



Editorial on "Characteristics and risk profiles of patients with pulmonary arterial or chronic thromboembolic pulmonary hypertension living permanently at >2500 m of high altitude in Ecuador"

Pulmonary hypertension (PH) is a complex cardiovascular disorder characterized by elevated mean pulmonary artery pressure >20 mmHg at rest. PH is classified into five groups based on etiology, each with unique underlying causes and pathophysiological mechanisms: pulmonary arterial hypertension (PAH), PH due to left heart disease, PH due to lung disease or hypoxia, chronic thromboembolic pulmonary hypertension (CTEPH), and PH with unclear multifactorial mechanisms. The global prevalence of PH is estimated to be around 1%, with the majority of cases classified as PH associated with left heart or chronic lung disease while the prevalence of PAH and CTEPH is considerably lower, estimated at approximately 100 per million population.² While the prevalence of PH is estimated to be similar worldwide, there are limited data on the characteristics and outcomes of PH patients living at high altitudes. Hypobaric hypoxia at high-altitude imposes several genetic and physiological changes that help individuals living at various altitudes to maintain adequate oxygenation and function in the face of chronic hypoxia.³ However, the chronic hypoxic environment may exacerbate the occurrence and management of pulmonary vascular diseases (PVD).4

In this issue of Pulmonary Circulation, Hoyos et al. (2024) address this knowledge gap by performing a cross-sectional study investigating the characteristics and risk profiles of patients with PAH or CTEPH living at high altitudes (>2500 m) in Ecuador. The study is notable for its focus on a unique and understudied population, as most research on PH has been conducted in low-altitude populations, offering valuable insights into the impact of high altitude on PVD. The study's strengths lie in its detailed characterization of the patient cohort, including hemodynamic parameters, functional class, and exercise performance. The authors also provide an overview of the treatment strategies employed in this setting. The

study found that despite living at high altitudes, these patients exhibit arterial oxygen levels similar to healthy newcomers at comparable altitudes and to PVD patients living at low altitudes.⁵ This finding challenges the traditional understanding of the impact of high altitude on PVD, which is typically associated with worsened hypoxemia and increased pulmonary vascular resistance.⁶ Interestingly, the study reveals that these patients have relatively low and stable risk profiles, as assessed by functional class, 6-min walk distance, and NT-pro-brain natriuretic peptide levels, despite having severe hemodynamic compromise.⁵ This finding is consistent with previous research that has shown that individuals living at high altitudes can adapt to chronic hypoxia and maintain relatively normal exercise capacity.⁴

The findings of this study have possible implications for understanding the pathogenesis of PH in different populations and environments. The study suggests that current risk assessment models, which are primarily based on data from low-altitude populations, may not be entirely applicable to high-altitude dwellers.⁵ This highlights the need for further research to develop risk stratification tools and treatment strategies that are specifically tailored to high-altitude populations. However, the small sample size (36 patients) dominated by female patient group limits the generalizability of these findings.⁵ Additionally, the cross-sectional design precludes any conclusions about the long-term outcomes of these patients, and further research, particularly longitudinal studies, are needed to confirm these findings and to investigate the long-term effects of high altitude on PVD. Further, the authors acknowledge the potential for selection bias, as the study only included ambulatory patients who were able to visit the clinic. This may have excluded patients with more severe disease, potentially skewing the results. Despite these limitations, the study

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2024 The Author(s). Pulmonary Circulation published by Wiley Periodicals LLC on behalf of the Pulmonary Vascular Research Institute.

highlights the implications in the management of PVD in high-altitude populations. The findings suggest that favorable outcomes are achievable for these patients, even in settings with limited resources. This is encouraging for healthcare providers working in high-altitude regions, as it suggests that effective treatment strategies can be implemented even with limited resources and expensive combination therapies.

In conclusion, Hoyos et al. provide valuable insights into the characteristics and risk profiles of PVD patients living at high altitudes. This study underscores the importance of considering the unique physiological challenges faced by high-altitude populations in the management of PH. This could open new avenues for research into the protective effects of hypoxia-induced adaptations and their potential in therapeutic applications.

AUTHOR CONTRIBUTIONS

Samantha Sharma and Naresh Singh conceived and contributed to writing the manuscript. Samantha Sharma and Naresh Singh contributed equally to this article.

ACKNOWLEDGMENTS

The authors have no funding to report.

CONFLICT OF INTEREST STATEMENT

The author declares no conflict of interest.

FUNDING INFORMATION

None.

ETHICS STATEMENT

The authors have nothing to report.

Samantha Sharma^{1,2} D Naresh Singh^{1,2}

¹Indiana University Simon Comprehensive Cancer Center, Indiana University School of Medicine, Indianapolis, Indiana, USA

²Department of Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, Indiana, USA

Correspondence

Samantha Sharma, Department of Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, IN 46202, USA. Email: samshar@iu.edu

ORCID

REFERENCES

- 1. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, Carlsen J, Coats AJS, Escribano-Subias P, Ferrari P, Ferreira DS, Ghofrani HA, Giannakoulas G, Kiely DG, Mayer E, Meszaros G, Nagavci B, Olsson KM, Pepke-Zaba J, Quint JK, Rådegran G, Simonneau G, Sitbon O, Tonia T, Toshner M, Vachiery JL, Vonk Noordegraaf A, Delcroix M, Rosenkranz S, Schwerzmann M, Dinh-Xuan AT, Bush A, Abdelhamid M, Aboyans V, Arbustini E, Asteggiano R, Barberà JA, Beghetti M, Čelutkienė J, Cikes M, Condliffe R, de Man F, Falk V, Fauchier L, Gaine S, Galié N, Gin-Sing W, Granton J, Grünig E, Hassoun PM, Hellemons M, Jaarsma T, Kjellström B, Klok FA, Konradi A, Koskinas KC, Kotecha D, Lang I, Lewis BS, Linhart A, Lip GYH, Løchen ML, Mathioudakis AG, Mindham R, Moledina S, Naeije R, Nielsen JC, Olschewski H, Opitz I, Petersen SE, Prescott E, Rakisheva A, Reis A, Ristić AD, Roche N, Rodrigues R, Selton-Suty C, Souza R, Swift AJ, Touyz RM, Ulrich S, Wilkins MR, Wort SJ. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Heart J. 2022;43: 3618-731. https://doi.org/10.1093/eurheartj/ehac237
- Hoeper MM, Humbert M, Souza R, Idrees M, Kawut SM, Sliwa-Hahnle K, Jing ZC, Gibbs JSR. A global view of pulmonary hypertension. Lancet Respir Med. 2016;4:306–22. 20160312. https://doi.org/10.1016/S2213-2600(15)00543-3
- Sharma S, Koshy R, Kumar R, Mohammad G, Thinlas T, Graham BB, Pasha Q. Hypobaric hypoxia drives selection of altitude-associated adaptative alleles in the himalayan population. Sci Total Environ. 2024;913:169605. https://doi.org/10. 1016/j.scitotenv.2023.169605
- Soria R, Egger M, Scherrer U, Bender N, Rimoldi SF. Pulmonary artery pressure and arterial oxygen saturation in people living at high or low altitude: systematic review and meta-analysis. J Appl Physiol. 2016;121:1151–9. https://doi.org/10.1152/japplphysiol.00394.2016
- Hoyos R, Lichtblau M, Cajamarca E, Mayer L, Schwarz EI, Ulrich S. Characteristics and risk profiles of patients with pulmonary arterial or chronic thromboembolic pulmonary hypertension living permanently at >2500 m of high altitude in Ecuador. Pulm Circ. 2024;14:e12404. https://doi.org/10. 1002/pul2.12404
- León-Velarde F, Maggiorini M, Reeves JT, Aldashev A, Asmus I, Bernardi L, Ge RL, Hackett P, Kobayashi T, Moore LG, Penaloza D, Richalet JP, Roach R, Wu T, Vargas E, Zubieta-Castillo G, Zubieta-Calleja G. Consensus statement on chronic and subacute high altitude diseases. High Alt Med Biol. 2005;6:147–57. https://doi.org/10.1089/ham.2005.6.147