meng ML, 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(3):511–20.
19. Rudienė V, Kaplerienė L, Jančauskaitė D, Meškėnė E, Palevičiūtė E, Laukytė-Slėnienė M, et al. Pregnancy in congenital heart disease, complicated by pulmonary arterial Hypertension-A challenging issue for the pregnant woman, the foetus, and healthcare professionals. Med (Kaunas). 2022;58(4):476.
20. Liu Y, Li Y, Zhang J, Zhang D, Li J, Zhao Y, et al. Maternal and fetal outcomes of pregnant women with pulmonary arterial hypertension associated with congenital heart disease in Beijing, China: A retrospective study. Pulm Circ. 2022;12(2):e12079.
21. Ladouceur M, Benoit L, Radojevic J, Basquin A, Dauphin C, Hascoet S, et al. Pregnancy outcomes in patients with pulmonary arterial hypertension associated with congenital heart disease. Heart. 2017;103(4):287–92.
22. Sliwa K, van Hagen IM, Budts W, Swan L, Sinagra G, Caruana M, et al. ROPAC investigators. 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(9):1119–28.
23. Vaidya A, Oliveros E, Mulla W, Feinstein D, Hart L, Forfia P. Management of pulmonary arterial hypertension in pregnancy: experience from a nationally accredited center. J Cardiovasc Dev Dis. 2022;9(6):195.
24. Luo J, Shi H, Xu L, Su W, Li J. Pregnancy outcomes in patients with pulmonary arterial hypertension: A retrospective study. Med (Baltim). 2020;99(23):e20285.
25. Benza RL, Gomberg-Maitland M, Elliott CG, Farber HW, Foreman AJ, Frost AE, et al. Predicting survival in patients with pulmonary arterial hypertension: the REVEAL risk score calculator 2.0 and comparison with ESC/ERS-Based risk assessment strategies. Chest. 2019;156(2):323–37.
26. Bédard E, Dimopoulos K, Gatzoulis MA. Has there been any progress made on pregnancy outcomes among women with pulmonary arterial hypertension? Eur Heart J. 2009;30(3):256–65.
27. Wolla CD, Matos JR, Wineland R. Anesthetic management of severe pulmonary hypertension in pregnancy. J Cardiothorac Vasc Anesth. 2022;36(2):542–5.
28. Deng X, Jin B, Li S, Li Y, Zhou H, Wu Y, et al. Guideline implementation and early risk assessment in pulmonary arterial hypertension associated with congenital heart disease: A retrospective cohort study. Clin Respir J. 2019;13(11):693–9.
29. Sun X, Feng J, Shi J. Pregnancy and pulmonary hypertension: an exploratory analysis of risk factors and outcomes. Med (Baltim). 2018;97(44):e13035.

Publisher's note