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Original Article

Clinical insights and outcomes of pulmonary arterial hypertension in pregnant women: Experience from a national center in Vietnam

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Abstract

Introduction: Pulmonary hypertension (PH) during pregnancy poses significant risks, including high maternal and fetal morbidity and mortality. Managing pregnant patients with PH in developing countries, presents unique challenges, underscoring the need for further research and resources in these areas.

Methods: This retrospective study at Cho Ray Hospital in Vietnam collected data from January 2011 to September 2023. It included pregnant women with confirmed PH. Data on clinical and subclinical characteristics and outcomes were analyzed using descriptive and inferential statistics.

Results: The present study involved 41 pregnant women diagnosed with PH, and the average age of the patients was 29.3 ± 5.1 years. The mean gestational age at diagnosis was 25.1 ± 8.5 weeks. Idiopathic pulmonary arterial hypertension (iPAH) affected 68.3% of patients, making it the leading cause, followed by congenital heart disease-associated with pulmonary arterial disease (CHD-PAH) at 26.8% and connective tissue disease associated pulmonary arterial hypertension (CTD-PAH) at 4.9%. Echocardiography revealed a mean pulmonary artery pressure of 81.1 ± 30 mmHg. The study found a high maternal mortality rate of 17.1%. Pregnancy termination was indicated in 70.7% of the patients, resulting in a strikingly high fetal mortality rate of 41.4%.

Conclusion: Our study shows that the most common causes of pulmonary arterial hypertension (PAH) associated with pregnancy are iPAH, CHD-PAH, and CTD-PAH, respectively. Contraception should be recommended for women with PAH. Furthermore, due to the high maternal and fetal mortality rates, patients with PAH during Pregnancy require close and individualized management strategies.

Introduction

Pulmonary hypertension is a pathophysiological condition affecting various clinical conditions, including cardiovascular and respiratory diseases. Pregnancy induces numerous anatomical, physiological, biochemical, and psychological changes in women. These changes place a significant load on the heart and circulatory system, including increased blood volume, heart rate, erythrocyte count, clotting factors, decreased peripheral vascular resistance, and blood pressure. These alterations are primarily physiological adaptations but can exacerbate underlying cardiovascular and respiratory conditions.[1,2] Pregnancy is considered contraindicated in women with pre-existing PH due to the high risk of maternal and fetal complications.[3-7] Management requires a multidisciplinary approach involving cardiologists, obstetricians, and anesthesiologists to optimize maternal and fetal outcomes.[8] Comprehensive preconception counseling is crucial for informing patients of the risks and necessary precautions during pregnancy.[2,9]

In developing countries, managing PH in pregnant women remains a significant clinical challenge.[10,11] In Vietnam, there have been no studies evaluating the clinical characteristics, paraclinical features, treatment, or prognosis of both mothers and children with pulmonary arterial hypertension during pregnancy. Therefore, this retrospective study was conducted to provide practical information and effective management strategies for pregnant women with pulmonary arterial hypertension.

Methods

This was a single-center study conducted at Cho Ray Hospital. This study was conducted in accordance with the Declaration of Helsinki and was approved by the

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Study Highlights

What is current knowledge?

- Pulmonary arterial hypertension (PAH) during pregnancy is associated with high maternal and fetal morbidity and mortality.
- Most available evidence comes from high-income countries, with limited data from developing settings.

What is new here?

- This study provides the first comprehensive real-world data on PAH during pregnancy from a national referral center in Vietnam.
- Idiopathic PAH was the most common etiology, with patients presenting with severe echocardiographic abnormalities and advanced disease.
- Maternal mortality (17.1%) and fetal mortality (41.4%) remained high, highlighting persistent gaps in early diagnosis, counseling, and access to advanced care in developing countries.

Ethics Committee for Biomedical Research at Cho Ray Hospital, Ho Chi Minh City, Vietnam. We retrospectively reviewed 41 medical records of patients with pulmonary arterial hypertension (PAH) associated with pregnancy or within 1 month postpartum. Pregnancy in the study was defined as having at least 1 fetal ultrasound result or pregnancy termination. The gestational age was defined as the gestational age at the time of hospital admission if the patient was still pregnant or the gestational age at the time of pregnancy termination (before admission). We diagnosed pulmonary hypertension based on echocardiographic results showing a tricuspid regurgitant velocity (TRV) peak > 2.8 m/s.[12] We only included patients with group 1 pulmonary hypertension according to the 2022 European Society of Cardiology guidelines for the diagnosis and treatment of pulmonary hypertension. The patients in the study were defined as having hypoglycemia if they had at least 1 instance of capillary or venous blood glucose < 70 mg/dL.

Statistical analysis

The data were processed and analyzed using Stata 16.0 software. Quantitative variables are presented as the mean ± standard deviation. The qualitative variables are shown as frequencies and percentages. The Shapiro-Wilk test was used to assess normality. The difference in means between 2 groups was compared using the t-test, if the variable was normally distributed. The difference in means between multiple groups (3 or more) was compared using ANOVA if the variable was normally distributed. The differences in the proportions of categorical or ordinal variables were compared using the chi-square test ($\chi 2$) or Fisher's exact test, when any expected value was less than 1 or when 20% or more of the expected values were less than 5. Statistical significance was set at P value < 0.05.

Results

Clinical characteristics

Figure 1 illustrates the study flow chart. The study included 41 women who were diagnosed with PAH during pregnancy or within 1 month postpartum. The average age of the patients was 29.3 ± 5.1 years, ranging from 18 to 38 years. The average gestational age was 25.1 ± 8.5 weeks (Table 1). Most patients were diagnosed with iPAH, accounting for 28 patients (68.3%), followed by CHD-PAH, accounting for 11 patients (26.8%), and CTD-PAH, accounting for 2 patients (4.9%). PH was diagnosed during pregnancy in 27 patients (65.9%), prior to pregnancy in 10 patients (24.3%), and outside of pregnancy in 2 patients (4.9%). Figure 2 shows the maternal and fetal outcomes in the study.

Laboratory tests

Table 2 shows patients' laboratory test results according to the etiology of PH. Additionally, in the present study, 6 patients (14.6%) experienced hypoglycemic events during hospitalization. Table 3. Tricuspid Annular Plane Systolic Excursion (TAPSE) was measured in 14 out of 41 patients,

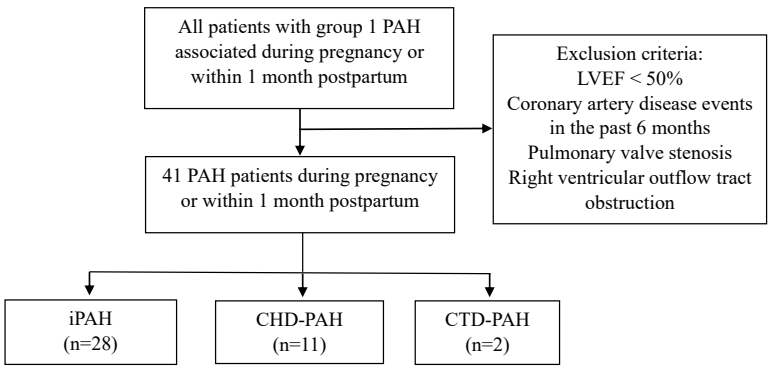

Figure 1. Flow chart of study. iPAH, idiopathic pulmonary arterial hypertension; CHD-PAH, congenital heart disease-associated pulmonary arterial hypertension; CTD-PAH, connective tissue disease-associated pulmonary arterial hypertension. LVEF: Left Ventricular Ejection Fraction

Table 1. Clinical characteristics of pulmonary hypertension groups

	Total N = 41	iPAH n = 28	CHD-PAH n = 11	CTD-PAH n = 2	*P* value
Age (years)	29.3 ± 5.1	29.2 ± 5.4	29.3 ± 4.9	30.5 ± 3.5	0.942
Gestational age (weeks)	25.1 ± 8.5	26.3 ± 8.1	23.7 ± 9.1	15 ± 4.2	0.156
Heart rate (beats/min)	102 ± 27.6	104 ± 30.1	93.1 ± 20	123.5 ± 9.2	0.293
Systolic pressure (mmHg)	110.2 ± 22	111.8 ± 25.1	108.2 ± 13.3	100 ± 14.1	0.726
Diastolic pressure (mmHg)	69.5 ± 11.8	69.6 ± 12.9	69.1 ± 9.4	70 ± 14.1	0.99

iPAH: idiopathic pulmonary hypertension, CHD-PAH: congenital heart disease-associated pulmonary arterial disease, CTD-PAH: connective tissue disease-associated pulmonary arterial hypertension.

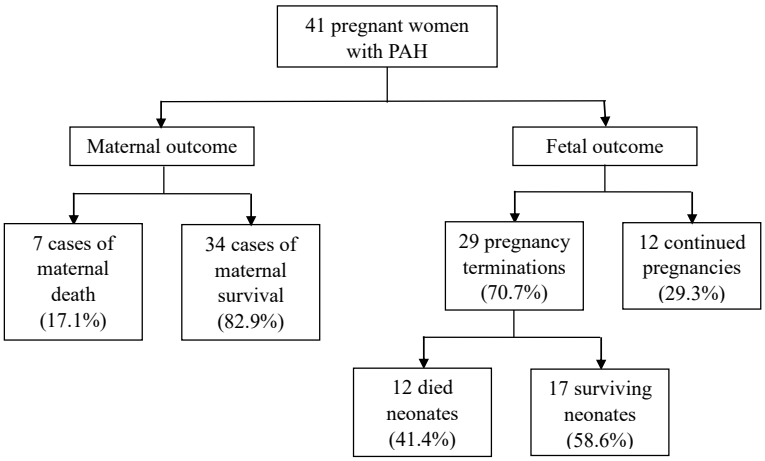

Figure 2. Diagram of maternal and fetal outcomes

with an average of 14.6 ± 5.7 mm.

Discussion

There are 3 main causes of PH in the studied population. IPAH was the most prevalent cause of PH, accounting for 68.3% of cases. Other significant causes included CHD-PAH (26.8%) and CTD-PAH (4.9%). In some research, conducted in Asia, the most common cause of pulmonary arterial hypertension associated with pregnancy is congenital heart disease, accounting for up to 64% of pulmonary hypertension cases.[7,13] The results of our study differed from those of previous studies, performed on the same population. However, the number of patients included in our study was not large enough to precisely estimate the causes of pulmonary hypertension in pregnant women in Vietnam. Moreover, due to medical, economic, and social barriers, some patients did not undergo more in-depth measures to investigate the cause of pulmonary hypertension. These patients are often classified as having "idiopathic" pulmonary hypertension. In recent years, as economic and healthcare conditions in Vietnam have improved, patients with pulmonary hypertension often undergo comprehensive testing to determine the cause of the condition. As a result, treatment plans have become clearer, significantly improving the prognosis for patients with pulmonary hypertension.

The echocardiographic findings revealed significantly elevated PAPs, with a mean value of 81.1 ± 30 mmHg and a peak TRV of 4.2 ± 0.8 m/s. Additionally, 80.5% of patients had right atrial enlargement, and 87.8% had right ventricular dilation. The echocardiographic characteristics in our study were more severe than those observed by William et al. In William's study: the mean right ventricular systolic pressure was 50 ± 17 mmHg, the peak TRV was 3.2 ± 0.5 m/s, the mean TAPSE was 23 ± 6 mm, and the rate of right ventricular dilation was 36%.[14] This highlights the severity of PH in our study population. In the study by Qiulan Dai et al,[3] the average pulmonary artery systolic pressure (PAPs) in pregnant women was 105.1 ± 22.7 mmHg, and the maternal mortality rate was 28%. This indicates that the high pulmonary pressures observed on echocardiography further clarify the severe clinical context in pregnant women with pulmonary hypertension, impacting outcomes in this population.[15] Cho Ray Hospital is a central-level hospital that frequently receives severe cases from provincial and district hospitals. Therefore, patients admitted here often present severe clinical conditions. These echocardiographic abnormalities underscore the need for thorough cardiac monitoring and management in pregnant women with PH to prevent severe complications and improve outcomes. Notably, our study revealed a significant hypoglycemia rate of 14.6% among pregnant women. Hypoglycemia is a serious event that can affect both maternal and fetal outcomes. Maternal blood glucose levels are directly related to fetal blood glucose levels; thus, hypoglycemia can lead to fetal malformations, abnormal neurological development, and fetal growth restriction.[16]

Table 2. Laboratory test results of pulmonary hypertension groups

	Total N = 41	iPAH n = 28	CHD-PAH n = 11	CTD-PAH n = 2	*P* value
Hb (g/dL)	116.5 ± 21.6	113.1 ± 23.3	126.9 ± 14.8	106.5 ± 7.8	0.161
WBC (G/L)	11.2 ± 5.7	11.2 ± 6.7	11.1 ± 2.7	11.8 ± 6.6	0.988
PLT (G/L)	183 ± 91.2	178.8 ± 100	216.1 ± 37.9	58.5 ± 68.6	0.07
BUN (mg/dL)	12.7 ± 8.9	14.3 ± 10.3	9 ± 1.7	12.5 ± 7.8	0.258
Creatinine (mg/dL)	0.7 ± 0.2	0.7 ± 0.3	0.7 ± 0.2	0.6 ± 0.2	0.783
Sodium (mmol/L)	134.9 ± 3.9	134.8 ± 3.8	135.9 ± 3.7	130 ± 1.4	0.137
Potassium (mmol/L)	3.5 ± 0.5	3.6 ± 0.5	3.2 ± 0.4	3.5 ± 0.4	0.065
AST (U/L)	144.7 ± 347.9	185.8 ± 411.7	35.1 ± 16.1	124 ± 117.4	0.549
ALT (U/L)	105.3 ± 238.2	132.4 ± 292.5	23.1 ± 11.8	136.5 ± 143.5	0.531

iPAH: idiopathic pulmonary hypertension, CHD-PAH: congenital heart disease-associated pulmonary arterial disease, CTD-PAH: connective tissue disease-associated pulmonary arterial hypertension, Hb: Hemoglobin, WBC: white blood count, PLT: Platelet count, BUN: blood urea nitrogen.

Table 3. Echocardiographic characteristics of pulmonary hypertension groups

	Total N = 41	iPAH n = 28	CHD-PAH n = 11	CTD-PAH n = 2	*P* value
Peak TRV (m/s)	4.2 ± 0.8	4.1 ± 0.8	4.5 ± 0.9	5.1 ± 0.9	0.115
PAPs (mmHg)	81.1 ± 30	75.5 ± 27.2	90.6 ± 34.1	108 ± 32.5	0.159
LVEF (%)	66.5 ± 8	65.8 ± 7.3	67.3 ± 9.3	72.5 ± 12	0.499
Right ventricular dilation, n (%)	36 (87.8)	23 (82.1)	11 (100)	2 (100)	N/A
Right atrial enlargement, n (%)	33 (80.5)	22 (78.6)	9 (81.2)	2 (100)	N/A
Pericardial effusion, n (%)	5 (12.2)	5 (17.9)	0 (0)	0 (0)	N/A

iPAH: idiopathic pulmonary hypertension, CHD-PAH: congenital heart disease-associated pulmonary arterial disease, CTD-PAH: connective tissue disease-associated pulmonary arterial hypertension, Peak TRV: peak tricuspid regurgitation velocity, PAPs: pulmonary artery systolic pressure, LVEF: left ventricular ejection fraction.

Pulmonary hypertension (PH) during pregnancy represents a significant clinical challenge due to its high maternal and fetal mortality rates.[2,5,13,17] The reported maternal mortality rate of 17.1% in this study is stark and concerning. The mortality rate in our study was greater than that reported by Lv et al (3.2%),[13] De La Cal et al (7.1%),[18] and Jun Luo et al (15.8%).[19] Previous data indicated that the mortality rate for pregnant women with pulmonary hypertension could be as high as 30-56%, with an average survival time of 2.8 years. Due to advances in the treatment and management of pulmonary hypertension, the mortality rate for these patients has decreased to 9-25% in recent years.[20,21] The high maternal mortality rate in our study can be explained by several factors. First, our hospital is a central-level hospital in Vietnam that typically admits and treats severe cases that exceed the capacity of provincial or district hospitals. As a result, patients often arrive at our facility in critical condition. Second, due to economic limitations, some patients are unable to access advanced treatments or afford intensive care costs. Lastly, the development of resuscitation facilities at our center has occasionally been limited at time in the past. This study provides an overall picture of maternal mortality in women with pulmonary arterial hypertension during pregnancy, motivating us to advance resuscitation techniques, improve care and treatment plans, and enhance health education for patients with pregnancy-associated pulmonary hypertension.

Current guidelines do not recommend pregnancy for women with pulmonary hypertension due to the elevated risk of mortality for both mothers and fetuses. Therefore, women with pulmonary hypertension should be advised on appropriate contraceptive methods. Moreover, counseling and advice should be repeated to enhance patient knowledge, especially in developing countries, where health education is not always widely disseminated. In the study by Jun Luo et al, most patients sought medical care in the third trimester.[19] This is largely because the study population consisted primarily of rural residents with limited access to health education. Most patients did not undergo routine check-ups with a cardiologist. The lack of consultations with both cardiologists and obstetricians increases the risk of complications for pregnant women with pulmonary arterial hypertension. Although early termination of pregnancy is recommended for patients with pulmonary arterial hypertension, few agree to early termination in the first trimester. After the 32nd week of pregnancy, when hemodynamic changes are severe, most pregnant women seek medical care during this period.[19] In our study, 12 fetuses (29.3%) died. Among them, 3 fetuses (25%) died in utero, and 9 fetuses (75%) died shortly after birth. This rate is higher than the 1.9% reported by Lv et al.[13] This significantly higher rate can be attributed to the fact that most patients in our study were in severe condition, leading to early termination of pregnancy to save the mother's life.

Study Limitations

Our study had some limitations. Firstly, it is a retrospective study, so there are many confounding factors, and it is not possible to determine the causes of patient mortality. Among these, the severity of the patients at admission, socioeconomic conditions, treatment provided by local hospitals before referral, and changes in clinical practices over time are potential confounding factors that may influence the study results. In our study, right heart catheterization was not performed. This was due to the lack of facilities and equipment, the severe condition of the patients, and concerns about the effects of radiation exposure during pregnancy. The number of patients enrolled in the study was low, which limited its generalizability. Therefore, more future studies with a more rigorous design and larger sample size are needed to provide a more comprehensive and accurate overview of the overall picture of pregnant or postpartum pulmonary hypertension patients, aiming to find the best management approach for these individuals.

Conclusion

In our study, the causes of pulmonary hypertension in pregnant patients were identified as iPAH, CHD-PAH, and CTD-PAH. Pregnancy in women with PH poses significant risks, with high maternal and fetal morbidity and mortality rates. A multidisciplinary approach is essential to provide comprehensive care and improve outcomes. In the future, studies on this topic with larger sample sizes and prospective designs are needed to provide useful information for the treatment and monitoring of patients with pulmonary arterial hypertension associated with pregnancy.

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Author's Contribution

Conceptualization: Hung Phi Truong, Sy Van Hoang.
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Software: Thanh Ngoc Trinh, Kha Minh Nguyen.
Formal analysis: Hung Phi Truong, Thanh Ngoc Trinh, Kha Minh Nguyen.
Investigation: Hung Phi Truong, Thanh Ngoc Trinh, Kha Minh Nguyen.
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Project administration: Hung Phi Truong, Sy Van Hoang.
Resources: Hung Phi Truong
Supervision: Hung Phi Truong, Sy Van Hoang.
Validation: Hung Phi Truong, Sy Van Hoang.
Visualization: Hung Phi Truong, Thanh Ngoc Trinh.
Writing–original draft: Hung Phi Truong, Thanh Ngoc Trinh, Kha Minh Nguyen, Sy Van Hoang.
Writing–review & editing: Hung Phi Truong, Thanh Ngoc Trinh, Kha Minh Nguyen, Sy Van Hoang.

Competing Interests

There is no conflict of interest.

Ethical Approval

This study was approved by the Ethics Committee of Cho Ray Hospital, Vietnam (No: 1699/GCN-HDDD).

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