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# Long-term maternal and fetal outcomes of pulmonary hypertension in pregnancy in the southwest plateau area of China: a retrospective study

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#### **Abstract**

**Objective** The objective was to investigate maternal, obstetric, and neonatal outcomes of pulmonary hypertension (PH) in pregnancy based on different altitudes of residence in the southwest plateau area of China.

**Methods** Data were collected from pregnant women with PH admitted to The First People's Hospital of Yunnan Province from January 1, 2012, to December 31, 2021. All pregnant women with PH were diagnosed via echocardiography according to a pulmonary arterial systolic pressure > 30 mmHg. Patients were classified into three groups according to the altitude of residence during pregnancy. Demographic characteristics, maternal and neonatal outcomes, complications, and follow-up outcomes after discharge were reported.

**Results** Fifty-two pregnant women with PH were included. Among the included women, eleven (21.2%) were in the low-altitude group, twenty-six (50.0%) were in the medium-altitude group, and fifteen (28.8%) were in the high-altitude group. The overall mortality rate was 5.8%: death up to 6 weeks after delivery occurred in one patient (1.9%), and the other two patients (4.9%) died within one to four years after delivery. Preterm delivery occurred in 22 (42.3%) patients. The incidences of maternal death (11.5% vs. 0.0, p < 0.01), cesarean delivery (80.8% vs. 70.7% vs. 80.0%, p = 0.001), and live birth (84.6% vs. 72.7% vs. 80.0%, p < 0.01) were higher in the medium-altitude group than in the low- and high-altitude groups. Therapeutic abortion was performed in 15.4% of the women, with the highest rate in the high-altitude group (p < 0.01). The rates of heart failure and respiratory failure were highest in the low-altitude group (p < 0.01). No fetal death occurred, and 22 neonates (42.3%) had a low birth weight. During a median follow-up of 2.4 years, two patients died (4.9%), and seven (17.1%) still had PH.

**Conclusion** The in-hospital mortality rate of pregnant women with PH in the plateau area is similar to that previously reported in the low-altitude region, but the long-term survival rate is lower. Therapeutic abortion is also higher in pregnant women with a high altitude of residence. These findings highlight that the risks associated with PH in

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pregnancy persist beyond delivery and underscore the importance of early risk assessment, rigorous multidisciplinary management, and prolonged postpartum follow-up, especially in plateau populations with limited access to specialized care.

Keywords Pulmonary hypertension, Pregnancy, Plateau area

#### Introduction

Pulmonary hypertension (PH) is a pathophysiological disorder characterized by narrowing of the pulmonary vasculature and often progresses to right heart failure and death. The prevalence of PH is reported to be 97 cases per million with a 1.8 female/male ratio [1]. Even with improved treatment and new approaches to managing PH during pregnancy and the peripartum period, the maternal mortality rate of pulmonary hypertension in pregnancy still ranges from 11 to 25% [2–7]. Pulmonary thrombosis events, respiratory failure and right heart failure are the most common causes of death in patients with PH [8]. Mortality and complication rates remain high in pregnant women with PH and their fetuses. Given the significant risks associated with PH, European guidelines and American consensus strongly advise against pregnancy in PH patients; however, if pregnancy does occur, termination is generally recommended following a thorough multidisciplinary evaluation [9, 10]. Even if pregnancy with PH is contraindicated, many women choose to continue the pregnancy, whether planned or unplanned, for social or individual reasons.

Globally, over 140 million people reside at altitudes above 2500 m, with a significant number in mountainous regions such as the Tibetan Plateau and Central Asia [11]. Chronic exposure to hypobaric hypoxia at high altitude is known to increase pulmonary arterial pressure (PAP), contributing to the development of high-altitude PH. Studies have demonstrated that pulmonary vascular resistance is elevated in individuals living at altitudes above 2500 m compared to low-altitude populations, with higher systolic PAP values and increased prevalence of PH [11, 12]. While some populations have developed genetic adaptations to high-altitude hypoxia, others exhibit varying degrees of susceptibility to altitude-related pulmonary complications.

All women with known cardiac disease, especially PH, who have pregnancy plans require timely prepregnancy counseling [13]. Given the impact of chronic hypoxia on pulmonary circulation, it remains uncertain whether pregnant women with PH at higher altitudes experience worse outcomes due to increased hypoxic stress or better outcomes due to long-term adaptation to altitude. The purpose of this study was to investigate maternal, obstetric, and neonatal outcomes of PH in pregnancy based on different altitudes of residence. The specific impacts of the altitude of residence, parity, anesthesia

use, delivery timing and mode, and PH target therapies were evaluated.

#### **Materials and methods**

## Study design

We reviewed the medical records of pregnant women with PH who were treated in the Department of Obstetrics and Gynecology, The First People's Hospital of Yunnan Province, in the southwest plateau area of China from January 1, 2012, to December 31, 2021. This study was approved by the Ethics Committee of Yunnan Province Hospital, China. And the requirement for informed consent from patients was waived.

In this study, right heart catheterization was not performed due to concerns over radiation exposure in pregnant women. While non-invasive echocardiography remains the standard diagnostic tool during pregnancy, invasive catheterization may be justified in certain highrisk scenarios if the benefits outweigh the risks, provided strict adherence to the ALARA (as low as reasonably achievable) principle is maintained. Pulmonary hypertension was defined as an increase in pulmonary arterial systolic pressure (PASP) greater than 30 mmHg on echocardiography [14]. All patients who met the diagnostic criteria during pregnancy to 42 days after delivery were included, including women pregnant for the first, second or multiple times. A PASP of 30 to 49 mm Hg, 50-79 mm Hg, or more than 80 mm Hg measured by echocardiography was classified into mild, moderate, or severe PH, respectively [8]. Pregnant women with different etiologies of PH, including PH associated with congenital heart disease (CHD-PH), PH associated with left heart disease (LHD), PH associated with connective tissue disease (CTD-PH) or PH caused by unclear multifactorial mechanisms, were included.

## **Data collection**

Data on the following were extracted: age, parity, etiology of PH, altitude of residence, delivery timing and mode, anesthesia use, complications, maternal or fetal mortality, management, the number of hospitalization days and costs. Obstetrical data included premature delivery, termination, low birth weight (LBW), and complications such as infection and CHDs. Data on maternal adverse events, including heart failure, pneumonia, postpartum hemorrhage, transfusion, and pulmonary embolism, were collected. The primary indication for pregnancy termination was maternal safety due to severe PH or

Patients	Preg- GP history Alti- Etiology PH Delivery	GP history	Alti-	Etiology	E .	Delivery	Delivery	Delivery	Anesthe		Maternal	Fetal	Hos-	Hospital-
	nancy age (y)		tude or residence (m)	<b>a</b> .	severity	(week)	Mode	6 E	-sia	e e	Death	status	pital stayb (d)	iza-tion costs (RMB)
No.1	27	G3P0	1773	Unknown	Moderate	31	8	Unknown	EPI	Yes	No	Alive	m	Unknown
No.2	31	G1P0	1773	CHD (PDA)	Severe	28	Termination	1	EPI	Yes	o N	Terminated	13	15,383
No.3	38	G4P1	1500	Unknown	Moderate	37	0	Unknown	EPI	No	No	Alive	11	9825
No.4	33	G2P0	1510	CHD	Moderate	35	0	Planned	EPI	Yes	No	Alive	12	38,036
No.5	76	G1P0	2000	Unknown	Moderate	35	0	Emergent	CSE	Yes	N <sub>O</sub>	Alive	9	21,805
No.6	30	G3P0	2000	CHD (ASD+VSD+FS)	Severe	25	Termination	ı	1	Yes	0 N	Terminated	13	23,269
V 0 N	24	C3PO	1500	CHD (ASD)	Seyere	32	5	Fmergent	J.	S	S	Alive	σ	14 901
No.8	21	G1P0	1510	CHD (PDA)	Moderate	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	, 10	17,318
No.9	25	G2P1	1510	Unknown	Mild	36	0	Planned	GETA	Yes	Yes	Alive	9	8104
No.10	28	G1P0	1500	Unknown	Mild	37	0	Planned	EPI	No	No	Alive	∞	6701
No.11	38	G2P1	2000	CHD (VSD) + RHD	Moderate	38	О	Emergent	EPI	o N	o N	Alive	9	7914
No.12	30	G6P1	1302	CHD (ASD)	Moderate	41	Termination		ı	No	No	Terminated	2	3501
No.13	30	G3P0	1500	CHD (ASD)	Severe	19	Termination		1	Yes	No	Terminated	7	9196
No.14	29	G1P0	1773	CHD (ASD)	Moderate	21	Termination		1	No	No	Terminated	31	54,453
No.15	23	G2P1	1500	CHD (ASD)	Severe	36	CD	Planned	GETA	Yes	No	Alive	7	16,725
No.16	26	G2P0	2416	Unknown	Mild	35	0	Emergent	EPI	No	o N	Alive	12	11,387
No.17	28	G1P0	1302	Unknown	Moderate	32	0	Emergent	EPI	Yes	No	Alive	7	12,473
No.18	30	G3P1	2000	Unknown	Moderate	38	0	Planned	EPI	No	No	Alive	∞	8764
No.19	20	G1P0	1510	CHD (ASD)	Moderate	34	0	Planned	GETA	No	o <sub>N</sub>	Alive	10	9307
No.20	28	G2P1	2000	CHD (TOF)	Moderate	39	CD	Planned	EPI	No	No	Alive	∞	8282
No.21	30	G3P1	1891	SLE	Severe	18	Termination	1	1	Yes	No	Terminated	21	38,429
No.22	41	G6P2	1891	Unknown	Mild	32	0	Emergent	CSE	Yes	No	Alive	6	9327
No.23	33	G3P2	1891	CHD (ASD)	Moderate	39	0	Planned	CSE	No	No	Alive	10	10,974
No.24	40	G5P3	1932	RHD	Mild	38	0	Planned	CSE	No	No	Alive	∞	11,462
No.25	27	G2P1	1750	Unknown	Severe	33	0	Planned	GETA	Yes	Yes	Alive	13	48,448
No.26	40	G1P0	1891	Unknown	Moderate	35	0	Planned	S	No	o <sub>N</sub>	Alive	11	12,604
No.27	22	G2P0	1800	CHD (ASD)	Moderate	39	9	Unknown	EPI	No	No	Alive	7	Unknown
No.28	38	G3P1	1500	CHD (ASD)	Mild	36	0	Planned	CSE	No	o <sub>N</sub>	Alive	∞	9042
No.29	28	G1PO	2000	Unknown	Mild	40	CD	Emergent	GETA	Yes	No	Alive	9	14,828
No.30	40	G6P2	1100	Unknown	Mild	31	CD	Emergent	CSE	No	o N	Alive	6	11,326
No.31	33	G2P0	1891	Unknown	Mild	39	CD	Emergent	EPI	No	o <sub>N</sub>	Alive	6	11,550
No.32	38	G4P1	2000	Unknown	Mild	30	Termination			No	o <sub>N</sub>	Terminated	6	10,915
No.33	32	G2P1	2000	Unknown	Mild	29	Termination			No	No	Terminated	∞	9953
No.34	35	G3P1	1891	Unknown	Mild	29	0	Emergent	CSE	No	o <sub>N</sub>	Alive	11	11,818
No.35	35	G2P0	2000	Unknown	Moderate	34	0	Unknown	Unknown	Yes	No	Alive	∞	39,997

Table 1 (continued)

Patients	Preg- nancy age (y)	GP history Alti- tude resid (m)	Alti- tude of residence (m)	Etiology	PH Severity	Delivery Timing (week)	Delivery Mode	Delivery timing	Anesthe -sia	ICU Care	Maternal Death	Fetal Status	Hos- pital stayb (d)	Hospital- iza-tion costs (RMB)
No.36	37	G1P0	2000	PE	Moderate	Unknown	CD	Unknown	Unknown	No	No	Unknown	8	9428
No.37	25	G1P0	1323	SLE	Mild	34	Unknown	Unknown	Unknown	o N	No	Alive	∞	27,719
No.38	33	G2P1	1891	Unknown	Moderate	38	0	Emergent	GETA	Yes	No	Alive	20	82,664
No.39	30	G4P2	2000	Unknown	Mild	38	0	Planned	CSE	N <sub>o</sub>	No	Alive	8	10,442
No.40	31	G2P1	1976	Unknown	Mild	39	NSVD	1	ı	N <sub>o</sub>	No	Alive	7	9801
No.41	42	G1P0	1891	Unknown	Moderate	38	0	Emergent	CSE	N <sub>o</sub>	No	Alive	∞	9913
No.42	35	G3P1	1800	Unknown	Mild	34	0	Emergent	GETA	N <sub>o</sub>	No	Alive	9	12,243
No.43	22	G2P0	2000	CHD (ASD)	Mild	37	0	Emergent	S	o N	No	Alive	∞	7972
No.44	34	G3P0	1891	Unknown	Mild	40		Emergent	GETA	N <sub>o</sub>	No	Alive	∞	16,316
Vo.45	37	G1P0	2416	CHD (ASD)	Mild	35	$\ominus$	Emergent	EPI	o N	No	Alive	13	18,007
No.46	31	G2P0	1500	Unknown	Mild	36	0	Planned	S	N <sub>o</sub>	No	Alive	13	13,772
Vo.47	38	G2P0	1891	THD	Moderate	37	CD	Planned	S	Yes	No	Alive	23	96,128
No.48	35	G3P2	1510	VHD (Severe TR)	Severe	31	0	Planned	S	Yes	No	Alive	20	43,187
No.49	29	G2P0	1976	VHD (Severe TR)	Severe	32	CD	Emergent	GETA	Yes	Yes	Alive	2	23,345
No.50	39	G2P1	1891	Unknown	Mild	37	CD	Planned	EPI	N <sub>o</sub>	No	Alive	7	10,484
No.51	36	G4P1	1891	RHD	Severe	40		Emergent	GETA	N <sub>o</sub>	No	Alive	10	12,435
No.52	25	G4P1	2000	CTD	Mild	30	CD	Emergent	GETA	No	No	Alive	7	36,113

AF: atrial fibrillation; AFE: amniotic fluid embolism; ASD: atrial septal defect; CHD: congenital heart disease; CD: cesarean delivery; CSE: combined spinal-epidural analgesia or analgesia; CTD: connective tissue disease; EPI: epidural anesthesia or analgesia; ES: eisemmenger syndrome; GETA: general endotracheal anesthesia; GP history; gravidity and parity history; ICU intensive care unit; LHD: left heart disease; PDA: patent ductus arteriosus; PFO: patent foramen ovale; PE: pulmonary embolism; NSVD: normal spontaneous vaginal delivery; RHD: rheumatic heart disease; S: spinal anesthesia; SLE: systematicness lupus erythematosus; TR: tricuspid incompetence; VSD: ventricular septal defect; VHD: valvular heart disease

Mild=30–49mmHg; Moderate=50–79mmHg; Severe≥80mmHg

other life-threatening complications. In some cases, fetal indications such as severe preeclampsia (defined by persistent hypertension accompanied by neurological symptoms, hematologic abnormalities, renal or liver dysfunction, pulmonary edema, or hypoproteinemia with effusion), fetal growth restriction (FGR, formerly known as IUGR)—defined as estimated fetal weight or abdominal circumference below the 10th percentile for gestational age—or non-reassuring fetal status also contributed to the decision. All abortion decisions were made by a multidisciplinary team (MDT), including obstetricians, cardiologists, neonatologists, and anesthesiologists, ensuring a comprehensive evaluation of maternal-fetal risks [4, 9, 15]. All data were extracted from the medical electronic system. Follow-up data included maternal status, cardiac function, and neonatal status. Follow-up data were available for all patients from 1 year to 5 years after delivery. Information after discharge was collected by telephone interviews.

All women lived at altitudes ranging from 1,100 m to 2,416 m during pregnancy (Supplementary File 1), so patients were classified into three groups: Group 1 (lowaltitude group): altitude of residence ≤ 1,500 m; Group 2 (medium-altitude group): altitude of residence between 1,501 and 1999 m; and Group 3 (high-altitude group): altitude of residence ≥ 2,000 m. Patients with PH were diagnosed at 42 days after delivery, and those with a PASP lower than 30 mmHg were excluded. An additional data file shows this in more detail [see Additional file 1].

#### Statistical analysis

The clinical baseline characteristics, as well as cardiac, maternal and fetal outcomes, are presented in detail. They were grouped and summarized according to altitude of residence during pregnancy. Data analysis was performed using SPSS 22.0 software (IBM Corp., Armonk, New York, USA). We compared and analyzed the outcomes between the low-, medium-and high-altitude groups. Categorical data are presented as frequencies and percentages, and chi-square tests were used for comparison. If there were fewer than five patients in a group, Fisher's exact test or continuity correction was used. Kolmogorov-Smirnov tests were used to check the normality of continuous data. Normally distributed data are presented as the mean ± standard deviation, and continuous parameters were compared using Student's *t* test. In the case of nonnormality, data are presented as the median and first and third quartiles (Q1-Q3) and were compared using Kruskal-Wallis tests. A P value < 0.05 was considered statistically significant.

#### Results

#### Baseline characteristics of the study population

From January 1, 2012, to December 31, 2021, a total of 52 patients were included in the study. Their baseline characteristics are summarized in Table 1. The mean age was  $31.46 \pm 5.75$  years, and 13 patients (25%) being nulliparous. Most pregnancies (90.4%) were conceived naturally, while 9.6% resulted from assisted reproductive technology. 18 patients (34.6%) had advanced maternal age (older than 35 years) [16]. Based on altitude of residence, patients were categorized into low-altitude (Group 1, n=11), medium-altitude (Group 2, n=26), and highaltitude (Group 3, n=15) groups. Twin pregnancies were reported in 8 patients (15.4%), distributed as follows: one in Group 1, five in Group 2, and two in Group 3.

As shown in Table 2, the mean age was  $31.2 \pm 5.9$  years in Group 1,  $30.8 \pm 5.6$  years in Group 2, and  $32.4 \pm 6.0$  years in Group 3, with no significant differences among groups (P=0.601). Advanced maternal age ( $\geq$ 35 years) was observed in 18 patients (34.6%), with rates of 27.3% in Group 1, 38.5% in Group 2, and 33.3% in Group 3, showing no significant differences among groups (P=0.927). The mean pulmonary arterial systolic pressure (PASP) was  $60.91 \pm 26.74$  mmHg in Group 1,  $60.73 \pm 22.33$  mmHg in Group 2, and  $50.53 \pm 16.07$  mmHg in Group 3 (P=0.315).

Moreover, regarding PH etiology, 17 (32.7%) patients had congenital heart disease-associated PH (CHD-PH), 5 (9.6%) had PH secondary to left heart disease (LHD-PH), 3 (5.8%) had PH related to connective tissue disease (CTD-PH), and 26 (50%) had PH of unknown etiology. Only one patient (1.9%) had PH associated with acute pulmonary embolism. CHD-PH was present in 45.5%, 26.9%, and 30.0% of patients in Groups 1, 2, and 3, respectively (P = 0.546, Table 2).

## Delivery outcomes and anesthesia use

Delivery details were available for 50 patients (96.2%, Table 1). The average gestational week at termination or delivery was 35 weeks (Q1-Q3=31-38). The overall cesarean delivery (CS) rate was 78.8%, while 1 patient underwent vaginal delivery. Among CS cases, 19 (46.3%) were emergency procedures performed due to cardiac or obstetric indications. The remaining CS cases were performed based on a comprehensive evaluation of maternal and fetal conditions by the attending physicians. Across the altitude groups, CS rates were 72.7% in Group 1, 92.3% in Group 2, and 66.7% in Group 3, with a significantly higher CS rate in the medium-altitude group (P=0.001, Table 2).

Among 39 cesarean deliveries with available anesthesia records, 5 (12.8%) patients received spinal anesthesia, 10 (25.6%) had combined spinal—epidural anesthesia, and 13 (33.3%) had epidural anesthesia. General endotracheal

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**Table 2** Baseline characteristics of PH patients with pregnancy based on altitude of residence

Variable	Total (N = 52)	Group 1 (N=11)	Group 2 ( $N = 26$ )	Group 3 ( $N = 15$ )	P value
Age (y)	31.46±5.75	30.45 ± 5.87	32.27 ± 6.10	30.80 ± 5.17	0.601
Altitude of Residence, m	1791.42 ± 270.17	1411.55 ± 135.53	1799.81 ± 155.43	2055.47 ± 146.38	0.000
mPASP, mmHg	57.83 ± 21.85	$60.91 \pm 26.74$	$60.73 \pm 22.33$	50.53 ± 16.07	0.315
Elderly Pregnant Women	18 (34.6)	3 (27.3)	10 (38.5)	5 (33.3)	0.927
PASP					
<50	22 (42.3)	5 (45.5)	9 (34.6)	8 (53.3)	0.504
50–79	20 (38.5)	3 (27.3)	11 (42.3)	6 (40.0)	0.701
≥80	10 (19.2)	3 (27.3)	6 (23.1)	1 (6.7)	0.000
CHD	17 (29.3)	5 (45.5)	7 (26.9)	5 (30.0)	0.5460
Delivery, median weeks of pregnancy (Q1–Q3)	35 (31.0-38.0)	34 (28.0-36.3)	35 (31.5-38.5)	35 (30.0-38.0)	0.295
Cesarean Section	41 (78.8)	8 (72.7)	21 (80.8)	12 (80.0)	0.001
Vaginal delivery	1 (1.9)	0 (0)	1 (3.8)	0 (0)	0.000
Medicine					
PH Targeted Therapy	7 (13.5)	0 (0)	6 (23.1)	1 (6.7)	0.000
Diuretic	20 (38.5)	5 (45.5)	10 (38.5)	5 (33.3)	0.215
Anticoagulants	27 (51.9)	2 (18.2)	18 (69.2)	7 (46.7)	0.017
Cardiotonic	5 (9.6)	1 (9.1)	4 (15.4)	0 (0)	0.000
CCB	4 (7.7)	2 (18.2)	1 (3.8)	2 (13.3)	0.000
General Anesthesia	11 (21.2)	1 (9.1)	8 (30.8)	2 (13.3)	0.000
Transfusion	10 (19.2)	1 (9.1)	5 (19.2)	4 (26.7)	0.000
Tracheal Intubation	10 (19.2)	1 (9.1)	8 (30.8)	1 (6.7)	0.000
Comorbidity					
Diabetes	12 (21.2)	2 (18.2)	8 (30.8)	2 (13.3)	0.000
Hypertension	4 (7.7)	0 (0)	3 (11.5)	1 (6.7)	0.000
Preeclampsia	8 (15.4)	2 (18.2)	3 (11.5)	3 (20.0)	0.000
Hypothyroidism	5 (9.6)	0 (0)	3 (11.5)	2 (13.3)	0.000
Maternal adverse events					
Postpartum hemorrhage	6 (11.5)	0 (0)	3 (11.5)	3 (20.0)	0.000
Pneumonia	6 (11.5)	1 (9.1)	4 (15.4)	1 (6.7)	0.000
Heart Failure	12 (23.1)	3 (27.3)	7 (26.9)	2 (13.3)	0.000
VTE/PE	2 (3.8)	0 (0)	2 (7.7)	0 (0)	0.000
Respiratory Failure	2 (3.8)	2 (18.2)	0 (0)	0 (0)	0.000
Hospital stays, d	9.81 ± 5.14	$8.36 \pm 2.16$	11.15 ± 6.73	$8.53 \pm 2.33$	0.442
Hospitalization costs (CYN)	19759.72 ± 18559.37	12289.18 ± 6343.36	25572.04 ± 24101.36	15938.4 ± 10253.28	0.119

G1: ≤ 1500 m; G2: 1501–1999 m; G3: ≥ 2000 m; PASP: pulmonary arterial systolic pressure; CCB: Calcium Channel Blocker; PE: pulmonary embolism; VTE: venous thromboembolism; CNY: Chinese Yuan

anesthesia was required in 11 patients (28.2%) due to severe cardiac or obstetric complications. In Group 1, one patient had severe tricuspid insufficiency. In Group 2, eight patients had complications, including intrahepatic cholestasis (n=1), heart failure (n=3), severe preclampsia (n=1), secondary epilepsy (n=1), and PROM (n=2). In Group 3, two patients had heart failure and placenta implantation abnormalities. Only one (2%) patient in Group 2 was reported to have vaginal delivery and no anesthesia.

## Management and cost

Details of patient management are presented in Tables 1 and 2. During pregnancy, 7 (13.5%) patients received targeted pulmonary hypertension (PH) therapy. The most commonly used medications were phosphodiesterase

type 5 inhibitors (PDE5-i, n=3), prostaglandin I2 (PGI2, n=2), and endothelin-receptor antagonists (ERA, n=1). One patient received a combination of PDE5-i and ERA. Six (23.1%) of these patients were in the medium-altitude group, and the targeted drug therapy rate was significantly higher in this group than the other two groups (P<0.01, Table 2). Among the six patients, four had severe PH, and two had moderate PH. Furthermore, therapeutic abortion was performed in two of these patients. One patient with severe PH in the high-altitude group used targeted drugs and experienced abortion.

Most patients (51.9%) were treated with anticoagulation therapy, while 38.5% received diuretic therapy. No patients underwent intrapartum pulmonary catheterization or extracorporeal membrane oxygenation. Anticoagulation therapy use was significantly higher in Group

2 (69.2%) compared to Group 1 (18.2%) and Group 3 (46.7%) (P = 0.017, Table 2), whereas diuretic therapy did not differ significantly among groups (P = 0.215, Table 2).

The mean hospital stay was  $9.81 \pm 5.14$  days, with the longest hospitalization recorded at 31 days for a patient who underwent therapeutic abortion at 21 weeks due to right heart failure. Across the altitude groups, the mean hospital stay was  $8.36 \pm 2.16$  days in Group 1,  $11.15 \pm 6.73$ days in Group 2, and  $8.53 \pm 2.33$  days in Group 3, with no significant differences among groups (P = 0.442, Table 2).

The average hospitalization cost was ¥19,759.72 ± 18,559.37 USD (approximately 2,906.00 ± 2,732.27, based on an average exchange rate of 1 USD ≈ 6.8 RMB during the study period). The highest recorded cost (¥96,128; ≈ USD 14,134) was observed in a Group 2 patient who developed severe postpartum hemorrhage, hemorrhagic shock, and peripartum cardiomyopathy (PPCM). Across groups, hospitalization costs were  $\$12,289.18 \pm 6,343.36 \ (\approx USD \ 1,807.23 \pm 932.85)$ Group  $\$25,572.04 \pm 24,101.36$ (≈USD in 1,  $3,761.18 \pm 3,544.31$ ) in Group 2, and  $\$15,938.4 \pm 10,253.28$ ( $\approx$  USD 2,344.76  $\pm$  1,507.84) in Group 3, with no significant differences among groups (P = 0.119, Table 2).

#### **Maternal outcomes**

Details of maternal mortality are presented in Table 3. No deaths occurred during pregnancy. One patient (1.9%) died during the early postpartum period (16 h after delivery), while two patients (4.9%) died more than one year postpartum. The patient who died early postpartum had severe tricuspid incompetence and severe PH and was nulliparous. She underwent emergency CS under general endotracheal anesthesia at 32 weeks of gestation and experienced sudden death due to heart failure, cardiogenic shock, and multisystem organ failure.

Among 8 patients (15.4%), therapeutic abortion was performed, with 2 (18.2%) patients in the low-altitude group, 3 (11.5%) patients in the medium-altitude group, and 3 (20.0%) patients in the high-altitude group (P < 0.01, Table 4). One (n = 1/8) patient in the medium-altitude group received epidural anesthesia. In Group 1, two patients underwent termination at 14 and 19 weeks, one of whom had severe CHD-PH. Three patients in Group 2 underwent termination at 18, 21, and 28 weeks. Two of these patients had CHD-PH, and one had severe PH. One patient with Eisenmenger's syndrome and severe PH in Group 3 underwent termination at 25 weeks' gestation. The other two patients with mild PH underwent termination at 29 and 30 weeks' gestation due to severe preeclampsia.

Preterm delivery (at less than 37 weeks of gestation) was reported in 22 patients (42.3%). All of the women with premature births had a mean gestational term of 35 (31–38) weeks. As shown in Table 4, the three groups had

Delivery 표 Altitude **Table 3** Specific characteristics of 3 dead patients with PH

Hospital- iza-tion costs (CNY)	8104	48,448	23,345
Hos- I pital i stay e (d) (d)			
PH therapy	No	Diuretic, 13 Cardiotonic	Cardiotonic 2
용	No	Š	PDA, ASD
ICU Transfusion Fetal Care Status	Alive	Alive	Alive
Transfusi	Yes No	8 0	Yes
Care	Yes	Yes	χes
Anesthe-sia	GETA	GETA	GETA
Delivery Deliv- Delivery Timing ery timing (Week) Mode	Planned	Planned	Emergent
Deliv- ery Mode	9	0	8
Delivery Timing (Week)	36	33	32
PH Severity	Mild	Severe	Severe
PASP, mmHg	49	68	68
Etiology	Unknown	Unknown	VHD (Severe TR)
Altitude of resi- dence (m)	1510	1750	1976
GP history	G2P1	G2P1	G2P0
Death Reason	Acute Myocarditis	HF	B-CS, HF, Pneumonia, Hypothyroidism, Anemia, Hypohepatia
Death Date	4 years after delivery Acute Myocarditis	1 years after delivery HF	2 days after delivery B-CS, HF, Pneumonia, Hypothyroidism, Anemia, Hypohepatia
Preg- nancy age (y)	25	27	53
Patients	No.9	No.25	No.49

ASD: atrial septal defect; B-CS: Budd-Chiari syndrome; CHD: congenital heart disease; CD: cesarean delivery; GETA: general endotracheal anesthesia; GP: gravidity parity; HF: heart failure; ICU: intensive care unit; PDA: patent ductus arteriosus; PASP: pulmonary arterial systolic pressure; PH: pulmonary hypertension; TR: tricuspid incompetence; VHD: valvular heart disease; CNY: Chinese Yuan Zhang et al. BMC Pulmonary Medicine

**Table 4** Maternal and fetal outcomes of PH patients with pregnancy

Variable	Total	Group	Group	Group	P
	(N=52)	1 (N=11)	2 (N=26)	3 (N=15)	
Maternal outcomes					
Maternal death	3(5.8)	0(0)	3(11.5)	0(0)	0.000
During pregnancy	0(0)	0(0)	0(0)	0(0)	
Postpartum(< 6weeks)	1(1.9)	0(0)	1(3.8)	0(0)	0.000
Postpartum(>6weeks)	2(4.9)*	0(0)	2(9.1)**	0(0)	0.000
Therapeutic abortion	8 (15.4)	2(18.2)	3(11.5)	3(20.0)	0.000
Premature delivery	22(42.3)	6(54.5)	11(42.3)	5(33.3)	0.317
ICU Care	18(34.6)	3(27.3)	11(42.3)	4(26.7)	0.048
Readmission postpar- tum 42 days	4(7.7)	0(0)	4(15.4)	0(0)	0.000
Fetal outcomes					
Low birth Weight	22(42.3)	5(45.5)	12(46.2)	5(33.3)	0.399
Live birth	42(80.8)	8(72.7)	22(84.6)	12(80.0)	0.000
Infection	15(28.8)	4(36.4)	6(23.1)	5(33.3)	0.020
CHD	13(25.0)	5(45.5)	5(19.2)	3(20.0)	0.211
RDS	5(9.6)	1(9.1)	3(11.5)	1(6.7)	0.000

<sup>\*:</sup> Follow up available in 41 cases; \*\*: Follow up available in 22 cases; PH: pulmonary hypertension; ICU: intensive care unit. CHD: congenital heart disease; RDS: respiratory distress syndrome

a similar gestational age at birth [34 weeks (28.0-36.3), 35 weeks (31.5–38.5) vs. 35 weeks (30.0–38.0), P=0.317]. The distribution of preterm deliveries was 6 (54.5%) in Group 1, 11 (42.3%) in Group 2, and 5 (33.3%) in Group 3.

Eighteen patients (34.6%) required ICU care, and the rate was significantly higher in Group 2 (42.3%) compared to Group 1 (27.3%) and Group 3 (26.7%) (P=0.048, Table 4). Heart failure was observed in 12 patients (23.1%), with rates of 27.3% in Group 1, 26.9% in Group 2, and 13.5% in Group 3 (P<0.01, Table 4). Other adverse maternal events included pneumonia (9.1% in Group 1, 15.4% in Group 2, and 6.7% in Group 3, P<0.01, Table 4), vein thrombotic events in 7.7% of Group 2, and respiratory failure in 18.2% of Group 1.

Four patients (7.7%) were readmitted 42 days after delivery. All four patients were in the medium-altitude group: two patients had an unclear mechanism and PH associated with left heart disease induced by peripartum cardiomyopathy (patient number 42 and patient number 47). Furthermore, both of these patients received anti-heart failure therapy and recovered in one year. One patient with PH associated with valvular heart disease (VHD-PH) experienced pulmonary embolism after delivery and recovered after treatment with anti-thrombosis therapy (patient number 48). One patient with PH associated with rheumatic heart disease (RHD-PH) was readmitted due to acute heart failure (patient number 51). However, the patient discontinued therapy after discharge despite poor heart function and was still alive during our follow-up period.

**Table 5** Maternal and fetal outcomes in CHD-PH vs. Non-CHD-PH patients

Variable	Total	CHD	Non-CHD	P
	(N = 52)	(N = 17)	(N = 35)	value
Maternal outcomes				
Maternal death	3 (5.8)	0 (0)	3 (8.6)	0.214
Premature delivery	22 (42.3)	5 (29.4)	17 (48.6)	0.190
ICU Care	18 (34.6)	5 (29.4)	13 (37.1)	0.583
Cesarean delivery	41 (78.8)	11 (64.7)	30 (85.7)	0.052

#### **Fetal outcomes**

No fetal deaths were reported among the three groups. Low birth weight (LBW, <2500 g) was observed in 22 neonates (42.3%), all of whom were delivered by CS. Among these, 11 (50%) were delivered via emergency CS, and 7 (31.8%) were from twin pregnancies. LBW rates did not significantly differ among groups (P = 0.399, Table 4), with 5 (45.5%) in Group 1, 12 (46.2%) in Group 2, and 5 (33.3%) in Group 3.Live births occurred in 42 patients (80.8%), with the highest rate in Group 2 (84.6%) compared to Group 1 (72.7%) and Group 3 (80.0%) (P < 0.01, Table 4).

Twenty-two (52.4%) newborns were transferred to the neonatology department immediately after birth due to complications. A total of 15 neonates (28.8%) suffered from infection, including 4 (36.4%) in the low-altitude group, 6 (23.1%) in the medium-altitude group and 5 (33.3%) in the high-altitude group (P = 0.020, Table 4). CHD was diagnosed in 13 neonates (25.0%), with a higher rate in Group 1 (45.5%) than in Group 2 (19.2%) and Group 3 (20.0%). Specifically, one newborn in Group 1 had an atrial septal defect (ASD), while in Group 2, five newborns had CHD, including one with persistent ductus arteriosus (PDA), two with ASD, and two with both PDA and ASD. In Group 3, two newborns had CHD, one with ASD and one with both PDA and ASD. No neonate was reported to have familial PH. Additionally, respiratory distress syndrome (RDS) was reported in 5 neonates (9.6%), with 1 (9.1%) in Group 1, 3 (11.5%) in Group 2, and 1 (6.7%) in Group 3 (*P*<0.01, Table 4).

## The effect of CHD on maternal and fetal outcomes

To further evaluate whether congenital heart disease-associated pulmonary hypertension (CHD-PH) influences maternal and neonatal outcomes, we conducted a subgroup analysis comparing CHD-PH (n = 17) and non-CHD-PH (n = 35) patients. As shown in Table 5, maternal mortality was 0% in the CHD-PH group compared to 8.6% in the non-CHD-PH group (P = 0.214). Similarly, there were no significant differences between the two groups in terms of premature delivery (29.4% vs. 48.6%, P = 0.190), ICU admission (29.4% vs. 37.1%, P = 0.583), or cesarean section rates (64.7% vs. 85.7%, P = 0.052).

Additionally, we analyzed the distribution of CHD-PH cases across different altitude groups and found no statistically significant association between CHD-PH prevalence and altitude (P=0.546, Table 2). These findings suggest that CHD-PH did not independently impact maternal or neonatal outcomes in this cohort, and altitude was not a major influencing factor in the prevalence of CHD-PH.

## Follow-up at postpartum

The follow-up period after discharge ranged from 1 year to 5 years (median 2.4 years). In 41 patients (78.8%), follow-up data during the postpartum period were available (Table 6). A total of 2 patients (4.9%) died during the follow-up period, both of whom were in the mediumaltitude group. The all-cause mortality rate in our cohort was 5.8%. One patient with PH with an unclear mechanism died of acute myocarditis 4 years after delivery and her pregnancy had been terminated by cesarean section under general endotracheal anesthesia at 36 weeks gestation (patient number 9). She was transferred to the ICU immediately after birth due to pulmonary infection and ICP (intrahepatic cholestasis of pregnancy). Another patient with severe PH with an unclear mechanism died due to cardiac failure 1 year after delivery (patient number 25). She terminated the pregnancy prematurely by cesarean section under general endotracheal anesthesia at 33 weeks gestation. Due to heart failure and pulmonary infection, she was transferred to the ICU after delivery. Both patients had multiple pregnancies and did not receive targeted PH therapy during pregnancy. PH was not reported during follow-up after discharge from the hospital. An additional data file shows this in more detail [see Additional file 2].

Seven patients (17.1%) still had PH in the postpartum period. The remaining patients did not have echocardiography after delivery and did not have heart-related symptoms. Only one patient (patient number 21) received a long-term pulmonary vascular-targeted drug (Bosentan), and her PASP was shown to have decreased from 110 mmHg to less than 25 mmHg by echocardiography. Three patients (7.3%) experienced chronic cardiac failure and had an New York Heart Association (NYHA) functional class of III-IV. Three women (7.3%) were pregnant again in our follow-up period, and all had conceived naturally. In two patients, abortion was performed (one patient in the medium-altitude group underwent therapeutic abortion, and one patient in the high-altitude group had spontaneous abortion). Another patient was 31 weeks pregnant and reported no PH.

No offspring death or familial PH occurred in the 41 patients. Only two children (4.9%) were reported to have CHD in our follow-up period (patient number 19 and patient number 45). Another six children were found

**Table 6** Follow-up data on mothers (n = 41) and offspring

(n=41)		
Variable	n	(%)
Mothers		
Death	2	4.9
PH after delivery	7	17.1
Targeted therapy	4	9.8
Symptoms of cardiac insuffciency	3	7.3
Re-pregnancy	3	7.3
Offspring		
Death	0	0.0
PH	0	0.0
Growth and development lag behind	3	7.3
CHD	2	4.9

PH: pulmonary arterial hypertension; CHD: congenital heart disease

to have closed defects after birth. Three children (7.3%) had mild growth restriction (one in the medium-altitude group and two in the high-altitude group). No intelligence development disorder or familial PH was observed in any of the children.

## **Discussion**

In this retrospective cohort study, we evaluated maternal and fetal outcomes in 52 pregnant women with PH residing in a high-altitude region. The findings revealed that pregnant women with PH in the medium-altitude group had higher maternal mortality, cesarean delivery, congenital heart disease (CHD) incidence in neonates, and live birth rates. In contrast, therapeutic abortion was more frequent in the high-altitude group, and heart or respiratory failure occurred more commonly in the low-altitude group. These results suggest that altitude may play a role in modifying pregnancy outcomes in PH patients, though the exact physiological mechanisms require further investigation.

Hypobaric hypoxia is a known contributor to increased pulmonary arterial pressure (PAP) and right ventricular strain, particularly in populations residing at high altitudes [17, 18]. Chronic exposure to reduced oxygen levels leads to pulmonary vasoconstriction and vascular remodeling, increasing the risk of PH progression. While some studies define 2500 m as a critical threshold for high-altitude PH [11, 12], research suggests that physiological changes in pulmonary circulation may begin at altitudes as low as 1500 m [1, 19, 20]. Given that the majority of our study population resided between 1100 and 2416 m, we classified patients into three groups—low altitude (≤1500 m), medium altitude (1501–1999 m), and high altitude (≥2000 m)—to better capture potential variations in pregnancy outcomes among PH patients across different altitude ranges. Interestingly, maternal mortality in our cohort was similar to reports from lower-altitude regions, suggesting that long-term residence at moderate to high altitudes may confer some degree of hypoxia tolerance. Prior studies have highlighted genetic and physiological adaptations in high-altitude populations, including increased oxygen transport efficiency and modified pulmonary vasoreactivity [21, 22]. However, these adaptations are population-dependent, and not all individuals at high altitudes exhibit protective mechanisms against PH progression.

In this study, most patients chose to undergo CS (78.8%), of which 46.3% were emergency operations for cardiac and obstetric reasons, such as heart failure, diabetes, preeclampsia, and premature rupture of membranes. Only one woman delivered vaginally. Although cesarean delivery is often preferred in PH pregnancies to minimize hemodynamic stress [23-25], evidence supporting its superiority over vaginal delivery remains limited [26, 27]. Prior studies have reported lower cesarean rates ranging from 44.9 to 63.4%, suggesting that delivery mode should be determined based on individual risk factors rather than a universal approach [14, 28]. Although recent management trends favor cesarean delivery, there is little evidence that CS improves maternal outcomes compared with vaginal delivery [26, 27]. In addition, CS results in higher rates of death, postpartum hemorrhage, shock, cardiac arrest and thrombotic events [29]. The high rates of therapeutic abortion in this study (15.4%), particularly in the high-altitude group (20%), may reflect clinical decisions aimed at reducing maternal mortality in severe PH cases [8, 14, 23, 24, 28, 30]. Additionally, in the present study, 42.3% of the patients had premature delivery, and the rate was higher than that reported by Miao et al. [8] (30.6%), Yang et al. [23] (26.9%), and K.Sliwa et al. [14] (21.7%). However, compared with recent reports from the Southwest and North Plains of China, our study observed a relatively lower incidence of preterm birth [24, 31]. Additionally, a meta-analysis including 20 studies and 589 patients reported a higher premature birth rate of 59.7% [32]. These differences may reflect variations in disease severity, management approaches, and regional healthcare resources, suggesting that standardized perinatal care strategies are essential to improving neonatal outcomes in PH pregnancies.

Our study reported a maternal mortality rate of 5.8%, comparable to that observed in other PH pregnancy cohorts [25]. Prior studies have demonstrated considerable variability in PH-related maternal mortality, influenced by disease severity, availability of specialized care, and perinatal management strategies. Reports from low-altitude regions in China and international registries have indicated relatively lower maternal mortality, with some studies reporting rates as low as 2.8–3.4% [8, 14, 30], often attributed to specialized PH management and multidisciplinary team (MDT) involvement. In contrast, studies conducted in settings with limited access to

PH-targeted therapy and specialized perinatal care have documented higher mortality rates, ranging from 7.2–16% [23, 24, 31], reflecting the impact of disease progression and delayed intervention on patient outcomes [28].

The higher therapeutic abortion rate in the high-altitude group may reflect a clinical decision to avoid severe maternal complications in advanced PH cases. Given the increased hypoxic burden at higher altitudes, the decision to terminate pregnancy may have been influenced by concerns over worsening right heart function and maternal decompensation. This is consistent with our finding that no deaths occurred in women who underwent pregnancy termination before 30 weeks, suggesting that early termination may improve maternal outcomes in high-risk PH cases. The high incidence of emergency cesarean sections and preterm births observed in our study is consistent with previous research, underscoring the clinical preference for cesarean delivery in managing pregnancies complicated by PH [8].

Neonatal outcomes were also affected by maternal PH status. No neonatal deaths occurred in our cohort, consistent with prior studies [28, 30]. This may be because the hospital currently emphasizes the need for delivery with neonatal intensive care. However, our cohort showed a higher LBW rate (42.3%) than that previously reported by Zhang et al. [24], Liu et al. [25], and Yang et al. [23] (34.8%, 33.8%, and 25.6%) in the eastern and northern low-altitude regions of China. This may be attributed to a high rate of preterm delivery (42.3%), as well as the presence of twin pregnancies (31.8% of LBW cases). In contrast, a European study reported a lower LBW rate (19%), suggesting that altitude, hypoxia, and maternal PH severity may contribute to fetal growth restriction [14]. CHD occurs in 0.8 – 0.9% of live births [9, 33, 34]. In our study, the prevalence of CHD in neonates was 4.9%, which aligns with prior studies conducted in low-altitude regions [14, 25, 35]. Interestingly, all CHD cases in our cohort occurred in neonates born to mothers with CHD-PH (ASD). While our sample size is limited, this clustering raises the possibility that genetic predisposition may play a more prominent role than altitude exposure in the development of CHD among offspring in this population. Further investigation is warranted to distinguish environmental from hereditary influences.

Long-term postpartum outcomes remain a major concern for PH patients. Previous studies have reported maternal mortality rates between 1.3% and 2.6% during long-term follow-up, with heart failure occurring in 2.7–7.8% of cases [14, 25]. Another study found that the cumulative survival rate exceeded 90% for women with moderate PH after long-term follow-up [30]. In this study, 41 patients (78.8%) were followed for a median of 2.4 years, during which two patients (4.9%) died from cardiac complications at one and four years postpartum.

Compared to reports from low-altitude regions, this cohort exhibited a lower long-term survival rate, possibly due to delayed access to specialized PH care or undetected cardiovascular deterioration after delivery. These findings highlight the importance of extended postpartum monitoring and continued PH-targeted therapy to optimize long-term maternal outcomes. Neonatal outcomes were generally favorable in this cohort, with no cases of neonatal death or familial PH reported during follow-up. Mild growth restriction was observed in 7.3% of infants, but these children exhibited normal development comparable to those born to healthy women. Additionally, three women (7.3%) became pregnant again during follow-up, two of whom opted for pregnancy termination, reflecting the ongoing challenges and clinical concerns associated with future pregnancies in PH survivors.

Pregnancy imposes a significant physiological burden on PH patients due to increased blood volume and cardiac output [10, 36, 37]. However, only 17.1% of women in this cohort exhibited persistently elevated pulmonary arterial systolic pressure (PASP) after delivery, and 7.3% developed chronic heart failure during follow-up. This suggests that a subset of PH cases may involve pregnancy-related hemodynamic changes that are at least partially reversible postpartum, potentially due to volume overload rather than permanent vascular remodeling. However, these patients remain at high cardiovascular risk, warranting long-term follow-up to assess the persistence or recurrence of PH symptoms. The European Society of Cardiology (ESC) guidelines recommend genetic counseling and a multidisciplinary evaluation for women with well-controlled PH before considering pregnancy, emphasizing the need for careful risk assessment in future pregnancies [38].

Due to a lack of medical resources and specialists, echocardiography was not a common examination during pregnancy. Patients who suffered from PH could not be diagnosed and treated in time in the present study. Many patients were transferred to specialized hospitals only in the middle or late stages of pregnancy, when symptoms became severe. Furthermore, most PH patients did not MDT management or standard supportive treatments such as oxygen therapy or heart failure management. Given the complex hemodynamic changes during pregnancy, timely risk assessment and close monitoring by an MDT are essential to optimize maternal and fetal outcomes [9]. The use of PH-targeted therapies in pregnancy remains controversial due to safety concerns and limited clinical evidence [31]. While previous studies suggest that PH therapies may improve maternal outcomes [1, 6, 20, 35, 39, 40], there is no consensus on the optimal drug regimen or dosing for pregnant women. Endothelin receptor antagonists and riociguat have potential teratogenic effects and are not recommended during pregnancy [38, 41] whereas calcium channel blockers (CCBs), phosphodiesterase type 5 inhibitors (PDE5is), and prostacyclin analogs are considered safer options, despite limited safety data [38, 42, 43]. In our cohort, only 13.5% of patients received PH-targeted therapy, and treatment duration was short, limited to the perinatal period. Given the lack of large-scale trials in pregnant PH patients, future studies should focus on establishing evidence-based treatment protocols to improve maternal and fetal outcomes.

Additionally, hospitalization costs were assessed to explore the economic burden associated with PH in pregnancy. Although the difference in cost among the altitude groups was not statistically significant, the highest cost was observed in a patient with severe complications including peripartum cardiomyopathy and hemorrhagic shock. These findings highlight the substantial resource utilization involved in managing high-risk PH pregnancies, especially in settings with delayed diagnosis or limited access to specialized care. Consideration of economic burden is essential when developing multidisciplinary management strategies and allocating healthcare resources for PH in pregnancy, particularly in underresourced or geographically remote areas.

This study has a few limitations. First, this was a retrospective study, and additional bias compared to prospective cohort studies cannot be ignored. All data were collected from medical electronic records, and some of the data were unavailable and incomplete. Second, all involved patients were hospitalized; thus, we were unable to obtain information from patients in outpatient departments or other hospitals. Third, no patient was diagnosed by right heart catheterization. Invasive tests that involve radiation are not feasible in pregnant women. The interpretation of our results must account for the limitations of diagnosing and treating PH by echocardiography. Additionally, while we conducted a subgroup analysis comparing CHD-PH and non-CHD-PH patients, a significant proportion of our cohort had PH of unknown etiology, which may introduce heterogeneity in the study population. Further research with more refined etiological classifications and larger sample sizes is needed to confirm whether different PH subtypes exhibit distinct maternal and fetal outcomes. Finally, the study was conducted at a single medical center, and the findings may not be fully generalizable to other regions with different demographic characteristics, healthcare systems, and clinical management protocols. Future prospective, multicenter studies are needed to further validate our results and provide a broader perspective on maternal and fetal outcomes in pregnant women with PH.

#### Conclusion

In conclusion, the present study revealed that PH increased the risks for adverse maternal and neonatal outcomes. Mortality in the present study cohort was similar to that previously reported in the low-altitude region. Our study indicates that pregnant women with PH residing in plateau areas experience in-hospital mortality rates similar to those in low-altitude regions; however, their long-term survival is reduced, and therapeutic abortion rates are higher, especially among those at higher altitudes. These findings suggest that altitude may influence the progression of PH and modify pregnancy outcomes likely through mechanisms related to hypoxic stress and cardiovascular adaptation. Although our data imply that pregnancy may not be absolutely contraindicated in these women, they underscore the need for rigorous, multidisciplinary management and further prospective studies to elucidate the underlying physiological mechanisms. When patients decide to continue pregnancy, close and regular monitoring by a MDT is essential, particularly in the postpartum period when the risk of cardiac complications remains high. In contrast, the incidence of LBW and CHD in the plateau population was similar to that reported in low-altitude regions, suggesting that these outcomes may be less influenced by altitude-related hypoxia than previously assumed. Pregnancies in women with PH remain clinically challenging, and large-scale prospective multicenter studies are warranted to confirm these findings and inform future care strategies.

#### **Abbreviations**

PH Pulmonary hypertension

ICU Intensive care unit

PASP Pulmonary arterial systolic pressure

 $\mathsf{CHD}$ Congenital heart disease B-CS Budd-Chiari syndrome LHD Left heart disease CTD Connective tissue disease Low birth weight I BW CS Cesarean section

PDE5-i Phosphodiesterase type 5 inhibitor

 $PGI_2$ Prostaglandin I<sub>2</sub>

**ERA** Endothelin-receptor antagonist VHD Valvular heart disease RHD Rheumatic heart disease ASD Atrial septal defect PDA Persistent ductus arteriosus NYHA New York Heart Association

MDT Multidisciplinary team RV Right ventricle

CCB Calcium Channel Blocker

CNY Chinese Yuan

**ESC** 

European Society of Cardiology

ΑF Atrial fibrillation CD Cesarean delivery

CSE Combined spinal-epidural analgesia or anesthesia

DM Diabetes Mellitus

Epidural anesthesia or analgesia FRA Endothelin-receptor antagonist **GETA** General endotracheal anesthesia GP History gravidity and parity history FS Eisenmenger syndrome

**GDM** Gestational diabetes mellitus

HF Heart failure

ICP Intrahepatic cholestasis of pregnancy **PROM** Premature rupture of membrane **PPCM** Peripartum cardiomyopathy PFO Patent foramen ovale RF Respiratory failure

Spinal anesthesia

SLE Systematicness lupus erythematosus

TR Tricuspid incompetence VSD Ventricular septal defect PF Pulmonary embolism VTF Venous thromboembolism RDS Respiratory Distress Syndrome General endotracheal anesthesia **GFTA** 

Heart Failure

## **Supplementary Information**

The online version contains supplementary material available at https://doi.or q/10.1186/s12890-025-03729-3.

Supplementary Material 1

Supplementary Material 2

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#### **Author contributions**

WH and XDZ designed the study and wrote the manuscript. PL, LLT and XMY collected and analyzed the data. WH critically reviewed and improved the drafts of the manuscript. All authors have read and approved the final manuscript.

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## Data availability

All data generated or analysed during this study are included in this published article [and its supplementary information files].

#### **Declarations**

#### Ethics approval and consent to participate

This study was approved by the Ethics Committee of Yunnan Province Hospital, China, and the requirement for informed consent from patients was waived. The study was conducted in accordance with the Declaration of Helsinki and relevant national guidelines.

## Consent for publication

Not applicable. This study does not contain any individual person's data in any form (including text, images, or supplementary materials) that could lead to the identification of study participants.

#### Human ethics and consent to participate

Not applicable.

## **Competing interests**

The authors declare no competing interests.

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#### References

- Galie N, Humbert M, Vachiery JL, Gibbs S, Lang I, Torbicki A, Simonneau G, Peacock A, Vonk Noordegraaf A, Beghetti M, et al. 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.
- Bedard 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.
- 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.
- 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.
- Jais X, Olsson KM, Barbera JA, Blanco I, Torbicki A, Peacock A, Vizza CD, Macdonald P, Humbert M, Hoeper MM. Pregnancy outcomes in pulmonary arterial hypertension in the modern management era. Eur Respir J. 2012;40(4):881–5.
- Kiely DG, Condliffe R, Webster V, Mills GH, Wrench I, Gandhi SV, Selby K, Armstrong IJ, Martin L, Howarth ES, et al. Improved survival in pregnancy and pulmonary hypertension using a multiprofessional approach. BJOG. 2010;117(5):565–74.
- 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.
- Miao H, Chen Y, Wang C, Huang T, Lin J. Pregnancies in women with moderate and severe pulmonary hypertension remain challenging: A single-center experience in East China. Int J Gynaecol Obstet. 2022;157(1):140–8.
- Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, Blomstrom-Lundqvist C, Cifkova R, De Bonis M, lung B, Johnson MR, Kintscher U, Kranke P, et al. 2018 ESC guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J. 2018;39(34):3165–241.
- Hemnes AR, Kiely DG, Cockrill BA, Safdar Z, Wilson VJ, Al Hazmi M, Preston IR, MacLean MR, Lahm T. Statement on pregnancy in pulmonary hypertension from the pulmonary vascular research Institute. Pulm Circ. 2015;5(3):435–65.
- Lichtblau M, Saxer S, Furian M, Mayer L, Bader PR, Scheiwiller PM, Mademilov M, Sheraliev U, Tanner FC, Sooronbaev TM et al. Cardiac function and pulmonary hypertension in central Asian Highlanders at 3250 m. Eur Respir J 2020, 56(2).
- Muller J, Titz A, Schneider SR, Bauer M, Mayer L, Luond L, Ulrich T, Furian M, Forrer A, Schwarz El et al. The effect of high altitude (2500m) on incremental cycling exercise in patients with pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension: a randomised controlled crossover trial. Eur Respir J 2024, 63(3).
- Roos-Hesselink JW, Budts W, Walker F, De Backer JFA, Swan L, Stones W, Kranke P, Sliwa-Hahnle K, Johnson MR. Organisation of care for pregnancy in patients with congenital heart disease. Heart. 2017;103(23):1854–9.
- Sliwa K, van Hagen IM, Budts W, Swan L, Sinagra G, Caruana M, Blanco MV, Wagenaar LJ, Johnson MR, Webb G, 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(9):1119–28.
- Hsu CH, Gomberg-Maitland M, Glassner C, Chen JH. The management of pregnancy and pregnancy-related medical conditions in pulmonary arterial hypertension patients. Int J Clin Pract Suppl 2011(172):6–14.
- Yogev Y, Melamed N, Bardin R, Tenenbaum-Gavish K, Ben-Shitrit G, Ben-Haroush A. Pregnancy outcome at extremely advanced maternal age. Am J Obstet Gynecol. 2010;203(6):e558551–557.
- Burns RM, Peacock AJ, Johnson MK, Church AC. Hypoxaemia in patients with pulmonary arterial hypertension during simulated air travel. Respir Med. 2013;107(2):298–304.
- Kylhammar D, Radegran G. The principal pathways involved in the in vivo modulation of hypoxic pulmonary vasoconstriction, pulmonary arterial remodelling and pulmonary hypertension. Acta Physiol (Oxf). 2017;219(4):728–56.
- Roubinian N, Elliott CG, Barnett CF, Blanc PD, Chen J, De Marco T, Chen H. Effects of commercial air travel on patients with pulmonary hypertension air travel and pulmonary hypertension. Chest. 2012;142(4):885–92.

- Galie N, Humbert M, Vachiery JL, Gibbs S, Lang I, Torbicki A, Simonneau G, Peacock A, Vonk Noordegraaf A, Beghetti M, et al. 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 Respir J. 2015;46(4):903–75.
- 21. Storz JF, Cheviron ZA. Physiological genomics of adaptation to High-Altitude hypoxia. Annu Rev Anim Biosci. 2021;9:149–71.
- Lee FS. Hypoxia inducible factor pathway proteins in high-altitude mammals. Trends Biochem Sci. 2024;49(1):79–92.
- 23. Yang M, Wang J, Zhang X, Zhuang Q, Wang R, Shen J, Lin J. Incidence and long-term outcomes of pregnant women complicated with pulmonary arterial hypertension during different pregnancies: A prospective cohort study from China. Int J Cardiol. 2021;326:178–83.
- Zhang L, Qie G, Yin X, Zhao H, Zhang F, Wang T, Meng M, Sha J, Chu Y. Pregnant outcomes of critically ill pregnant patients with pulmonary hypertension: A multicenter retrospective study. Front Cardiovasc Med. 2022;9:872833.
- Liu Y, Li Y, Zhang J, Zhang D, Li J, Zhao Y, Liu K, Ma X, Bai C, Gu H, 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.
- Sahni S, Palkar AV, Rochelson BL, Kepa W, Talwar A. Pregnancy and pulmonary arterial hypertension: A clinical conundrum. Pregnancy Hypertens. 2015;5(2):157–64.
- 27. Obican SG, Cleary KL. Pulmonary arterial hypertension in pregnancy. Semin Perinatol. 2014;38(5):289–94.
- 28. Meng ML, Landau R, Viktorsdottir O, Banayan J, Grant T, Bateman B, Smiley R, Reitman E. Pulmonary hypertension in pregnancy: A report of 49 cases at four tertiary North American sites. Obstet Gynecol. 2017;129(3):511–20.
- American College of O, Gynecologists, Society for Maternal-Fetal M, Caughey AB, Cahill AG, Guise JM, Rouse DJ. Safe prevention of the primary Cesarean delivery. Am J Obstet Gynecol. 2014;210(3):179–93.
- Lai W, Ding Y, Wen L. Long-term outcomes of pregnant women with pulmonary hypertension diagnosed by echocardiography: a retrospective cohort study in a single center from China. Pulm Circ. 2021;11(1):2045894020966876.
- Shu T, Feng P, Liu X, Wen L, Chen H, Chen Y, Huang W. Multidisciplinary team managements and clinical outcomes in patients with pulmonary arterial hypertension during the perinatal period. Front Cardiovasc Med. 2021;8:795765.
- 32. 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.
- van der Linde D, Konings EE, Slager MA, Witsenburg M, Helbing WA, Takkenberg JJ, Roos-Hesselink JW. Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. J Am Coll Cardiol. 2011;58(21):2241–7.
- Marelli AJ, Ionescu-Ittu R, Mackie AS, Guo L, Dendukuri N, Kaouache M. Lifetime prevalence of congenital heart disease in the general population from 2000 to 2010. Circulation. 2014;130(9):749–56.
- 35. Li Q, Dimopoulos K, Liu T, Xu Z, Liu Q, Li Y, Zhang J, Gu H. Peripartum outcomes in a large population of women with pulmonary arterial hypertension associated with congenital heart disease. Eur J Prev Cardiol. 2019;26(10):1067–76.
- Olsson KM, Channick R. Pregnancy in pulmonary arterial hypertension. Eur Respir Rev. 2016;25(142):431–7.
- Canobbio MM, Warnes CA, Aboulhosn J, Connolly HM, Khanna A, Koos BJ, Mital S, Rose C, Silversides C, Stout K, et al. Management of pregnancy in patients with complex congenital heart disease: A scientific statement for healthcare professionals from the American heart association. Circulation. 2017;135(8):e50–87.
- Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, Carlsen J, Coats AJS, Escribano-Subias P, Ferrari P, et al. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Heart J. 2022;43(38):3618–731.
- 39. Cartago RS, Alan PA, Benedicto J. Pregnancy outcomes in patients with severe pulmonary hypertension and eisenmenger syndrome treated with sildenafil monotherapy. Obstet Med. 2014;7(1):40–2.
- 40. Rosengarten D, Kramer R. Pregnancy in a woman with pulmonary hypertension: favorable outcome with intravenous treprostinil. Clin Exp Obstet Gynecol. 2015;42(3):390–1.

- de Raaf MA, Beekhuijzen M, Guignabert C, Vonk Noordegraaf A, Bogaard HJ. Endothelin-1 receptor antagonists in fetal development and pulmonary arterial hypertension. Reprod Toxicol. 2015;56:45–51.
- Kamp JC, von Kaisenberg C, Greve S, Winter L, Park DH, Fuge J, Kuhn 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.
- 43. Dunn L, Greer R, Flenady V, Kumar S. Sildenafil in pregnancy: A systematic review of maternal tolerance and obstetric and perinatal outcomes. Fetal Diagn Ther. 2017;41 (2):81–8.

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