Recent Advances in Pulmonary Non-infectious Diseases in High-Altitude Areas: Postprint

Authors: Zhao Xuedan, Ai Yue, Jin Guoen, Jia Guoqiang, Jia Guoqiang

Date: 2025-02-24T00:00:00+00:00

Abstract

High-altitude regions are characterized by low temperature, low humidity, low pressure, and hypoxia, which can trigger a series of physiological responses that significantly affect pulmonary health. This article comprehensively summarizes the effects of the unique high-altitude environment on acute and chronic non-infectious pulmonary diseases, analyzing factors including incidence, pathogenesis, clinical indicators, and prognosis. The influence of the high-altitude environment on acute diseases such as high-altitude pulmonary edema (HAPE) and pulmonary embolism (PE), as well as on chronic diseases including chronic obstructive pulmonary disease (COPD), chronic pulmonary heart disease (CPHD), asthma, high-altitude pulmonary hypertension (HAPH), pulmonary fibrosis (PF), obstructive sleep apnea syndrome (OSAS), and lung cancer, is examined through comparative analysis of influencing factors with low-altitude regions. This review aims to summarize the mechanisms of lung tissue injury induced by the high-altitude environment and analyze its relationship with various non-infectious pulmonary diseases, in order to provide targeted guidance for the diagnosis and treatment of non-infectious pulmonary diseases in patients residing in high-altitude regions.

Full Text

The New Research Progress of Non-infectious Lung Diseases in High Altitude Areas

ZHAO Xuedan[1], AI Yue[1], JING Guoen[1], JIA Guoqiang[2]*

[1]Graduate School of Qinghai University, Xining 810001, China
[2]Affiliated Hospital of Qinghai University, Xining 810001, China

Corresponding author: JIA Guoqiang, Chief physician; E-mail: gqjqhxn@163.com

Abstract

High-altitude areas are characterized by hypothermia, low humidity, hypobaric pressure, and hypoxia, which may trigger a series of physiological responses that significantly affect lung health. This article provides a comprehensive summary of the impact of the unique environment in high-altitude areas on acute and chronic non-infectious lung diseases, analyzing factors such as morbidity, pathogenesis, clinical indicators, and prognosis. The environmental conditions of high-altitude areas affect acute diseases such as high-altitude pulmonary edema (HAPE) and pulmonary embolism (PE), as well as chronic diseases like chronic obstructive pulmonary disease (COPD), chronic pulmonary heart disease (CPHD), asthma, high-altitude pulmonary hypertension (HAPH), pulmonary fibrosis (PF), obstructive sleep apnea syndrome (OSAS), and lung cancer. A comparative analysis of influencing factors between high-altitude and low-altitude areas is conducted, aiming to review the mechanisms of lung tissue damage in high-altitude environments and analyze its relationship with different non-infectious pulmonary diseases. This review aims to provide targeted guidance for the diagnosis and treatment of non-infectious pulmonary diseases in high-altitude areas.

Keywords: High altitude; Lung diseases; Pulmonary inflammatory disease; Chronic obstructive pulmonary disease; Asthma; High altitude pulmonary edema

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High-altitude areas are defined as regions exceeding 2,500 meters in elevation. Globally, over 81.6 million people live in high-altitude areas, representing 1.07% of the world' s total population, with China having the largest number of residents in areas above 3,500 meters [1]. As altitude increases, oxygen partial pressure decreases from 90–100 mmHg (1 mmHg = 0.133 kPa) at low altitudes to less than 50 mmHg at 5,300 meters [2]. Exposure to high-altitude environments can be categorized as acute exposure (permanent residents), chronic exposure (short-term visitors), and chronic intermittent hypobaric hypoxia exposure (frequent travelers between high and low altitudes) [3]. Acute exposure may lead to conditions such as high-altitude pulmonary edema (HAPE) and pulmonary embolism (PE), while chronic and intermittent exposure can trigger chronic diseases including chronic obstructive pulmonary disease (COPD), high-altitude pulmonary hypertension (HAPH), chronic pulmonary heart disease (CPHD), pulmonary fibrosis (PF), and lung cancer. These high-altitude environmental conditions can exacerbate lung injury and increase the incidence and mortality of non-infectious lung diseases. Therefore, in-depth study of the mechanisms of lung tissue damage in high-altitude areas and their relationship with various non-infectious pulmonary diseases may provide a basis for developing targeted diagnosis and treatment protocols, thereby reducing disease incidence and improving prognosis. This review elaborates on the latest understanding of acute and chronic non-infectious lung diseases in high-altitude areas, offering multidi-

mensional perspectives on adaptation for patients in these regions and providing theoretical support for clinical practice and intervention strategies.

Literature Search Strategy

We conducted computerized searches of PubMed, CNKI, Wanfang, VIP, and the Chinese Medical Full-Text Database. Chinese search terms included "high-altitude areas/plateau regions," "non-infectious lung diseases," "respiratory system diseases," "high-altitude pulmonary edema," "pulmonary embolism," "COPD," "high-altitude pulmonary hypertension," "chronic pulmonary heart disease," "asthma," "pulmonary fibrosis," "lung cancer," and "obstructive sleep apnea syndrome." English search terms included "High altitude/plateau," "Sickness, Altitude/Altitude Hypoxia," "high altitude pulmonary edema," "pulmonary embolism," "chronic pulmonary hypertension," "chronic pulmonary heart disease," "pulmonary fibrosis," and "Neoplasms, Pulmonary/Lung Cancer." The search timeframe was 2019–2025, though for diseases with limited research, the timeframe was extended to 2015. Inclusion criteria comprised studies related to high-altitude environments and HAPE, PE, COPD, CPHD, asthma, HAPH, PF, OSAS, and lung cancer. Exclusion criteria included irrelevant studies, unpublished works, inaccessible full texts, and retracted articles.

1. High-Altitude Environment and Acute Lung Diseases

1.1 High-Altitude Pulmonary Edema (HAPE)

HAPE is a non-cardiogenic pulmonary edema caused by acute hypoxia, primarily resulting from pulmonary vasoconstriction and elevated pulmonary artery pressure (PAP), which leads to fluid extravasation into the interstitium and alveoli. The disease has an acute onset and rapid progression, with a recurrence rate of up to 60% in susceptible individuals upon re-exposure to high altitudes [4]. Early symptoms include dry cough and shortness of breath, while later stages may present with pink frothy sputum, fever, headache, cyanosis, and in severe cases, loss of consciousness [5]. Diagnosis typically relies on chest X-ray and CT scans showing cotton-wool opacities, while electrocardiography reveals sinus tachycardia and increased right ventricular load [6]. The incidence increases with altitude: 0.01%–0.1% at 2,500 m, 2%–6% at 4,000 m, and 2%–15% at 5,500 m. Men have a higher incidence than women, children recover more quickly, while adults may require several days for recovery. Timely treatment can prevent life-threatening complications and sequelae [7,8].

The pathogenesis of HAPE is closely related to vascular remodeling, lymphatic vessel contraction, and mitochondrial dysfunction. Within 5–10 minutes of hypoxia, small arteries and veins constrict, reducing ventilation-perfusion and increasing pulmonary vascular resistance, followed by elevated PAP within 2–8 hours. Persistent hypoxia leads to vascular hypertrophy and thickening, ultimately causing vascular remodeling. In the lymphatic system, lymphatic ves-

sels do not initially show dilation or fluid leakage. However, when microvascular fluid extravasation exceeds lymphatic clearance capacity, fluid accumulates in the interstitial space. Under various influencing factors, this leads to lymphatic vessel contraction, persistently elevated interstitial pressure, compromised extracellular matrix integrity, and fluid entry into alveoli, resulting in hypoxemia and dyspnea. Plasma and red blood cell leakage damages the alveolar-capillary barrier, potentially leading to pulmonary hypertension (PH) [9]. Hypoxia induces mitochondrial dysfunction through the hypoxia-inducible factor-1α (HIF-1α) pathway, causing electron transport chain imbalance, mitochondrial damage, reactive oxygen species (ROS) production, and inflammatory responses, ultimately resulting in cellular injury [10]. Mitochondrial DNA mutations can adapt to hypoxia, and OXPHOS gene mutations are associated with HAPE susceptibility, affecting protein subunit stability and leading to mitochondrial dysfunction with altered HIF signaling and metabolic pathways under hypobaric hypoxia [11]. Additionally, studies show that hypoxia increases intracellular calcium concentration, activates pro-apoptotic proteins, enhances P53 stability, and translocates it to mitochondria, further exacerbating apoptosis and mitochondrial dysfunction [12]. Throughout this process, HIF plays a crucial role, being highly expressed in pulmonary artery smooth muscle cells and endothelial cells [13]. HIF-1α participates in both oxygen-dependent regulation and interacts with multiple non-oxygen-dependent pathways, affecting HIF-1α stability and activity and regulating gene transcription and cellular function [14]. The interaction mechanisms of various HIF regulatory pathways are illustrated in Figure 1 [Figure 1: see original paper].

Furthermore, genetic inheritance plays an important role in HAPE susceptibility [15]. In-depth investigation of HAPE pathogenesis and related signaling pathways will facilitate the development of novel prevention and treatment strategies, providing more effective clinical interventions for patients in high-altitude areas.

1.2 High-Altitude Pulmonary Embolism (PE)

PE is characterized by circulatory and respiratory dysfunction caused by thrombi from the venous system or right heart obstructing pulmonary arteries or their branches, with main symptoms including progressive dyspnea, tachycardia, chest pain, and hemoptysis [16]. The incidence of PE in COPD patients in high-altitude areas is 29.6%, compared to 16.8% in low-altitude areas [17]. PE occurrence is related to Virchow' s triad: hypoxia and low temperature can cause venous stasis, endothelial injury, and hypercoagulable states, leading to vascular endothelial dysfunction and imbalance of coagulation and fibrinolysis systems [18]. High-altitude environments stimulate increased HIF-1 expression, promoting erythropoietin (EPO) synthesis, which enhances platelet aggregation and adhesion, reduces plasma volume, causes venous stasis, and increases PE risk. Additionally, hypoxia, dehydration, low temperature, and venous stasis at high altitudes induce hypercoagulable states, further elevating PE incidence [17]. The main clinical manifestations of PE in high-altitude areas are chest

pain and dyspnea, with syncope as the first symptom in some patients and hemoptysis being rare [18]. Moreover, COPD is an important risk factor for PE, with autopsy studies showing a PE incidence of 28%–51% [19]. In laboratory tests, heart rate variability is significantly reduced in chronic HAPH patients, showing a significant negative correlation with disease severity [20], with poor prognoses including right ventricular hypertrophy, severe right heart failure, and left ventricular outflow tract obstruction [21–23]. Research on PE in high-altitude areas still has many unexplored domains, and future studies should focus on long-term follow-up and specific populations to provide more comprehensive understanding and effective clinical management strategies.

2. High-Altitude Environment and Chronic Lung Diseases

2.1 Chronic Obstructive Pulmonary Disease (COPD)

COPD is characterized by persistent, progressive, and irreversible airflow limitation, typically caused by chronic inflammation of airways and lung tissues in response to harmful particles. High-altitude environments cause oxidative stress and tissue damage, leading to decreased lung elasticity, alveolar enlargement, increased residual volume, and ventilation-perfusion mismatch, resulting in impaired gas exchange. The main clinical symptoms include chronic cough, sputum production, shortness of breath, wheezing, and chest tightness. Global COPD prevalence is rising annually, with a prevalence of 13.7% among Chinese individuals over 40 years old, higher than the global average of 12.38%, and significantly higher in men than women, closely related to differences in smoking rates [24]. The impact of altitude on COPD incidence remains controversial. The prevalence among patients $ $40 years in high-altitude areas is 9.0%, relatively low [25]. In Xinjiang and Tibet, COPD incidence in high-altitude areas is 8.2% (9.3% in men, lower than 11.9% in low-altitude men; 7.1% in women, higher than 5.4% in low-altitude women) [26]. This lower incidence may be related to physiological adaptation of lung function, lower smoking rates, and less household air pollution and tuberculosis detection, with 67.8% of subjects exposed to indoor air pollution, affecting women more severely [26]. However, a meta-analysis indicated that COPD prevalence in high-altitude areas is higher than the global average, though altitude is not an independent risk factor [27]. In Gansu, the overall prevalence is 19.7%, higher than low-altitude areas, associated with frequent use of unclean fuels [28]. COPD mortality increases with acute exacerbation frequency and altitude, rising by 1/10 for every 95 m increase in altitude, with severe patients having a 50% mortality rate within 3.6 years and 75% within 7.7 years [29,30].

COPD patients on the Tibetan Plateau face severe respiratory symptom burden and limited medical accessibility, with few patients understanding their condition and receiving regular treatment. Previous tuberculosis and indoor air pollution from biomass fuels are important risk factors. Approximately 90% of COPD patients in high-altitude areas experience significant dyspnea, especially in extremely high-altitude regions of Tibet ($ $3,000 m), where symptom

burden is heavy: 87.2% of patients have COPD Assessment Test (CAT) scores $ $10, with severe disease progression and increased hospitalization rates. In contrast, only 39.8% of low-altitude patients have typical symptoms, suggesting altitude-induced hypoxemia causes this difference. Radiologically, despite severe symptoms, CT shows mild to moderate emphysema, likely because inhaled biomass particles deposit less in alveolar regions compared to cigarette smoke [31]. High-altitude COPD patients are more likely to have comorbidities such as PH and erythrocytosis than low-altitude patients, with poorer overall health status that can be life-threatening [17]. In summary, differences in COPD incidence, symptoms, and complication severity between high and low altitudes are mainly related to indoor air pollution from unclean fuels, previous tuberculosis history, and inadequate medical awareness.

2.2 High-Altitude Pulmonary Hypertension (HAPH)

PH is a progressive disease that can lead to premature death. Diagnostic criteria include mean pulmonary artery pressure (mPAP) >20 mmHg, pulmonary artery wedge pressure (PAWP) $ $15 mmHg, and pulmonary vascular resistance (PVR) >2 WU. PH is classified into five groups, including arterial PH, left heart disease, chronic lung disease and/or hypoxia, chronic thromboembolism, and PH with unknown etiology, with HAPH belonging to group 3 [32]. HAPH prevalence varies significantly by diagnostic criteria: 6%–12% using high-altitude standards versus 35% using low-altitude standards [33]. Among Tibetan populations in Sichuan Province, China, HAPH prevalence is 6.2%, with age increase, metabolic syndrome, and decreased percutaneous arterial oxygen saturation (SpO2) being independent susceptibility factors [34]. Long-term residence at high altitude causes chronic and intermittent hypoxia, triggering hypoxic pulmonary vasoconstriction (HPV) and leading to HAPH. This process involves multiple biological mechanisms, including Rho-associated protein kinases (ROCKs), calcium release from actin, uncoupling of endothelial nitric oxide synthase, release of pro-inflammatory cytokines such as interleukin-1 (IL-1) and interleukin-6 (IL-6), and increased oxidative stress, ultimately causing pulmonary artery remodeling [3,35]. Studies show that PH increases during exercise or hypoxia in both HAPE-susceptible patients and healthy BMPR2 mutation carriers [36]. HAPH symptoms include exertional dyspnea, cough, and fatigue, with disease progression potentially causing right ventricular hypertrophy and other complications. Severe cases require heart-lung transplantation, though the median survival of combined heart-lung transplantation is 3.4 years, lower than isolated heart (10.7 years) or lung (6.2 years) transplantation. Therefore, lung transplantation should be considered early in the disease course to avoid progression to right heart failure [37]. PAP normalizes within 2 years at low altitude but increases again upon re-exposure to high altitude [38].

Clinical assessment of PH can be performed through echocardiography, right heart catheterization, and comprehensive evaluation of patient history and high-altitude exposure. In individuals without COPD or chronic heart disease, a his-

tory of high-altitude exposure with PAP >30 mmHg and/or systolic pulmonary artery pressure >50 mmHg establishes a HAPH diagnosis [39]. Additionally, ventilation/perfusion (V/Q) scanning is needed to exclude chronic thromboembolic PH by identifying mismatched perfusion defects [40]. HAPH is primarily triggered by the high-altitude environment through interactions of multiple biological mechanisms with high prevalence, requiring exclusion of other causes of PH for diagnosis to enable early treatment.

2.3 Chronic Pulmonary Heart Disease (CPHD)

CPHD results from various lung diseases causing reduction of the pulmonary vascular bed, pulmonary artery constriction, and vascular remodeling, leading to right ventricular hypertrophy and enlargement, and eventually right heart dysfunction. Main symptoms include cough, sputum production, fatigue, palpitations, and gastrointestinal symptoms. The incidence of CPHD in high-altitude COPD patients is 29.13%, with higher prevalence in men than women [41]. Studies show that high-altitude environments cause decreased body weight, whole heart mass, and right ventricular mass in rats, while increasing the proportion of right heart mass relative to body weight and whole heart mass [42]. Research indicates that below 2,500 m, myocardial injury is a mortality risk factor, while at or above 2,500 m, D-dimer is a mortality risk factor [43]. Abnormally high expression of serum hypersensitive C-reactive protein (hs-CRP), N-terminal pro-brain natriuretic peptide (NT-proBNP), and tumor necrosis factor-alpha (TNF-α) are important influencing factors for CPHD [41]. Studies show that brain natriuretic peptide (BNP) is elevated in CPHD regardless of heart failure status (mean 975 pg/mL), with a suggested cutoff point of $ $130 pg/mL [44]. High-altitude areas also show significant positive correlation with left ventricular diastolic dysfunction (LVDD), which may be related to unhealthy diet, smoking, and alcohol consumption [45]. Electrocardiography shows increased right ventricular load, and CT scans demonstrate right ventricular dilation. To adapt to high-altitude hypoxia, blood circulation may shunt from poorly oxygenated lung regions to healthy alveoli to reduce ventilation-perfusion mismatch [6]. Patients with hypercapnia and respiratory acidosis have higher intubation and mortality rates, and may develop life-threatening complications such as PE [43]. CPHD represents a continuation of COPD, with similar clinical manifestations between high and low altitudes, including right heart dysfunction symptoms, but with more sensitive indicator changes at high altitude.

2.4 Asthma

Asthma is a heterogeneous disease characterized by wheezing, chest tightness, cough, and dyspnea, affecting approximately 300 million people globally, with about 461,000 asthma-related deaths in 2019 [46]. The prevalence of asthma among Chinese individuals $ $20 years old is 4.2% and rising annually [47]. The incidence of asthma in preschool children in high-altitude areas is 17.8%, with overall prevalence of 3.7% and higher rates in women than men [48]. Increased

ambient particulate matter concentration positively correlates with asthma incidence. With PM2.5 exposure at $ 35$\mu g/m^{\{3\},26–34\mu g/m}\{3\}, and < 26\mu g/m\hat{}\{3\}$, asthma incidence rates are 7.5%, 3.7%, and 1.5%, respectively. With PM10 exposure at $ 91$\mu g/m^{\{3\},48–90\mu g/m}\{3\}, and < 48\mu g/m\hat{}\{3\}, asthmaprevalenceratesare7.1 $ levels causing lung injury, potentially involving the nuclear factor kappa-B (NF- B)/vascular permeability factor signaling pathway [52]. In most mild asthma patients, PAP increases with altitude and remains elevated for up to 3 weeks [53].

High-altitude climate therapy (AACT) for severe asthma reduces exacerbation frequency, improves lung function, decreases inflammation and circulating Th2 cell numbers, IgE levels, and reduces interferon-γ (IFN-γ) and IL-13 mRNA levels, significantly controlling asthma symptoms. However, these indicators rebound after repeated allergen exposure [5,54,55], and controlled conditions worsen upon return to low altitude [56]. AACT efficacy correlates with residence duration: short-term exposure increases bronchial hyperreactivity and spasm, while long-term residence is beneficial and reduces airway reactivity [57]. High-altitude environments are generally beneficial for asthma patients, though sex differences and immune variations exist, requiring further long-term research to optimize treatment strategies.

2.5 Pulmonary Fibrosis (PF)

PF is a chronic, progressive, age-related interstitial lung disease (ILD) with high morbidity and mortality. Among COPD patients, PF incidence is significantly higher in high-altitude areas than low-altitude areas (37% vs. 19%) [58]. High-altitude PF is closely related to hypoxia and cold, with pathogenesis involving low-pressure hypoxia triggering "inflammatory storm" core promoter FIZZ1 overexpression in the lungs (alveolitis, parenchymal injury), leading to gradual extracellular matrix and collagen deposition, inducing migration and proliferation of pulmonary vascular smooth muscle cells and causing vascular remodeling, ultimately forming pulmonary fibrosis [59]. Additionally, high-altitude environments cause expression changes in hypoxia tolerance-related genes (such as ZFP36L1, FN1, and NEDD9), and with oxygen therapy, HIF-1α, EPO, and vascular endothelial growth factor (VEGF) levels increase [60]. Pathological features include excessive collagen deposition, enlarged alveolar interstitium, thickened alveolar walls, and inflammatory cell infiltration, eventually causing scarring and decreased lung compliance, potentially leading to respiratory failure. PF may be related to abnormal wound healing of alveolar epithelial cells after repeated injury [61]. Radiological manifestations correlate with disease progression: early stage shows small interstitial thickening and vascular coarsening, followed by bullae, honeycombing, and bronchiectasis, with advanced stages showing bullae and destruction of acinar architecture. The disease course exceeds 3 years in 48.8% of patients, with poor treatment response and prognosis [62]. Studies show that ILD patients have more severe hypoxemia than COPD patients at rest and during walking tests, with SpO2 decreasing from 87% at

low altitude to 79.5% at high altitude [57]. Future research should focus on improving early diagnosis and treatment strategies to enhance patient prognosis and quality of life.

2.6 Lung Cancer

Lung cancer is a common and fatal malignancy, with hypoxia considered an important factor in its progression and treatment resistance. As altitude increases, changes in inhaled particulate matter, sunlight exposure, and atmospheric pressure occur, with hypoxia significantly increasing cancer cell migration and invasion in vitro [63]. Hypoxia promotes tumor drug resistance, epithelial-mesenchymal transition, extracellular matrix remodeling, cancer stem cell support, and immune evasion. Studies show that m6A-modified mRNA binding protein YTHDF1 plays a key role in high-altitude adaptation, and its deficiency inhibits non-small cell lung cancer cell proliferation and tumor formation [64]. Global lung cancer incidence and mortality rates are 13.2% and 18.8%, respectively. In 2022, China had 1.06 million new lung cancer cases (42.8% of global cases) and 730,000 deaths (40.3% of global deaths), ranking second and third in incidence in Qinghai and Tibet, respectively, with smoking as the main risk factor [65]. In high-altitude areas, unclean fuel use is also an important risk factor for lung cancer. For example, Himalayan residents have higher lung cancer risk closely related to seasonal use of unclean fuels [66]. There is a strong negative correlation between altitude and lung cancer incidence, with each 1,000 m increase reducing incidence by 12.7% [67]. Studies show that 81.2% of high-altitude patients present at stage IIIB–IV, likely due to poor health awareness and lack of standardized screening [68]. Regarding treatment, nucleotide excision repair pathway variants XPD and XPF are associated with lung cancer risk, and XPF can modulate cisplatin chemotherapy toxicity in high-altitude Han Chinese populations [69]. Future research should refine studies on characteristics and epidemiological data of different lung cancer types in high-altitude areas to provide more precise diagnosis and treatment.

2.7 Obstructive Sleep Apnea Syndrome (OSAS)

OSAS is a common respiratory disorder caused by repeated upper airway obstruction at night, leading to chronic hypoxia. The prevalence of OSAS in China is 11%, with 4% in Southwest China and 16% in Northwest China [70]. In high-altitude hypoxic environments, OSAS promotes acute mountain sickness development and correlates with prognosis. High-altitude environmental effects on neurological function cause sleep structure changes, impaired analytical ability, and memory deficits [71]. Surveys show that 67.9% of military personnel stationed at high altitudes experience sleep disorders, primarily due to hypoxemia, manifesting as insomnia (52.53%), insufficient sleep syndrome (48.34%), and snoring (41.01%) [72]. High-altitude sleep disorders not only reduce arterial oxygen partial pressure and increase cerebral blood flow, causing cerebral vasodilation and brain cell edema that affects sleep center function, but

also cause deeper and faster breathing, leading to hypocapnia and respiratory alkalosis, triggering periodic central sleep apnea that worsens sleep disruption and brain hypoxia. Cold and dry high-altitude environments also reduce respiratory defense function, causing inflammatory responses and airway edema that further affect sleep quality [73].

When high-altitude populations move to low altitudes, although apnea-hypopnea index (AHI) decreases, the duration of obstructive apnea prolongs. The proportion of Tibetan highlanders with apnea duration $ $2 minutes reaches 25%, compared to 10% in Han highlanders, possibly because low-altitude oxygen is more abundant [74]. Conversely, when lowlanders move to high altitudes, unstable ventilatory control due to hypobaric hypoxia causes enhanced breathing that weakens high-altitude-related periodic breathing. As altitude increases, the proportion of periodic breathing increases and its cycle time shortens, correlating with high-altitude residence duration [75]. When moving from low to high altitude, sleep breathing events show sex differences, with greater increases in AHI and event types in men than women [76].

In high-altitude environments, increased PAP and right ventricular injury correlate with OSAS severity. OSAS also independently correlates with cardiovascular diseases such as atrial fibrillation, coronary artery disease, heart failure, and stroke. Studies show that OSAS patients living at moderate high altitude have higher systolic pulmonary pressure and more pronounced right ventricular remodeling than healthy high-altitude residents [77]. The incidence of sleep apnea syndrome in high-altitude populations reaches 30%, with more obvious intermittent hypoxemia than in low-altitude areas [78]. In summary, high-altitude environments affect neurological and respiratory functions in OSAS patients, causing decreased sleep quality and increased cardiovascular disease risk. Future research should focus on management and treatment strategies for OSAS patients in high-altitude environments.

3. Summary

The high-altitude environment significantly impacts non-infectious lung diseases. This review detailed the incidence, risk factors, and pathogenesis of various non-infectious lung diseases, revealing that these conditions in high-altitude areas are primarily induced by hypoxia, low pressure, cold, and air pollution. Additionally, important factors affecting patient incidence and prognosis include poor high-altitude acclimatization, insufficient medical awareness, and inadequate health attention among high-altitude residents. Future research urgently requires more in-depth and detailed investigation of non-infectious lung diseases in high-altitude areas, with emphasis on early diagnosis, optimized treatment, and enhanced public education to improve health outcomes for high-altitude populations and provide scientific basis and guidance for diagnosis and treatment of lung diseases in these regions.

Author Contributions: ZHAO Xuedan was responsible for conceptualization,

literature collection, and manuscript writing; AI Yue participated in literature collection and data extraction; JING Guoen and JIA Guoqiang developed the research framework and revised the manuscript for quality control.

Conflict of Interest: The authors declare no conflict of interest.

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Received: 2024-10-10; Revised: 2025-01-15
Edited by: MAO Yamin