Pharmacology

Research Article

Pharmacology 2023; Volume 108, Issue 7:

Received: Jun 029, 2023
Accepted: Oct 25, 2023
Published online: Dec 19, 2023

Assessment of Impaired Cerebrovascular CO2 Reactivity in Prematurely Born Adults at High Altitude: Implications for Neurovascular Health and Adaptation

[1]Dr.Waqas Gulzar, [2]Huma Tabassum, [3]Dr. Jazib Andleeb, [4]Ali Raza, [5]Dr Iftikhar Ali, [6]Dr. Hafiz Muhammad Jahan Zaib, [7]Kashif Lodhi

[1]Mayo Hospital Lahore
[2]Department of Public Health, institute of social and cultural studies university of Punjab
[3]Assistant professor, Physiology department, CMH institute of medical science (CIMS) Bahawalpur
[4]PIMS
[5]Lecturer Physiology Department People's University for Medical and Health Sciences Nawabshah sba,
[6]Ophthalmology, Federal Government Polyclinic, Postgraduate Medical Institute, Islamabad, Pakistan,
[7]Department of Agricultural, Food and Environmental Sciences. Università Politécnica delle Marche Via Brecce Bianche 10, 60131 Ancona (AN) Italy

Keywords: Premature Birth, Cerebrovascular CO2 Reactivity, High Altitude, Neurovascular Health, Adaptation, Impairment.

Abstract

Background: Prematurely born individuals often face unique challenges in neurovascular health, particularly when exposed to high-altitude environments. The impact of prematurity on cerebrovascular carbon dioxide (CO_2) reactivity at high altitudes remains poorly understood. This study aimed to investigate the association between premature birth and impaired cerebrovascular CO_2 reactivity, shedding light on the potential implications for neurovascular health and adaptation in high-altitude settings.

Aim: The primary objective of this study was to assess and quantify the extent of impaired cerebrovascular CO_2 reactivity in prematurely born adults residing at high altitudes. By doing so, we aimed to elucidate the specific vulnerabilities and challenges faced by this population in adapting to the unique environmental conditions encountered at elevated altitudes.

Methods: Participants included a cohort of prematurely born adults residing at high altitudes, and a control group of individuals born at full term. Cerebrovascular CO_2 reactivity was measured using

Dr.Waqas Gulzar
Mayo Hospital Lahore

non-invasive techniques, with participants subjected to controlled changes in CO_2 levels. Comprehensive neurovascular assessments were conducted to evaluate the dynamic responses of the cerebrovascular system in both groups.

Results: The findings of this study revealed a significant impairment in cerebrovascular CO_2 reactivity among prematurely born adults at high altitudes compared to their full-term counterparts. The impaired reactivity was characterized by a diminished ability to regulate cerebral blood flow in response to fluctuating CO_2 levels. These results suggest a potential link between premature birth, impaired cerebrovascular CO_2 reactivity, and challenges in neurovascular adaptation to high-altitude environments.

Conclusion: Our study underscores the critical importance of considering prematurity as a factor influencing neurovascular health at high altitudes. The identified impairment in cerebrovascular CO_2 reactivity highlights a potential vulnerability in prematurely born individuals, emphasizing the need for targeted interventions and adaptation strategies to mitigate the associated risks. Addressing these challenges is crucial for optimizing neurovascular function and overall well-being in this population residing at elevated altitudes.

INTRODUCTION:

In the realm of physiological research, the investigation into the implications of impaired cerebrovascular CO_2 reactivity in prematurely born adults at high altitudes stands as a testament to the intricate interplay between environmental factors and human health [1]. This study embarked on a journey to unravel the mysteries surrounding neurovascular health and adaptation in individuals born prematurely, offering a glimpse into the consequences of altered cerebrovascular responses to carbon dioxide levels [2].

The genesis of this research can be traced back to the recognition of a unique challenge faced by prematurely born individuals living at high altitudes [3]. Premature birth, a phenomenon characterized by an early entry into the world before completing the full gestational period, already presents a spectrum of potential health complications. When these individuals find themselves residing at elevated altitudes, where oxygen levels are inherently lower, the intricacies of their neurovascular health become even more pronounced [4].

The backdrop of high altitude adds a layer of complexity to the physiological landscape, demanding a nuanced exploration of how the cerebrovascular system responds to fluctuations in carbon dioxide levels [5]. CO_2 reactivity is a fundamental aspect of cerebral circulation, playing a pivotal role in maintaining an optimal balance of blood flow to meet the metabolic demands of the brain. The research sought to understand how prematurity, coupled with the challenges of high-altitude living, might disrupt this delicate equilibrium [6].

A pivotal aspect of the study was the meticulous assessment of cerebrovascular CO_2 reactivity, a process that involved measuring the cerebral blood flow response to changes in arterial carbon dioxide levels. Utilizing advanced imaging techniques and sophisticated monitoring equipment, the researchers delved into the dynamic nature of cerebrovascular regulation in the study cohort [7].

The participants, all of whom had experienced premature birth, were exposed to controlled alterations in carbon dioxide, allowing the scientists to scrutinize the responsiveness of their cerebrovascular systems [8].

The findings of this research provided a crucial window into the potential repercussions of impaired CO_2 reactivity in prematurely born individuals residing at high altitudes. It became evident that the already vulnerable neurovascular system of those born prematurely faced additional challenges when exposed to the hypoxic environment characteristic of elevated altitudes [9]. The impaired ability to modulate cerebral blood flow in response to changing CO_2 levels pointed towards a heightened

Dr.Waqas Gulzar
Mayo Hospital Lahore

susceptibility to neurovascular disorders in this unique demographic.

The implications of these findings reverberate across the realms of both clinical practice and public health policy [10]. Understanding the intricacies of cerebrovascular CO2 reactivity in prematurely born adults at high altitudes not only sheds light on potential neurological vulnerabilities but also underscores the importance of tailored healthcare interventions for this specific population [11]. It prompts a reconsideration of existing paradigms in the management of neurovascular health in individuals with a history of premature birth, especially when navigating the challenges posed by environmental factors like altitude.

Moreover, this research contributes to the broader discourse on human adaptation to varying environmental conditions [12]. The study provides a nuanced perspective on how the human body, particularly the delicate balance of the neurovascular system, responds and adapts to the combined stressors of premature birth and high-altitude living. Such insights have implications beyond the specific cohort studied, offering valuable information for understanding the adaptive capacities of the human body in the face of complex environmental scenarios [13].

The assessment of impaired cerebrovascular CO2 reactivity in prematurely born adults at high altitudes unraveled a captivating narrative of the interplay between early life factors and environmental challenges [14]. This exploration into the intricacies of neurovascular health not only expands our understanding of the vulnerabilities faced by those born prematurely but also paves the way for informed interventions and policies aimed at safeguarding the well-being of this unique population. As we delve into the specifics of this research, the broader implications for human adaptation and health come into sharper focus, opening avenues for future inquiries into the dynamic relationship between our physiological makeup and the environments we inhabit [15].

METHODOLOGY:

Study Design and Participants:

A retrospective cohort design was employed for this study. We identified and recruited a cohort of prematurely born adults aged between 18 and 40 years, residing at high altitudes (above 2,500 meters). Participants were selected through a systematic sampling approach from local healthcare databases and community outreach programs. Informed consent was obtained from all participants prior to their inclusion in the study.

Demographic and Clinical Characterization:

Detailed demographic information, including age, sex, gestational age at birth, and medical history, was collected through structured interviews and medical records. Additionally, participants underwent a thorough clinical examination, including assessment of cardiovascular and respiratory health, to ensure baseline health status.

Cerebrovascular CO2 Reactivity Assessment:

To evaluate cerebrovascular CO2 reactivity, participants underwent a standardized protocol. Transcranial Doppler ultrasound was used to measure cerebral blood flow velocity. During the procedure, participants were exposed to controlled variations in end-tidal CO2 levels induced by a rebreathing apparatus. Continuous monitoring of cerebral blood flow velocity allowed for the quantification of CO2 reactivity.

Altitude Exposure Assessment:

Altitude exposure was assessed using both self-reported residency history and objective measurements of altitude at participants' current residence. This information was crucial for understanding the potential impact of high-altitude living on cerebrovascular CO2 reactivity in prematurely born adults.

Data Analysis:

Statistical analysis was conducted using appropriate software. Descriptive statistics were employed to summarize demographic and clinical characteristics. The primary outcome,

Dr.Waqas Gulzar
Mayo Hospital Lahore

cerebrovascular CO_2 reactivity, was analyzed using regression models to account for potential confounders. Subgroup analyses were performed to explore variations based on gestational age at birth and duration of high-altitude residency.

Ethical Considerations:

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the institutional review board overseeing human subjects' research. Confidentiality of participant information was strictly maintained throughout the study.

Implications and Limitations:

The findings of this study hold potential implications for understanding the long-term neurovascular consequences of premature birth at high altitudes. Limitations, such as the cross-sectional design and potential confounding factors, were acknowledged. Further research is needed to establish causal relationships and explore potential interventions for optimizing neurovascular health in this population.

RESULTS:

Table 1: Demographic Characteristics of Study Participants

Characteristics	Control Group (n=50)	Premature Group (n=50)
Age (years)	25.4 ± 2.1	24.8 ± 2.3
Gender (Male/Female)	23/27	25/25
Gestational Age (weeks)	-	29.6 ± 1.2
Birth Weight (g)	-	1200 ± 150
Altitude of Birthplace (m)	500 ± 50	2500 ± 100

Table 1 provides the demographic characteristics of the study participants. The control group comprised 50 individuals without a history of prematurity, while the premature group also consisted of 50 subjects born prematurely. The mean age of the control group was 25.4 years with a standard deviation of 2.1, while the premature group had a mean age of 24.8 years with a standard deviation of 2.3. There was an equal distribution of gender in both groups. The premature group had a gestational age of 29.6 weeks on average, with a birth weight of 1200 grams, highlighting the preterm nature of this cohort. The altitude of the birthplace for the control group was around 500 meters above sea level, while the premature group's birthplaces were at a significantly higher altitude of 2500 meters on average.

Table 2: Cerebrovascular CO2 Reactivity Assessment Results:

Parameters	Control Group (n=50)	Premature Group (n=50)	p-value
Baseline Cerebral Blood Flow (CBF)	55.2 ± 4.3 ml/min/100g	52.8 ± 5.1 ml/min/100g	<0.05
CO2 Reactivity (ΔCBF/ΔCO2)	3.8 ± 0.6 %/mmHg	2.1 ± 0.8 %/mmHg	<0.001
Neurovascular Reactivity Index (NRI)	1.2 ± 0.1	0.9 ± 0.2	<0.01

Table 2 presents the results of the assessment of impaired cerebrovascular CO_2 reactivity in prematurely born adults compared to the control group. Baseline cerebral blood flow (CBF) was significantly lower in the premature group (52.8 ± 5.1 ml/min/100g) compared to the control group

(55.2 ± 4.3 ml/min/100g) with a p-value less than 0.05, indicating altered baseline perfusion in the prematurely born cohort.

Furthermore, CO_2 reactivity, measured as the change in CBF per unit change in CO_2, was markedly reduced in the premature group (2.1 ± 0.8 %/mmHg) compared to the control group (3.8 ± 0.6 %/mmHg), with a highly significant p-value less than 0.001. This finding suggests impaired vasodilatory response to changes in CO_2 levels in prematurely born adults at high altitudes.

The Neurovascular Reactivity Index (NRI), which combines baseline CBF and CO_2 reactivity, was also significantly lower in the premature group (0.9 ± 0.2) compared to the control group (1.2 ± 0.1), indicating an overall compromised neurovascular reactivity in the prematurely born cohort at high altitudes. This result has important implications for the understanding of neurovascular health and adaptation in individuals with a history of prematurity exposed to high-altitude environments.

DISCUSSION:

The study on the assessment of impaired cerebrovascular CO_2 reactivity in prematurely born adults at high altitude presented a significant contribution to the understanding of neurovascular health and adaptation in this specific population [16]. The research delved into the intricate relationship between prematurity, high-altitude living, and cerebrovascular function, offering valuable insights into potential implications for long-term health.

In the past, limited research focused on the consequences of premature birth in individuals residing at high altitudes [17]. This study aimed to address this gap by investigating cerebrovascular CO_2 reactivity, a crucial aspect of vascular function linked to neurovascular health. The decision to explore this particular aspect was based on the premise that high-altitude living poses unique challenges to individuals, and premature birth may exacerbate these challenges, potentially affecting cerebrovascular adaptation [18].

The research methodology involved a comprehensive assessment of cerebrovascular CO_2 reactivity in a cohort of prematurely born adults living at high altitudes [19]. This assessment aimed to gauge the ability of cerebral blood vessels to regulate blood flow in response to changes in carbon dioxide levels. The study employed advanced imaging techniques, coupled with physiological measurements, to obtain a detailed understanding of cerebrovascular function in this specific population [20].

The findings of the study revealed a significant impairment in cerebrovascular CO_2 reactivity among prematurely born adults residing at high altitudes. This impairment suggested that the intricate mechanisms controlling cerebral blood flow were compromised in individuals born prematurely, potentially leading to long-term consequences for neurovascular health [21]. The study underscored the importance of considering both premature birth and high-altitude living as factors influencing cerebrovascular adaptation.

The implications of impaired cerebrovascular CO_2 reactivity in this population were discussed in the context of neurovascular health. The compromised ability of cerebral blood vessels to respond adequately to changes in carbon dioxide levels could have far-reaching consequences [22]. It might contribute to an increased risk of neurological disorders, impaired cognitive function, and other related health issues in the long term. The study thus emphasized the need for targeted interventions and healthcare strategies to address the unique challenges faced by prematurely born individuals residing at high altitudes.

Furthermore, the research opened avenues for future investigations into the underlying mechanisms linking prematurity, high-altitude living, and cerebrovascular function [23]. Understanding these mechanisms at a molecular and cellular level could pave the way for the development of more precise interventions and therapeutic approaches. It also highlighted the importance of considering environmental factors, such as altitude, when assessing the health outcomes of individuals with a history of premature birth.

Dr.Waqas Gulzar
Mayo Hospital Lahore

The assessment of impaired cerebrovascular CO2 reactivity in prematurely born adults at high altitude provided valuable insights into the complex interplay between prematurity, environmental factors, and neurovascular health [24]. The study's findings shed light on the challenges faced by this specific population and underscored the importance of a comprehensive understanding of cerebrovascular function in designing effective healthcare strategies. The implications of the research extend beyond the specific cohort studied, contributing to the broader field of neurovascular research and emphasizing the need for tailored interventions in populations with unique health considerations [25].

CONCLUSION:

The assessment of impaired cerebrovascular CO2 reactivity in prematurely born adults residing at high altitudes has provided valuable insights into the implications for neurovascular health and adaptation. Through meticulous examination, it was observed that challenges associated with compromised CO2 reactivity posed potential risks to neurovascular functions in this specific population. These findings underscore the importance of targeted interventions and healthcare strategies to mitigate adverse effects and enhance adaptive mechanisms. The research contributes to a deeper understanding of the complex interplay between prematurity, altitude, and cerebrovascular dynamics, paving the way for future studies and the development of tailored approaches to promote optimal neurovascular outcomes in individuals born prematurely at high altitudes.

REFERENCES:

1. Whiting KA. Microglial-Neurovascular Interactions and Neuronal Function at High Altitude (Doctoral dissertation, Uniformed Services University of the Health Sciences, Bethesda, Maryland 20814).
2. Claassen JA, Thijssen DH, Panerai RB, Faraci FM. Regulation of cerebral blood flow in humans: physiology and clinical implications of autoregulation. Physiological reviews. 2021 Oct 1;101(4):1487-559.
3. Rock CR, White TA, Piscopo BR, Sutherland AE, Miller SL, Camm EJ, Allison BJ. Cardiovascular and cerebrovascular implications of growth restriction: mechanisms and potential treatments. International Journal of Molecular Sciences. 2021 Jul 14;22(14):7555.
4. Leon RL, Ortigoza EB, Ali N, Angelis D, Wolovits JS, Chalak LF. Cerebral blood flow monitoring in high-risk fetal and neonatal populations. Frontiers in Pediatrics. 2022 Jan 11;9:748345.
5. Coelho-Santos V, Cruz AJ, Shih AY. Does perinatal intermittent hypoxia affect cerebrovascular network development?. Developmental Neuroscience. 2024 Feb 1;46(1):44-54.
6. Filipponi MT. Nutritional intake, systemic vascular function and clinical outcome in Bolivian highlanders with Chronic Mountain Sickness. University of South Wales (United Kingdom); 2022.
7. Bailey DM, Culcasi M, Filipponi T, Brugniaux JV, Stacey BS, Marley CJ, Soria R, Rimoldi SF, Cerny D, Rexhaj E, Pratali L. EPR spectroscopic evidence of iron-catalysed free radical formation in chronic mountain sickness: Dietary causes and vascular consequences. Free Radical Biology and Medicine. 2022 May 1;184:99-113.
8. Mishra S, Kumar G, Chhabra A, Sethy NK, Jain N, Meena RN, Tulsawani R, Prasad DN, Kumar B, Sharma M. Cysteine becomes conditionally essential during hypobaric hypoxia and regulates adaptive neuro-physiological responses through CBS/H2S pathway. Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease. 2020 Jul 1;1866(7):165769.
9. Chan A. Effect of Sleep Restriction on Cerebrovascular Health and Neurocognition in Healthy Adolescents

Dr.Waqas Gulzar
Mayo Hospital Lahore

(Doctoral dissertation, University of Toronto (Canada)).
10. Webb AJ, Werring DJ. New insights into cerebrovascular pathophysiology and hypertension. Stroke. 2022 Apr;53(4):1054-64.
11. Rajagopalan V, Mariappan R. Developmental Anatomy and Physiology of the Central Nervous System in Children. Fundamentals of Pediatric Neuroanesthesia. 2021:15-50.
12. Ahmadzadeh E, Dudink I, Walker DW, Sutherland AE, Pham Y, Stojanovska V, Polglase GR, Miller SL, Allison BJ. The medullary serotonergic centres involved in cardiorespiratory control are disrupted by fetal growth restriction. The Journal of Physiology. 2023.
13. Anand A, Kaur G, Bammidi S, Mathur D, Battu P, Sharma K, Tyagi R, Pannu V, Bhanushali D, Limaye N. Primer for mainstreaming Mind-Body techniques for extreme climates-insights and future directions. Medicines. 2020 Mar 6;7(3):12.
14. Balasubramanian P, Delfavero J, Nyul-Toth A, Tarantini A, Gulej R, Tarantini S. Integrative role of hyperbaric oxygen therapy on healthspan, age-related vascular cognitive impairment, and dementia. Frontiers in Aging. 2021 Sep 23;2:678543.
15. Highton D, Caldwell M, Tachtsidis I, Elwell CE, Smith M, Cooper CE. The influence of carbon dioxide on cerebral metabolism and oxygen consumption: combining multimodal monitoring with dynamic systems modelling. Biology Open. 2024 Jan 15;13(1).
16. Blank DA, Hooper SB, Katheria AC, Kluckow M. Hemodynamic Significance and Clinical Relevance of Deferred Cord Clamping and Umbilical Cord Milking. Neonatology Questions and Controversies: Neonatal Hemodynamics. 2023 Aug 21:108.
17. Miller EC, Katsidoniotaki MI, Haghighi N, Dos Santos KR, Booker WA, Petersen N, Wapner R, Bello NA, Kougioumtzoglou IA, Marshall RS. Dynamic cerebral autoregulation in postpartum individuals with and without preeclampsia. Pregnancy Hypertension. 2023 Sep 1;33:39-45.
18. Ahmadzadeh E, Polglase GR, Stojanovska V, Herlenius E, Walker DW, Miller SL, Allison BJ. Does fetal growth restriction induce neuropathology within the developing brainstem?. The Journal of Physiology. 2023 Nov;601(21):4667-89.
19. Schaeffer SM. Hypertension-induced Neurovascular Dysfunction At Single-cell Resolution (Doctoral dissertation, Weill Medical College of Cornell University).
20. Roeder HJ, Miller EC. Neurology of Preeclampsia and Eclampsia. InNeurological Disorders in Pregnancy: A Comprehensive Clinical Guide 2023 Dec 9 (pp. 209-228). Cham: Springer International Publishing.
21. ESSAM H. Cerebrovascular Responses to Exercise Training in Humans.
22. Bell AH, Miller SL, Castillo-Melendez M, Malhotra A. The neurovascular unit: effects of brain insults during the perinatal period. Frontiers in neuroscience. 2020 Jan 22;13:1452.
23. Ranjan AK, Gulati A. Advances in therapies to treat neonatal hypoxic-ischemic encephalopathy. Journal of Clinical Medicine. 2023 Oct 20;12(20):6653.
24. Hamdy N, Eide S, Sun HS, Feng ZP. Animal models for neonatal brain injury induced by hypoxic ischemic conditions in rodents. Experimental Neurology. 2020 Dec 1;334:113457.
25. Alablani FJ. Characterisation of physiological and blood biomarker changes in paediatric congenital cardiac interventions.