Original Article

Analysis of clinical characteristics of patients with pulmonary hypertension in Chaya County, Chamdo, Tibet

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Background: Pulmonary hypertension (PH) is a critical health issue marked by high blood pressure in the pulmonary arteries, with limited data on its clinical characteristics in the Tibetan population. The objective of this study was to examine the clinical characteristics of PH patients among Tibetan population residing in Chaya County, Changdu, Tibet.

Methods: This was a retrospective cross-sectional study. A total of 94 PH patients diagnosed via echocardiography at the Internal Medicine Department of Chaya County People's Hospital in Changdu (Tibet, China) between March 2019 and October 2020 were included. Additionally, 52 non-PH inpatients were selected as the control group. Patient medical records were reviewed for demographic and clinical data, lab results, and echocardiographic findings. Student's *t*-test/chi-squared test between PH and control group, one-way analysis of variance (ANOVA) among control and PH subgroups, Pearson's and Spearman's correlation coefficient were used to analysis the results.

Results: Out of 1,689 inpatients in the Internal Medicine Department, 94 were identified as PH patients for analysis. The average hemoglobin level among PH patients (150.64±21.67 g/L) was similar to that observed in the normal population (146.65±17.51 g/L) at high altitude (P=0.28). Abnormal liver function indexes were observed, with 51.06% of PH patients exhibiting hyperuricemia (P<0.001 compared to control's 15.38%). The PH group demonstrated significantly elevated red blood cell distribution width (RDW)-standard deviation (50.59±6.49 *vs.* 43.67±3.40 fL, P<0.001) and RDW-coefficient of variation of (16.18%±3.04% *vs.* 13.52%±1.32%, P<0.001), along with a decreased platelet level compared to the control group [(202.55±73.67) *vs.* (256.63±72.85) $\times 10^9$/L]. Furthermore, echocardiographic indicators related to right heart function showed correlations with red blood cell count, bilirubin, albumin, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol (multiple significant correlation coefficient r, magnitude from 0.22 to 0.54).

Conclusions: Chronic pulmonary disease and left heart disease were identified as common etiologies of PH among Tibetan patients residing in high-altitude regions. The Tibetan population residing in high-altitude regions and diagnosed with PH displayed abnormal changes in numerous liver functional and metabolic indices, which were correlated with the morphological indices observed via cardiac ultrasound.

Keywords: Pulmonary hypertension (PH); high-altitude; Tibetans; etiology; correlation

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Introduction

Pulmonary hypertension (PH) refers to elevated pressures in the pulmonary vascular bed and is defined as a mean pulmonary artery pressure (PAP) exceeding 20 mmHg during resting assessment via right heart catheterization (RHC), as per the 2022 guidelines of the European Society of Cardiology/European Respiratory Society (ESC/ERS) (1). PH is classified into five major groups: (I) idiopathic pulmonary arterial hypertension (PAH); (II) PH secondary to left heart disease; (III) PH secondary to lung diseases and/or hypoxia; (IV) PH associated with pulmonary artery obstructions; and (V) PH with unclear and/or multifactorial mechanisms (2).

Typical symptoms of PH encompass chest pain, exertional dyspnea, syncope, fatigue, presyncope, and weakness (3). The prevalence of PH globally is estimated to be approximately 1% (4). Literature reports indicate varying rates of high-altitude pulmonary hypertension (HAPH) in certain regions. Studies from South America, for example, have demonstrated HAPH prevalence ranging from 5% to 18% (5,6). Negi *et al.* found a HAPH prevalence of 3.23% among natives of Spiti Valley, India (7). These studies indicate that the prevalence of HAPH exceeds that of PH in the global population. However, there is still a lack of precise epidemiological data on HAPH, especially in the Qinghai-Tibet Plateau region. The Qinghai-Tibet Plateau, located in the southwest of China, boasts an average elevation of 4,000 m. The oxygen level in its atmosphere is approximately 60% of that found in lowland areas. The plateau hypoxic environment itself is considered one of the etiological factors for PH, specifically classified as high-altitude hypoxia-induced PH (group 3) (8). Furthermore, the hypoxic and low-pressure environment prevalent in high-altitude regions may exert deleterious effects on chronic pulmonary disease while exhibiting protective effects on cardiovascular diseases (9). The confluence of these conditions may pose challenges in analyzing the characteristics of PH patients residing in plateau areas.

On the other hand, studies on high-altitude PH are globally limited due to environmental constraints and the availability of limited testing methods. Tibetan individuals, inhabiting the plateau hypoxic environment for generations, exhibit a distinctive array of physiological adaptations induced by the plateau environment (10). Therefore, the features of PH in plateau-dwelling Tibetans may diverge from those observed in the general population. Currently, research on the etiology and clinical traits of PH patients among Tibetan populations residing on the plateau in China remains limited.

RHC serves as the "gold standard" for diagnosing and distinguishing between different groups of PH (11). However, the diagnostic infrastructure in Tibetan regions is relatively constrained, with the majority of county hospitals lacking the capability to conduct RHC. Echocardiography represents a simple, non-invasive, and efficient diagnostic tool widely used for clinical screening, diagnosis, and assessment of PH. It holds the highest level of evidence among current methods utilized for PH screening (12,13). The purpose of this study is to analyze the clinical characteristics of PH patients among the Tibetan population residing in Chaya County, Changdu, Tibet utilizing echocardiographic diagnosis. It should be pointed out that the current study utilized the same cohort of patients

Highlight box

Key findings

- Pulmonary hypertension (PH) patients in Chaya County Hospital, Tibet, displayed abnormal liver function and metabolic indexes, including elevated levels of alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, γ-glutamyltransferase, total bilirubin, and indirect bilirubin, and decreased levels of albumin.
- Echocardiographic indicators related to right heart function correlated with red blood cell count, bilirubin levels, and lipid profiles in PH patients.
- Left heart disease and chronic pulmonary disease were identified as prevalent causes of PH among Tibetan patients residing in high-altitude regions.

What is known and what is new?

- Previous research has highlighted the prevalence of PH in high-altitude areas, particularly among Tibetan populations. However, the specific clinical characteristics and etiologies of PH in this context remain poorly understood.
- This study adds to existing knowledge by revealing abnormal liver function and metabolic indexes in Tibetan PH patients, underscoring the multifaceted nature of PH in high-altitude settings.

What is the implication, and what should change now?

- The findings emphasize the need for tailored interventions to address. Left heart disease and chronic pulmonary disease, which are prevalent causes of PH among Tibetan populations.
- Comprehensive patient management strategies should incorporate monitoring of liver function and metabolic indexes in PH patients, particularly in high-altitude regions. Future research should focus on conducting large-scale prospective studies to validate these findings and explore potential risk factors for PH in Tibetan populations.

and control subjects but focus on different aspects of their medical data with our previous study (14). Specifically, this study investigated echocardiographic parameters, while our previous study (14) examined electrocardiogram (ECG) parameters associated with PH diagnosis in high-altitude Tibetan populations. We present this article in accordance with the STROBE reporting checklist (available at https://cdt.amegroups.com/article/view/10.21037/cdt-23-486/rc).

Methods

Study design and subjects

This is a retrospective study. From March 2019 to October 2020, the medical records of 1,689 inpatients in the Internal Medicine Department of Chaya County People's Hospital in Changdu (Tibet, China) were reviewed. Patients who had undergone echocardiography and determine PAP were screened. Of them, 116 cases were diagnosed with PH based on echocardiographic measurement indicating a pulmonary artery systolic pressure (PASP) ≥35 mmHg (15). Inclusion criteria for the PH patients were as follows: (I) age over 18 years; (II) presenting clinical symptoms such as dyspnea, fatigue, chest discomfort, dizziness, edema, wheezing, and abdominal distension; (III) during hospitalization, echocardiography revealed a PASP ≥35 mmHg. Exclusion criteria for the PH group are: (I) incomplete data; (II) presence of tumors; (III) chronic kidney disease stage 5; (IV) liver failure. Following the exclusion of cases with unclear medical histories or missing data, 94 PH patients (44 males and 50 females, mean age =66.51±12.35 years) were included. Patients with anemia were excluded from the analyses of blood routine examination, while patients with hepatobiliary diseases were excluded from the analyses of liver function indices. Anemia was defined as a hemoglobin concentration (Hb) <120 g/L for males and <110 g/L for females.

During the same period, 52 non-PH inpatients were selected as the control group, matched based on age and gender with the PH group. Inclusion criteria for the control group include: (I) age over 18 years; (II) absence of dyspnea, chest tightness, chest pain, edema, or chronic cough history; (III) during hospitalization, echocardiography revealed a PASP <35 mmHg. Exclusion criteria for the control group are: (I) incomplete data; (II) diagnosis of conditions such as hypertension, chronic heart disease, chronic lung disease, connective tissue disease, tumor, chronic kidney disease stage 5, or liver failure. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study received approval from the Ethics Committee of the Third Affiliated Hospital of Sun Yat-sen University (No. [2021]02-272-01). Patient informed consent was exempted given the retrospective nature of the study.

Subgroup analysis stratified by disease causes in PH patients

To assess the impact of different etiologies of PH on the patients' characteristics, PH patients were divided into three subgroups: (I) patients with a history of chronic lung disease and chest imaging examinations indicating PH secondary to chronic lung disease were classified into the chronic pulmonary disease subgroup (n=26); (II) patients with a history of heart disease and cardiac color Doppler ultrasound suggesting PH secondary to left heart disease were classified into the left heart disease subgroup (n=37); (III) patients without the aforementioned medical history and abnormal examination were classified into the unknown reason subgroup (n=31).

Data collection

The medical records of patient's were reviewed to gather the following information: (I) demographic and baseline clinical characteristics: gender, age, altitude of residence, symptoms, medical history, New York Heart Association (NYHA) classification, and physical examination findings upon admission; (II) laboratory test results, including routine blood test, parameters of liver and kidney function, and metabolic indicators; (III) echocardiographic examination findings: various echocardiographic indicators, the E/A ratio, and the ratio of right ventricular end-diastolic inner diameter/left ventricular end-diastolic inner diameter. The primary author, R.D., undertook the task of documenting general information, laboratory results, and echocardiography data. The secondary author, X.S., was in charge of statistical data analysis. The team ensured the accuracy and consistency of the research by collectively resolving any discrepancies in data collection and analysis through discussion, thereby reaching a consensus.

Statistical analysis

Continuous variables were presented as mean ± standard deviation (SD) and compared using Student's independent *t*-test or Mann-Whitney *U* test (if normality assumptions

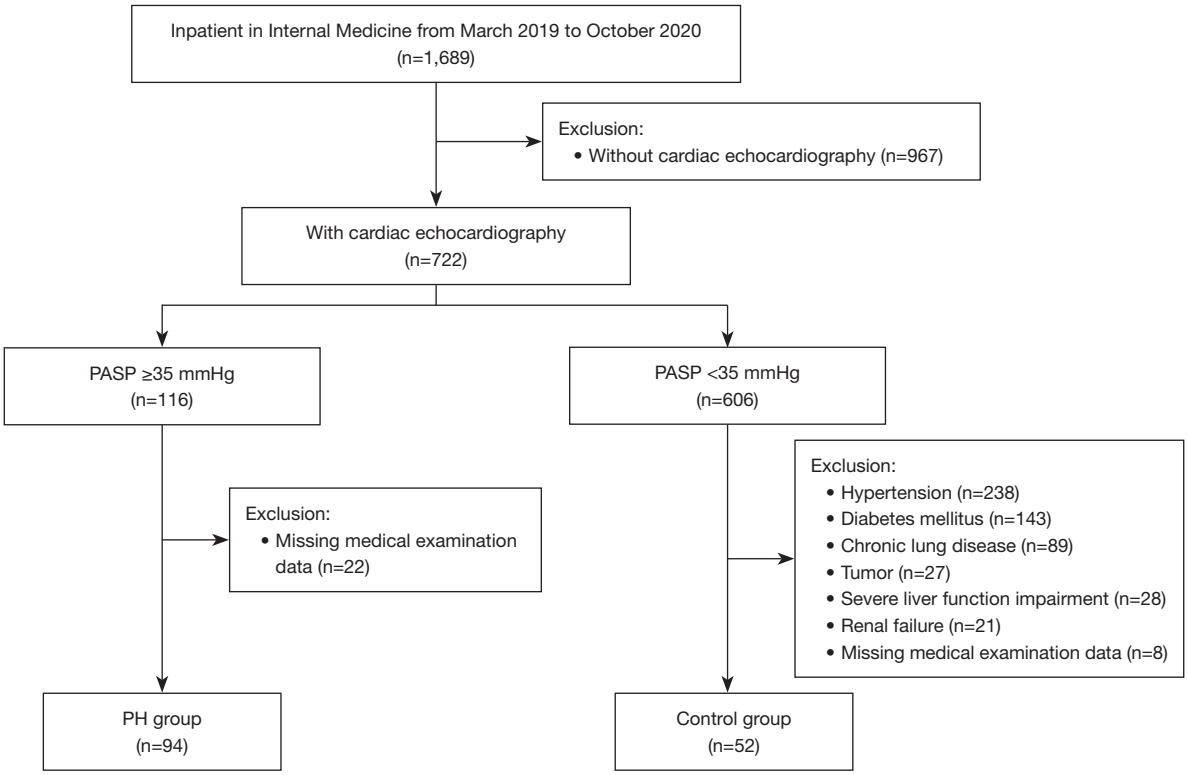

Figure 1 Flow diagram of patient selection. PASP, pulmonary artery systolic pressure; PH, pulmonary hypertension.

were not met). Categorical variables were described as numbers and percentages and compared using the Chi-squared test or Fisher's exact test (if expected values were ≤5). One-way analysis of variance (ANOVA) test and Fisher's LSD test for post-hoc comparison were utilized for comparing means among groups (more than 2). Pearson's correlation coefficient or Spearman rank correlation coefficient were employed to illustrate relationships between variables. A significance level of $P<0.05$ was considered statistically significant for all tests, two-tailed. All analyses were conducted using IBM SPSS Version 25 (SPSS Statistics V25, IBM Corporation, Somers, New York, NY, USA).

Results

Patient's demographic and clinical characteristics

The patient population of inpatient in internal medicine from March 2019 to October 2020 is 1,689. According to the inclusion criteria, a total of 146 patients were ultimately included in this study. The flow diagram refers to *Figure 1*. The PH group comprised a total of 94 patients (44 males and 50 females) with a mean age of 66.51±12.35 years, while 52 non-PH patients were included in the control group. As shown in *Table 1*, 64.89% of PH patients resided at an altitude of 3,000–4,000 m, while the remaining 35.11% lived over 4,000 m. Combined chronic diseases among the PH group included 14.89% with chronic obstructive pulmonary disease (COPD), 17.02% with a history of tuberculosis, 53.19% with systemic hypertension, 4.26% with type II diabetes mellitus (DM), 7.23% with hypercholesterolemia, 0% with hypertriglyceridemia, 51.06% with hyperuricemia, and 16.30% with anemia.

Compared to the control group, the PH group had significantly higher age ($P<0.001$), systolic blood pressure (SBP) ($P<0.001$), diastolic blood pressure (DBP) ($P<0.001$), while oxygen saturation upon admission was significantly lower ($P<0.001$).

Comparison of laboratory results between the two groups

Table 2 demonstrated the laboratory findings of the two groups. Compared to the control group, the PH group had

Table 1 Patients demographic and clinical characteristics

Parameters	Control (n=52)	PH (n=94)	All (n=146)	P
Gender				0.60
Male	22 (42.31)	44 (46.81)	66 (45.21)	
Female	30 (57.69)	50 (53.19)	80 (54.79)	
Age, years	57.69±13.40	66.51±12.35	63.37±13.38	<0.001
Weight, kg	62.30±13.19	59.23±10.88	60.48±11.92	0.16
Height, cm	163.70±8.02	162.45±8.62	162.96±8.37	0.41
BMI, kg/m^2	23.12±3.83	22.47±3.42	22.74±3.60	0.33
Living altitude				0.68
3,000–4,000 m	32 (61.54)	61 (64.89)	93 (63.70)	
>4,000 m	20 (38.46)	33 (35.11)	53 (36.30)	
Tuberculosis history				0.002
Yes	0	16 (17.02)	16 (10.96)	
No	52 (100.00)	78 (82.98)	130 (89.04)	
COPD history				0.002
Yes	0	14 (14.89)	14 (9.59)	
No	52 (100.00)	80 (85.11)	132 (90.41)	
Systemic hypertension				<0.001
Yes	0	50 (53.19)	50 (34.25)	
No	52 (100.00)	44 (46.81)	96 (65.75)	
Diabetes mellitus				0.65
Yes	1 (1.92)	4 (4.26)	5 (3.42)	
No	51 (98.08)	90 (95.74)	141 (96.58)	
Anemia				0.009
Yes	1 (1.96)	15 (16.30)	16 (11.19)	
No	50 (98.04)	77 (83.70)	127 (88.81)	
Hepatobiliary diseases				0.69
Yes	6 (11.54)	13 (13.83)	19 (13.01)	
No	46 (88.46)	81 (86.17)	127 (86.99)	
Hyperuricemia				<0.001
Yes	8 (15.38)	48 (51.06)	56 (38.36)	
No	44 (84.62)	46 (48.94)	90 (61.64)	
Hyperlipidemia type				0.08
Hypercholesterolemia	5 (11.36)	6 (7.23)	11 (8.66)	
hypertriglyceridemia	2 (4.55)	0	2 (1.57)	
No	37 (84.09)	77 (92.77)	114 (89.76)	

Table 1 (*continued*)

Table 1 (*continued*)

Parameters	Control (n=52)	PH (n=94)	All (n=146)	P
Lower limb edema				<0.001
No	52 (100.00)	48 (51.06)	100 (68.49)	
Slight	0	13 (13.83)	13 (8.90)	
Moderate	0	31 (32.98)	31 (21.23)	
Severe	0	2 (2.13)	2 (1.37)	
NYHA functional classification				<0.001
I	52 (100.00)	23 (24.47)	75 (51.37)	
II	0	32 (34.04)	32 (21.92)	
III	0	29 (30.85)	29 (19.86)	
IV	0	10 (10.64)	10 (6.85)	
Oxygen saturation on admission, %	92.83±3.35	87.12±7.86	89.20±7.12	<0.001
Heart rate on admission, bpm	78.23±10.29	84.55±16.23	82.00±14.43	0.01
SBP, mmHg	117.54±11.34	137.57±24.39	130.44±22.79	<0.001
DBP, mmHg	78.96±7.35	92.51±19.25	87.68±17.29	<0.001
Pleural effusion				<0.001
No	52 (100.00)	58 (61.70)	110 (75.34)	
Slight	0	27 (28.72)	27 (18.49)	
Moderate	0	9 (9.57)	9 (6.16)	
Pericardial effusion				<0.001
No	52 (100.00)	68 (72.34)	120 (82.19)	
Slight	0	18 (19.15)	18 (12.33)	
Moderate	0	8 (8.51)	8 (5.48)	
Calcific aortic valve disease				<0.001
Yes	1 (1.96)	27 (28.72)	28 (19.31)	
No	50 (98.04)	67 (71.28)	117 (80.69)	

Data are presented as mean ± standard deviation or number (percentage). Anemia has three missing values (1 control, 2 PH), Hyperlipidemia type has 19 missing values (8 control, 11 PH), and Calcific aortic valve disease has one missing value in the control group. BMI, body mass index; COPD, chronic obstructive pulmonary disease; NYHA, New York Heart Association; SBP, systolic blood pressure; DBP, diastolic blood pressure; PH, pulmonary hypertension.

significantly elevated levels of red blood cell (RBC) (P=0.02), red blood cell distribution width (RDW)-SD (P<0.001), coefficient of variation (CV) (P<0.001), platelet-large cell ratio (P-LCR) (P=0.03), aspartate aminotransferase (AST) (P=0.049), alkaline phosphatase (ALP) (P<0.001), γ-glutamyltransferase (γ-GT) (P=0.006), total bilirubin (TB) (P=0.002), direct bilirubin (DB) (P<0.001), urine acid (UA) (P<0.001), and positive rate of urine protein (P=0.008), as well as lower levels of platelet (PLT) (P<0.001), albumin (ALB) (P<0.001), low density lipoprotein-cholesterol (LDL-C) (P<0.001), high density lipoprotein-cholesterol (HDL-C) (P=0.008), and triacylglycerol (P=0.003).

Comparison of echocardiography results between the two groups

Echocardiography results were compared between the two groups. As shown in *Table 3*, the PH group exhibited significantly increased measurements of ascending aorta

Table 2 Patient's laboratory results

Parameters	Control (n=52)	PH (n=94)	All (n=146)	P
Hb, g/L	146.65±17.51	150.64±21.67	149.09±20.18	0.28
RBC, $\times10^{12}$/L	4.95±0.53	5.25±0.87	5.13±0.76	0.02
HCT, %	43.70±5.01	45.81±6.73	44.98±6.17	0.06
MCV, fL	88.46±5.91	87.86±8.47	88.10±7.54	0.67
MCH, pg	29.71±2.41	29.06±3.69	29.32±3.25	0.27
MCHC, g/L	334.90±12.04	330.03±16.15	331.95±14.81	0.07
RDW-SD, fL	43.67±3.40	50.59±6.49	47.85±6.43	<0.001
RDW-CV, %	13.52±1.32	16.18±3.04	15.13±2.82	<0.001
PLT, $\times10^{9}$/L	256.63±72.85	202.55±73.67	223.92±77.72	<0.001
PLT PDW, %	12.23±2.93	12.75±2.66	12.54±2.77	0.30
PLT MPV, fL	9.16±1.37	9.54±1.25	9.39±1.30	0.11
PLT P-LCR, %	21.79±7.67	24.56±6.71	23.46±7.21	0.03
PLT PCT, %	4.88±32.54	0.19±0.07	2.06±20.54	0.21
ALT, U/L	32.31±22.47	47.90±70.15	42.29±58.06	0.150
AST, U/L	24.87±10.57	48.66±79.66	40.10±64.91	0.049
ALP, U/L	98.33±31.17	138.99±61.30	124.35±55.88	<0.001
γ-GT, U/L	41.82±34.73	75.88±76.96	63.62±66.86	0.006
TB, μmol/L	12.27±4.60	22.29±20.76	18.68±17.47	0.002
DB, μmol/L	3.95±1.93	12.19±16.24	9.20±13.58	<0.001
IB, μmol/L	8.32±3.18	10.86±9.89	9.94±8.21	0.09
ALB, g/L	42.23±3.50	37.25±5.42	39.10±5.36	<0.001
UA, μmol/L	297.89±99.70	419.60±174.77	376.50±162.90	<0.001
GLU, mmol/L	4.85±1.18	4.81±1.40	4.82±1.32	0.84
Cr, μmol/L	74.31±17.08	84.22±34.88	80.39±29.62	0.06
LDL-C, mmol/L	3.24±1.03	2.56±0.90	2.79±0.99	<0.001
HDL-C, mmol/L	1.30±0.31	1.08±0.41	1.15±0.39	0.008
TG, mmol/L	1.30±0.80	0.96±0.47	1.07±0.62	0.003
Urine protein, positive	0	11 (11.70)	11 (7.53)	0.008

Data are presented as mean ± standard deviation or number (percentage). Hb, hemoglobin; RBC, red blood cell; HCT, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RDW-SD, red blood cell volume distribution width-standard deviation; RDW-CV, red blood cell volume distribution width-coefficient of variance; PLT, platelet; PDW, platelet distribution width; MPV, mean platelet volume; P-LCR, platelet-large cell ratio; PCT, plateletcrit; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; γ-GT, γ-glutamyltransferase; TB, total bilirubin; DB, direct bilirubin; IB, indirect bilirubin; ALB, albumin; UA, urine acid; GLU, glucose; Cr, creatinine; LDL-C, low density lipoprotein-cholesterol; HDL-C, high density lipoprotein-cholesterol; TG, triacylglycerol.

Table 3 Echocardiography results

Parameters	Control (n=52)	PH (n=94)	All (n=146)	P
Ascending aorta, mm	27.75±4.15	31.67±7.67	30.29±6.89	<0.001
LA, mm	28.86±4.13	39.38±8.80	35.68±9.02	<0.001
LVEDd, mm	41.80±5.40	44.89±9.91	43.81±8.70	0.04
LVESd, mm	27.50±3.74	32.14±10.12	30.53±8.73	0.002
Ventricular septum, mm	9.39±1.69	11.22±2.51	10.59±2.42	<0.001
LV posterior wall thickness, mm	9.00±1.21	10.88±2.47	10.23±2.30	<0.001
RVOT, mm	25.62±3.56	29.51±4.73	28.14±4.72	<0.001
Pulmonary artery diameter, mm	19.89±3.02	24.68±4.60	23.06±4.71	<0.001
RA transverse diameter, mm	32.29±3.45	45.68±8.08	41.06±9.35	<0.001
RV transverse diameter, mm	31.29±3.84	40.96±7.02	37.62±7.65	<0.001
RV/LV end-diastolic diameter	0.77±0.15	0.96±0.27	0.89±0.26	<0.001
EF, %	64.47±8.23	55.52±12.03	58.67±11.63	<0.001
E, cm/s	57.04±18.85	59.52±23.39	58.52±21.62	0.52
A, cm/s	68.78±14.65	68.94±19.07	68.87±17.24	0.96
E/A	0.85±0.27	0.89±0.57	0.87±0.47	0.59
PA pressure, mmHg	–	56.36±16.15	56.36±16.15	–

Data are presented as mean ± standard deviation. LA, left atrium; LV, left ventricle; LVEDd, left ventricular end-diastolic diameter; LVESd, left ventricular end-systolic diameter; RVOT, right ventricular outflow tract; RA, right atrium; RV, right ventricle; EF, ejection fraction; E, early diastole; A, atrial contraction; PA pressure, pulmonary artery pressure; PH, pulmonary hypertension.

(P<0.001), left atrium (LA) (P<0.001), left ventricular end-diastolic diameter (LVEDd) (P=0.04), left ventricular end-systolic diameter (LVESd) (P=0.002), ventricular septum (P<0.001), left ventricle (LV) posterior wall thickness (P<0.001), right ventricular outflow tract (RVOT) (P<0.001), pulmonary artery diameter (P<0.001), right atrium (RA) transverse diameter (P<0.001), right ventricle (RV) transverse diameter (P<0.001), RV/LV end-diastolic diameter (P<0.001), along with significantly decreased ejection fraction (EF) percentage (P<0.001) compared to the control group.

Subgroup analysis stratified by the disease history of the PH patients

Within the PH group, patients were divided into 3 subgroups based on disease history, including chronic pulmonary disease (n=26), left heart disease (n=37), and unknown reason (n=31). *Table 4* demonstrates the results of subgroup analyses and the post-hoc comparison between the two groups were as follows.

Age was significantly higher in the chronic pulmonary and left heart disease subgroups than in the control group (P<0.001 and P=0.004). Heart rate was significantly higher in the left heart disease subgroup than in the control group (P=0.005). RBC count was significantly elevated in the chronic pulmonary disease subgroup than in the left heart disease subgroups and control group (P=0.01 and P=0.02).

The mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) were significantly higher in the chronic pulmonary disease subgroup than the other 3 groups (MCH, P<0.001 to control, P=0.007 to left heart disease, P=0.005 to unknown reason; MCHC, P<0.001 to control, P=0.002 to left heart disease, P=0.003 to unknown reason). RDW-SD and RDW-CV in the 3 PH subgroups were all significantly higher than those of the control group (all six P<0.001). PLT count in the left heart disease subgroup and unknown reason subgroup was significantly lower than the control group (P=0.02 and P=0.001). PLT P-LCR in the left heart disease subgroup and unknown reason subgroup was significantly higher than the control group (P=0.008 and

Table 4 Comparisons among control group and subtypes of PH

Parameters	Control (n=52)	PH (n=94)				P values of Fisher's LSD comparisons					
		Chronic pulmonary disease (n=26)	Left heart disease (n=37)	Unknown reason (n=31)	P_{ANOVA}	Control *vs.* chronic pulmonary disease	Control *vs.* left heart disease	Control *vs.* unknown reason	Chronic pulmonary disease *vs.* left heart disease	Chronic pulmonary disease *vs.* unknown reason	Left heart disease *vs.* unknown reason
Gender					0.935						
Male	22 (42.31)	13 (50.00)	17 (45.95)	14 (45.16)							
Female	30 (57.69)	13 (50.00)	20 (54.05)	17 (54.84)							
Age, year	57.69±13.40	70.35±12.53	65.59±12.15	64.39±12.10	<0.001	<0.001	0.004	0.021	0.145	0.079	0.696
Anemia					0.021						
Yes	1 (1.96)	6 (23.08)	5 (13.89)	4 (13.33)							
No	50 (98.04)	20 (76.92)	31 (86.11)	26 (86.67)							
Heart rate on admission, bpm	78.23±10.29	87.27±17.69	87.64±17.95	79.11±11.65	0.007	0.012	0.005	0.790	0.926	0.043	0.025
Hb, g/L	145.67±18.68	138.69±34.57	139.44±26.71	144.27±32.24	0.619	0.288	0.294	0.823	0.914	0.445	0.474
RBC, 10^{12}/L	4.95±0.52	5.38±1.07	4.88±0.67	5.07±0.98	0.069	0.023	0.678	0.509	0.013	0.136	0.328
HCT, %	43.43±5.25	43.97±9.67	42.33±6.87	43.95±9.48	0.798	0.769	0.505	0.768	0.401	0.995	0.395
MCV, fL	87.85±6.72	81.66±10.65	86.85±7.58	87.39±12.19	0.034	0.005	0.612	0.827	0.027	0.021	0.815
MCH, pg	29.49±2.72	25.73±4.89	28.56±3.65	28.84±5.21	0.002	<0.001	0.282	0.485	0.007	0.005	0.780
MCHC, g/L	334.63±12.47	312.85±24.43	327.75±18.57	328.32±21.12	<0.001	<0.001	0.090	0.149	0.002	0.003	0.903
RDW-SD, fL	43.56±3.38	51.98±7.08	51.28±5.62	50.38±6.88	<0.001	<0.001	<0.001	<0.001	0.629	0.294	0.517
RDW-CV, %	13.60±1.39	18.48±4.53	16.49±2.69	16.28±3.46	<0.001	<0.001	<0.001	<0.001	0.010	0.007	0.776
PLT, 10^9/L	262.49±86.63	223.00±86.32	221.81±68.19	197.29±88.60	0.007	0.052	0.025	0.001	0.956	0.260	0.241
PLT P-LCR, %	21.41±7.77	23.52±7.64	25.53±5.08	25.16±7.44	0.034	0.232	0.008	0.026	0.283	0.406	0.836
ALP, U/L	105.64±49.45	171.51±134.04	140.34±53.09	124.00±48.92	0.002	<0.001	0.030	0.270	0.098	0.015	0.361
γ-GT, U/L	48.92±50.37	83.85±121.01	87.33±92.64	67.52±67.43	0.127	0.077	0.032	0.318	0.869	0.452	0.323
TB, μmol/L	11.92±4.45	40.48±58.86	24.15±13.28	20.98±24.78	<0.001	<0.001	0.049	0.162	0.027	0.011	0.649
DB, μmol/L	3.89±1.88	31.40±57.09	11.62±8.00	10.76±15.17	<0.001	<0.001	0.159	0.231	0.003	0.003	0.889
ALB, g/L	41.67±3.86	37.36±5.36	37.51±5.66	35.89±4.86	<0.001	<0.001	<0.001	<0.001	0.906	0.264	0.178
UA, μmol/L	297.89±99.70	442.48±225.73	439.75±133.94	377.01±165.71	<0.001	<0.001	<0.001	0.024	0.945	0.107	0.094
GLU, mmol/L	4.85±1.18	4.13±1.25	5.11±1.37	5.00±1.41	0.037	0.030	0.387	0.627	0.007	0.017	0.739

Table 4 (*continued*)

Table 4 (*continued*)

Parameters	Control (n=52)	PH (n=94)			P_{ANOVA}	P values of Fisher's LSD comparisons					
		Chronic pulmonary disease (n=26)	Left heart disease (n=37)	Unknown reason (n=31)		Control *vs.* chronic pulmonary disease	Control *vs.* left heart disease	Control *vs.* unknown reason	Chronic pulmonary disease *vs.* left heart disease	Chronic pulmonary disease *vs.* unknown reason	Left heart disease *vs.* unknown reason
Cr, μmol/L	74.31±17.08	74.61±18.62	95.07±49.48	80.39±19.60	0.01	0.96	0.002	0.38	0.009	0.47	0.06
LDL-C, mmol/L	3.24±1.03	2.34±0.87	3.05±0.86	2.14±0.67	<0.001	<0.001	0.40	<0.001	0.006	0.48	<0.001
HDL-C, mmol/L	1.30±0.31	1.06±0.56	1.18±0.32	0.98±0.31	0.01	0.02	0.22	0.003	0.26	0.48	0.07
TG, mmol/L	1.30±0.80	0.90±0.37	0.99±0.57	0.97±0.40	0.03	0.01	0.02	0.03	0.57	0.69	0.88

Data are presented as mean ± standard deviation or number (percentage). Hb, hemoglobin; RBC, red blood cell; HCT, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RDW-SD, red blood cell volume distribution width-standard deviation; RDW-CV, red blood cell volume distribution width-coefficient of variation; PLT, platelet; PDW, platelet distribution width; MPV, mean platelet volume; P-LCR, platelet-large cell ratio; PCT, plateletcrit; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; γ-GT, γ-glutamyltransferase; TB, total bilirubin; DB, direct bilirubin; IB, indirect bilirubin; ALB, albumin; UA, urine acid; GLU, glucose; Cr, creatinine; LDL-C, low density lipoprotein-cholesterol; HDL-C, high density lipoprotein-cholesterol; TG, triacylglycerol.

P=0.03). ALP levels in the chronic pulmonary and left heart disease subgroups were significantly higher than those in the control group (P<0.001 and P=0.03). γ-GT levels in the left heart disease subgroup were notably elevated compared to those in the control group (P=0.03). TB and DB levels in the chronic pulmonary disease subgroup were significantly higher than those in the control group (both P<0.001).

ALB levels in all three PH subgroups were significantly lower than those in the control group (all three P<0.001). UA levels in the chronic pulmonary and left heart disease subgroups were significantly higher than those in the control group (both P<0.001). GLU levels in the chronic pulmonary disease subgroup was significantly lower than those in the left heart disease subgroup (P=0.03). Cr levels in the left heart disease group were notably higher compared to those in the control group (P=0.002) and chronic pulmonary disease subgroup (P=0.009).

Overall, PH patients exhibited a comparatively lower levels of LDL-C than the control group, however, significances were observed only in the chronic pulmonary disease and unknown reason subgroups (both P<0.001). Additionally, the LDL-C level of the chronic pulmonary disease subgroup was also significantly lower than that of the left heart disease subgroup (P=0.006). HDL-C was significantly lower in the chronic pulmonary disease subgroup and unknown reason PH subgroup than in the control group (P=0.02 and P=0.003). TG levels in all three PH subgroups were significantly lower than those in the control group (P=0.01, P=0.02, and P=0.03).

Correlation coefficients analysis among variables

Correlations among the blood routine examination, liver function index, metabolic index, and selected echocardiography parameters were analyzed. Patients with anemia or hepatobiliary diseases were excluded from these analyses. Coefficient (r) exceeding 0.3 were considered significant and are reported below.

Table 5 presents the results of correlation analyses among the blood biochemical indexes. RBC exhibited positive correlations with Hb, hematocrit (HCT), and UA. Hb showed positive correlations with RBC, HCT, UA, and negatively correlations with PLT. HCT demonstrated positive correlations with RBC, Hb, UA, and negative correlations with PLT. PLT showed negative correlations with Hb, HCT, TB, and DB. Alanine aminotransferase (ALT) was exhibited positive correlations with AST, γ-GT, TB, and DB. AST showed positive correlations with ALT,

Table 5 Correlation coefficient analysis of laboratory results and other variables

Correlation coefficient, r	RBC	Hb	HCT	PLT	ALT	AST	ALP	γ-GT	TB	DB	IB	ALB	UA	HDL-C	LDL-C
RBC	–	0.60*	0.79*	−0.06	0.15	0.16	0.25*	0.25*	0.18	0.25*	−0.02	−0.02	0.42*	−0.19	−0.21
Hb	0.60*	–	0.94*	−0.37*	0.24*	0.24*	0.12	0.25*	0.20*	0.19	0.17	−0.06	0.32*	0.02	−0.05
HCT	0.79*	0.94*	–	−0.32*	0.21*	0.22*	0.20*	0.28*	0.20*	0.21*	0.12	−0.06	0.37*	−0.09	−0.12
PLT	−0.06	−0.37*	−0.32*	–	−0.11	−0.21*	−0.19*	−0.17	−0.33*	−0.30*	−0.20*	0.29*	−0.17	0.13	0.18
ALT	0.15	0.24*	0.21*	−0.11	–	0.76*	0.29*	0.44*	0.31*	0.31*	0.12	−0.12	0.27*	−0.14	0.07
AST	0.16	0.24*	0.22*	−0.21*	0.76*	–	0.41*	0.39*	0.41*	0.44*	0.13	−0.35*	0.39*	−0.32*	−0.18
ALP	0.25*	0.12	0.20*	−0.19*	0.29*	0.41*	–	0.48*	0.47*	0.58*	0.12	−0.13	0.47*	−0.29*	−0.19
γ-GT	0.25*	0.25*	0.28*	−0.17	0.44*	0.39*	0.48*	–	0.26*	0.24*	0.16	−0.01	0.32*	−0.05	0.00
TB	0.18	0.20*	0.20*	−0.33*	0.31*	0.41*	0.47*	0.26*	–	0.95*	0.63*	−0.38*	0.55*	−0.34*	−0.21
DB	0.25*	0.19	0.21*	−0.30*	0.31*	0.44*	0.58*	0.24*	0.95*	–	0.44*	−0.40*	0.61*	−0.43*	−0.30*
IB	−0.02	0.17	0.12	−0.20*	0.12	0.13	0.12	0.16	0.63*	0.44*	–	−0.19*	0.28*	0.15	0.21
ALB	−0.02	−0.06	−0.06	0.29*	−0.12	−0.35*	−0.13	−0.01	−0.38*	−0.40*	−0.19*	–	−0.18	0.57*	0.48*
UA	0.42*	0.32*	0.37*	−0.17	0.27*	0.39*	0.47*	0.32*	0.55*	0.61*	0.28*	−0.18	–	−0.32*	−0.02
HDL-C	−0.19	0.02	−0.09	0.13	−0.14	−0.32*	−0.29*	−0.05	−0.34*	−0.43*	0.15	0.57*	−0.32*	–	0.36*
LDL-C	−0.21	−0.05	−0.12	0.18	0.07	−0.18	−0.19	0.00	−0.21	−0.30*	0.21	0.48*	−0.02	0.36*	–
RA transverse diameter	0.25*	0.22*	0.24*	−0.40*	0.22*	0.41*	0.34*	0.32*	0.48*	0.46*	0.32*	−0.54*	0.44*	−0.35*	−0.34*
Pulmonary artery diameter	−0.02	0.13	0.10	−0.34*	0.03	0.12	0.21*	0.03	0.33*	0.32*	0.25*	−0.42*	0.19	−0.24*	−0.25*
RVOT	0.20*	0.22*	0.22*	−0.20*	0.15	0.21*	0.17	0.18	0.21*	0.20*	0.33*	−0.17	0.42*	−0.10	−0.11
RV transverse diameter	0.35*	0.25*	0.34*	−0.27*	0.14	0.26*	0.42*	0.28*	0.30*	0.34*	0.18	−0.34*	0.47*	−0.30*	−0.26*
RV/LV end-diastolic diameter	0.41*	0.26*	0.39*	−0.26*	−0.02	0.19	0.32*	0.14	0.27*	0.31*	0.08	−0.27*	0.30*	−0.18	−0.27*

*, P<0.05. RBC, red blood cell; Hb, hemoglobin; HCT, hematocrit; PLT, platelet; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; γ-GT, γ-glutamyltransferase; TB, total bilirubin; DB, direct bilirubin; IB, indirect bilirubin; ALB, albumin; UA, urine acid; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; RA, right atrium; RVOT, right ventricular outflow tract; RV, right ventricle; LV, left ventricle.

ALP, γ-GT, TB, DB, UA, and negative correlations with ALB and HDL-C. ALP demonstrated positive correlations with AST, γ-GT, TB, DB, and UA. γ-GT was positively correlated with ALT, AST, ALP, and UA. Both TB and DB were positively correlated with each other, ALT, AST, ALP, indirect bilirubin (IB), UA, and negatively correlated with PLT, ALB, HDL-C and LDL-C. IB was positively correlated with TB and DB. ALB was negatively correlated with AST, TB, DB, and positively correlated with HDL-C and LDL-C. UA was positively correlated with RBC, Hb, HCT, AST, ALP, γ-GT, TB, DB, and negatively correlated with HDL-C. HDL-C displayed negative correlations with AST, TB, DB, UA, and positive correlations with ALB and LDL-C. LDL-C exhibited positive correlations with ALB, HDL-C, and negative correlations with DB.

Table 6 presents the results of correlation analyses of the five echocardiography indices. The RA transverse diameter showed positive correlations with AST, ALP, γ-GT, TB, DB, IB, UA, pulmonary artery diameter, RVOT, RV transverse diameter, RV/LV end-diastolic diameter, and negative correlations with PLT, ALB, HDL-C, and LDL-C. Pulmonary artery diameter exhibited positive

Table 6 Correlation coefficient analysis of echocardiography results and other variables

Correlation coefficient, r	RA transverse diameter	Pulmonary artery diameter	RVOT	RV transverse diameter	RV/LV end-diastolic diameter
RBC	0.25*	–0.02	0.20*	0.35*	0.41*
Hb	0.22*	0.13	0.22*	0.25*	0.26*
HCT	0.24*	0.10	0.22*	0.34*	0.39*
PLT	–0.40*	–0.34*	–0.20*	–0.27*	–0.26*
ALT	0.22*	0.03	0.15	0.14	–0.02
AST	0.41*	0.12	0.21*	0.26*	0.19
ALP	0.34*	0.21*	0.17	0.42*	0.32*
γ-GT	0.32*	0.03	0.18	0.28*	0.14
TB	0.48*	0.33*	0.21*	0.30*	0.27*
DB	0.46*	0.32*	0.20*	0.34*	0.31*
IB	0.32*	0.25*	0.33*	0.18	0.08
ALB	–0.54*	–0.42*	–0.17	–0.34*	–0.27*
UA	0.44*	0.19	0.42*	0.47*	0.30*
HDL-C	–0.35*	–0.24*	–0.10	–0.30*	–0.18
LDL-C	–0.34*	–0.25*	–0.11	–0.26*	–0.27*
RA transverse diameter	–	0.53*	0.44*	0.72*	0.59*
Pulmonary artery diameter	0.53*	–	0.39*	0.38*	0.20*
RVOT	0.44*	0.39*	–	0.52*	0.19*
RV transverse diameter	0.72*	0.38*	0.52*	–	0.73*
RV/LV end-diastolic diameter	0.59*	0.20*	0.19*	0.73*	–

*, P<0.05. RBC, red blood cell; Hb, hemoglobin; HCT, hematocrit; PLT, platelet; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; γ-GT, γ-glutamyltransferase; TB, total bilirubin; DB, direct bilirubin; IB, indirect bilirubin; ALB, albumin; UA, urine acid; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; RA, right atrium; RVOT, right ventricular outflow tract; RV, right ventricle; LV, left ventricle.

correlations with TB, DB, RA transverse diameter, RVOT, RV transverse diameter, and negative correlations with PLT and ALB. RVOT showed positive correlations with IB, UA, RA transverse diameter, pulmonary artery diameter, and RV transverse diameter. RV transverse diameter displayed positive correlations with RBC, HCT, ALP, TB, DB, UA, RA transverse diameter, pulmonary artery diameter, RVOT, RV/LV end-diastolic diameter, and negative correlations with ALB and HDL-C. RV/LV end-diastolic diameter was positively correlated with RBC, HCT, ALP, DB, UA, RA transverse diameter, and RV transverse diameter.

Discussion

Currently, large-scale epidemiological data on the incidence of PH in people living at high altitude are lacking. Qadar Pasha *et al.* reported a PH prevalence of 1.2% among native Tibetans living on the Yunnan-Guizhou-Sichuan Plateau in China (16). This study reviewed 18-month data from a county-level hospital in Tibet, revealing that PH patients comprised 6.87% of the inpatients in the internal medicine department during the same period. This finding suggested that PH is a significant concern in hospitals located in high-altitude areas. In this study, the mean age of PH patients was 66.51±12.35 years, consistent with a previous study conducted in the Qinghai-Tibet Plateau (17). Additionally, 67% of PH patients in our study presented with concurrent chronic pulmonary disease and left heart disease, implying that these conditions might be the primary etiologies of PH in Tibetan regions.

It has been reported that left heart disease accounts for approximately 50% of PH cases (18). In this study, 39.4% of PH patients had concurrent left heart disease. In 2019, Wang *et al.* have reported congenital heart disease as a common cause of PH in the local area of Chongqing (19), China. However, no PH patients with congenital heart disease were identified in this study. These discrepancies suggest that the etiology of PH in high-altitude areas differs from that in plain areas. Despite the relatively high prevalence of systemic hypertension (53.19%) among high-altitude Tibetan PH patients, the incidences of diabetes, hyperlipidemia, and obesity were all low. This may account for the low occurrence of left heart disease in these PH patients. In this study, 33% of PH patients had unknown etiologies, warranting special attention to two important causes. Firstly, HAPH is noteworthy. The diagnostic criteria for HAPH include long-term residence at high-altitudes, absence of other underlying conditions causing PH, and reversible resolution of PH upon leaving high-altitude regions. Therefore, it is challenging to ascertain whether these patients had HAPH. Secondly, PH induced by rheumatic diseases is another consideration. Due to the lack of diagnostic tools for detecting indicators of rheumatic diseases, this etiology remains undetermined.

Chronic high-altitude disease encompass high-altitude polycythemia (HAPC) (20) and HAPH. This study identified only two cases of HAPC. Beall *et al.* have demonstrated that Tibetans dwelling on the plateau exhibit lower Hb levels compared to other ethnicities residing at the plateau (21). Specifically, the mean Hb levels of healthy Tibetan men and women are 156 and 142 g/L, respectively (21). In this study, the mean Hb level among PH patients was 150.64± 21.67 g/L, suggesting that Tibetan PH patients did not exhibit abnormally RBC and Hb levels.

Additionally, it is worth noting that PH patients with chronic pulmonary disease had a significantly higher RBC level than those with left heart disease. Correlation analysis revealed a negative correlation between LVEDd and Hb, RBC, and HCT, while a positive correlation was observed between these indicators and RV/LV end-diastolic diameter. These results indicated that appropriately elevated RBC and Hb may confer a protective effect on left ventricular function in the high-altitude environment.

In this study, all three PH subgroups had significantly elevated RDW-SD and RDW-CV as compared with the control group. RDW, an indicator of the variability in circulating erythrocyte volume, was assessed to characterize these differences. An elevated RDW indicates potential dysfunctions in erythropoiesis, augmented RBC degradation, or shortened RBC lifespan (20). Accumulating evidence has suggested that hemolysis, leading to the release of hemoglobin and heme, plays a significant role in the pathogenesis of PH (22,23). Yang *et al.* have demonstrated a significant increase in RDW among patients with COPD patients who also had PH, indicating that RDW serves as a predictive factor for PH secondary to COPD (24). RDW can serve as a prognostic indicator for adverse outcomes and mortality in PH patients (25-27). Therefore, monitoring RDW is advisable for individuals with PH living in high-altitude regions like Tibet. In this study, PH patients exhibited significantly decreased PLT levels as compared with the control group. Taguchi *et al.* have shown that idiopathic PAH patients with a PLT count below 20×10^4/μL at baseline had significantly lower survival rates and proposed that PLT count serves as an independent prognostic factor in idiopathic PAH patients (28).

Research has demonstrated that the prevalence of hyperuricemia can reach up to 80% in adult PH patients (29). Additionally, a meta-analysis shows that PH patients with elevated level of serum UA levels tend to have higher pulmonary arterial pressure compared to those with normal UA levels (30). Consistent with the aforementioned observations, this study revealed that over half of the Tibetan patients with (PH living at high altitude exhibited hyperuricemia, with significantly elevated serum uric acid levels as compared with the control group. In the PH patients with hyperuricemia, the risk of mortality was found to increase by 19% (30), indicating that hyperuricemia serves as an indicator of poor prognosis. Hence, it is worthwhile to further investigate the prognostic values of thrombocytopenia and hyperuricemia in PH patients living on the Tibetan plateau.

In this study, the LDL-C levels of PH patients with left heart disease was markedly higher compared to those of the other two groups, indicating that hypercholesterolemia could be one of the primary pathogenic factors contributing to cardiovascular disease. Correlation analysis showed that HDL-C exhibited a negative correlation with the RA transverse diameter and RV transverse diameter, suggesting a potential protective role of HDL-C in PH. Heresi *et al.* has demonstrated that PAH patients often present with reduced plasma levels of HDL-C, and this decrease in plasma HDL-C is associated with higher mortality and the disease severity (31). Supporting this notion, it is well established that HDL-C exerts vasoprotective effects in PAH patients, contributing to the long-term survival (32). However, the

molecular mechanism underlying the protective effect of HDL-C in PH still require further investigated.

In this study, PH patients had elevated serum levels of ALT, AST, ALP, γ-GT, TB, and IB, along with decreased levels of ALB as compared with the control group, suggesting an impaired liver function in PH patients. The RVOT, the RA transverse diameter, and the RV transverse diameter were all positively correlated with TB, DB, and IB, and negatively correlated with ALB. During PH, tricuspid regurgitation elevates pressure in the RA, potentially causing hepatic vein congestion and subsequent hyperbilirubinemia. Hypoalbuminemia arises from chronic liver damage and may exacerbate symptoms of water retention. In the context of right heart failure, hyperbilirubinemia serves as a prognostic indicator for poor prognosis (33). Takeda *et al.* have similarly noted an association between TB levels and right atrial pressure in PH patients, and patients with elevated TB levels have a worse prognosis (34). Therefore, monitoring bilirubin levels during the follow-up of high-altitude PH patients is advisable.

Our study focuses on analyzing the clinical characteristics of PH patients in high-altitude Tibetans. Compared to individuals from low-altitude regions, Tibetan PH patients face unique environmental challenges, particularly chronic hypoxia, which is a recognized risk factor for PH development. Additionally, the Tibetan population has undergone physiological adaptations to high-altitude conditions over generations, potentially leading to differences in the clinical presentation and etiology of PH when compared to low-altitude populations. This study highlights the significance of PH in high-altitude regions, shedding light on the prevalence of chronic pulmonary and left heart diseases as common causes. This underscores the importance of implementing tailored interventions to address these specific conditions effectively. Moreover, our findings reveal systemic impacts of PH, as evidenced by abnormal liver and metabolic indexes. Understanding these associations can guide comprehensive patient management, emphasizing the necessity for tailored approaches in high-altitude settings. Furthermore, our research contributes to the understanding of PH characteristics in regions with limited medical resources and sparse population distribution. Given that over 1.4 million people globally live at high altitudes, with approximately 800,000 in Asia alone, providing insights into PH disease characteristics in these areas holds significant research value, particularly for medical practices in specialized regions.

Our findings regarding the clinical attributes of PH patients among the Tibetan population in Chaya County, Changdu, Tibet, contribute to the growing body of literature on this topic. It is noteworthy that the current study complements our recent investigation (14), where we focused on analyzing ECG parameters associated with PH diagnosis in high-altitude Tibetan populations. While the current study primarily examines echocardiographic parameters, the findings from both studies collectively provide a comprehensive understanding of the multifaceted nature of PH in this population. Specifically, the abnormalities observed in liver function and metabolic indexes among Tibetan PH patients in the current study align with the ECG parameters identified as independent factors associated with PH diagnosis in our previous investigation (14). These converging findings underscore the complex interplay between cardiac and systemic manifestations of PH in high-altitude settings and highlight the importance of multimodal approaches in its diagnosis and management.

Several limitations to this study should be pointed out. First, PH diagnosis was not confirmed by RHC and the etiology grouping is not rigorous. A primary limitation was our inability to conduct comprehensive etiological investigations and RHC due to logistical constraints. Consequently, we were unable to classify the PH cases according to the 2022 ESC/ERS Guidelines. It should be pointed out that the "unknown reason" group in this study should be interpreted with caution. Strictly speaking, it cannot be solely attributed to HAPH as it may include cases with rheumatic diseases, idiopathic PAH, chronic thromboembolic PH, or other types of PH that were not definitively ruled out. Furthermore, the control group comprised hospitalized patients, resulting in an age mismatch and potential bias. In the control group, the right heart structure and tricuspid regurgitation fell within the normal range, thus PAP measurements were not taken. Also, this retrospective study lacked data on lifestyle characteristics such as smoking, alcohol consumption, and physical activity. Such information could offer valuable insights into potential risk factors for PH. Incorporating these factors into future prospective studies will be considered. Furthermore, many PH patients experience shortness of breath and difficulty walking, making it challenging to conduct a 6-minute walk test to assess the severity of PH, particularly among elderly individuals with joint issues. Therefore, future research should focus on conducting large, well-designed prospective studies to

validate the findings of this study.

Conclusions

Chronic pulmonary disease and left heart disease were identified as common etiologies of PH among Tibetan patients residing in high-altitude regions. Tibetan individuals with PH living at high altitudes exhibited abnormal alterations in various liver functional and metabolic indices, which demonstrated correlations with morphological parameters derived from cardiac ultrasound assessments.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://cdt.amegroups.com/article/view/10.21037/cdt-23-486/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study conformed to the provisions of the Declaration of Helsinki (as revised in 2013). The study received approval from the Ethics Committee of the Third Affiliated Hospital of Sun Yat-sen University (No. [2021]02-272-01). The need for patient informed consent was waived due to the retrospective nature of the study.

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