Original Article

Assessment of altitude induced effects on serum liver function, renal function and lipid profile within the population of Gilgit Baltistan's District Gamba, reporting to Combined Military Hospital Skardu

Mustajab Alam[1], Hunain Habib[2], Naveed Asif[3], Bushra Anwar[2], Tahir Asad[1], Khizar Hameed[1]

[1]Armed Forces Institute of Pathology (National University of Medical Sciences) Rawalpindi Pakistan
[2]Fazaia Medical College, Islamabad Pakistan
[3]Watim Medical College, Islamabad Pakistan

ABSTRACT

Objective: The objective of this study was to evaluate impact of high altitude on various parameters of Liver Function Tests, Renal Function Tests, and Lipid profiles in local population reporting to CMH Skardu.

Material and Methods: This Cross-sectional observational study was conducted in the department of pathology of CMH Skardu from January 2023 to August 2023. Participants underwent a comprehensive medical examination. Serum samples were obtained for the assessment of Liver Function Tests (LFTs), Renal Function Tests (RFTs) and lipid profiles of patients in clot activator vaccutainers and analyzed on Selectra Pro XI by their respective spectrophotometric methods. One way ANOVA and Pearson correlation were used to statistical analysis between different groups according to altitude and p value <0.05 was considered significant.

Results: The study involved 150 participants, with ages ranging from 28 to 71 years with the mean age of 46.5 ±10.71 years. Altitude varied between 1700 and 2500 meters among participants with mean altitude of 2018.6±21.9 meters. A total of 105(70%) participants were male, and 45(30%) participants were female. Significant negative correlations were observed between altitude and ALT (-0.227, p = 0.005) and AST (-0.212, p = 0.009) For ALT, AST, ALP, BUN, TGs, HDL, and LDL, there are significant differences among groups (p-values < 0.05). For BIL and Creatinine, there are no significant differences among groups (p-values > 0.05)

Conclusion: This study underscores the multifaceted nature of altitude's impact on human physiology, highlighting the need for comprehensive research to optimize health and performance in high-altitude environments.

Keywords: Altitude, Gilgit, Liver Function Tests, Renal Function Tests, Lipid

This article can be cited as: Butt A, Raja K, Awan FJ, Khan WA, Zaid F, Hassan FU. Assessment of altitude induced effects on serum liver function, renal function and lipid profile within the population of Gilgit Baltistan's District Gamba, reporting to Combined Military Hospital Skardu. Pak J Pathol. 2024; 35(3): 124-129.

DOI: https://doi.org/10.55629/pakjpathol.v35i3.816

INTRODUCTION

High-altitude environment, characterized by reduced barometric pressure and lower oxygen level, have been a subject of considerable research interest, particularly regarding their impact on human physiology. Effects of high altitude on various physiological parameters, such as Liver Function Tests (LFTs), Renal Function Tests (RFTs), and Lipid profiles, collectively referred to as "LFTs-RFTs-Lipid profile," have been extensively investigated.

Liver, as a pivotal metabolic organ, is crucial for maintaining metabolic homeostasis. Studies by Lala *et al*. [1] and Cornelius *et al* [2] have explored liver function tests, including Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), revealing alterations in response to factors such as hypobaric hypoxia and hepatotoxicity. RFTs, encompassing parameters like serum Creatinine and Blood Urea Nitrogen (BUN), are indicative of kidney function. Arshad *et al*. [3] investigated renal vein thrombosis at high altitudes, shedding light on

Correspondence: Dr. Hunain Habib, Consultant Chemical Pathologist, Fazaia Medical College, Islamabad Pakistan

Email: ssdd2391@gmail.com

Receiving Date: **26 Feb 2024**
Revision Date: **05 Jul 2024**
Acceptance Date: **01 Sep 2024**

the impact of altitude on kidney health. Lipid profile, an essential component in assessing cardiovascular health, has also been the focus of studies related to high-altitude exposure.

Additionally, high-altitude regions, defined as areas above 1,500 meters, provide a unique natural laboratory for studying adaptive responses to hypobaric hypoxia. Studies by Naeije *et al*. [4] and He *et al*. [5] delved into the effects of high altitude on pulmonary artery pressure, exercise capacity, and vascular endothelial function.

Understanding the impact of high altitude on LFTs, RFTs, and Lipid profiles is not only academically intriguing but also holds practical implications for individuals such as mountain climbers, trekkers, and residents of high-altitude regions. Furthermore, insights into cardiovascular functions and body composition at high altitudes, as studied by Vats *et al*. [6] and Ortiz-Prado *et al*. [7], contribute significantly to the growing body of knowledge in altitude medicine. Human adaptation to high-altitude is due to characteristic adjustments at every physiological level. Differences in lipid profile and cardiovascular risk factors in altitude dwellers have been previously explored [8]. Aryal *et al*. [9] and others explored Lipid profiles, Glycosylated hemoglobin (HbA1c), and Diabetes prevalence in populations residing at high altitudes.

In this study, we have aimed to synthesize existing literature, examining the mechanisms behind changes in LFTs, RFTs, and Lipid profiles at high altitudes, and discussing their clinical implications. The study seeks to provide a holistic understanding of the effects of high-altitude exposure on these physiological parameters, contributing to the broader field of altitude medicine.

MATERIAL AND METHODS

This Cross-sectional observational study was conducted in the department of pathology of CMH Skardu from January 2023 to August 2023. Determination of sample size for this study is based on a power analysis that considers following factors: the anticipated effect size based on previous research, the desired level of statistical power, and the significance level (alpha) for the statistical tests. Given the variability in the impact of high-altitude exposure on LFTs, RFTs, and Lipid profiles reported in previous studies, a moderate effect size is anticipated.

Sample size was calculated separately for each of these parameters (LFTs, RFTs, and Lipid profiles) to ensure adequate statistical power. Previous research, such as the study by Garcia, C. M [10], will be used as a reference for effect size estimation. With 95% confidence interval and 5% margin of error sample size is estimated to be approximately 150 participants for each parameter using the WHO sample size calculator [20]. The inclusion criteria for the study are participants aged between 18 and 65 years who have resided at altitudes of 1,500 meters (4,921 feet) or higher for a minimum of six months, and who have provided written informed consent to participate. Exclusion criteria include individuals under the age of 18 or over the age of 65, patients with chronic renal or hepatobiliary diseases, and those currently taking lipid-lowering medications.

Participants underwent a comprehensive medical examination, including the measurement of vital signs including Blood pressure, pulse rate, respiratory rate and body temperature and a review of medical history. Serum samples were obtained for the assessment of LFTs including serum Bilirubin, serum alanine amino- transferase (ALT), serum aspartate amino-transferase AST, serum alkaline phosphatase (ALP), RFTs that included serum creatinine and blood urea nitrogen (BUN), and lipid profiles of patients consisting of serum Total Cholesterol, serum Triglycerides (TGs), serum low density lipoprotein (LDL) and serum High density lipoprotein (HDL) in clot activator vaccutainers. All parameters were analyzed on Selektra Pro-M Clinical Chemistry analyzer after running calibration and Quality Control for each parameter following Standard operating procedures.

Statistical analysis involved the use of t-tests, analysis of variance (ANOVA), to examine the relationships between altitude exposure and the selected physiological parameters. Adjustments for potential confounding variables, such as age and gender, was made in the analysis with at a p-value of 0.05 considered statistically significant.

This study adhered to all relevant ethical guidelines and Ethical approval was obtained from the hospital ethical review board vide letter no. CMH Skardu /ERB/23/02.

RESULTS

The study involved 150 participants, with ages ranging from 28 to 71 years with the mean age of 46.5 ±10.71 years. Altitude varied between 1700 and 2500 meters among participants with mean altitude of 2018.6±21.9 meters. A total of 105(70%) participants were male, and 45 (30%) participants were female

Means of various parameters have been shown in Table-I Below. Significant negative correlations were observed between altitude and ALT (-0.227, p = 0.005) and AST (-0.212, p = 0.009) as shown in Table-II below. For ALT, AST, ALP, BUN, TGs, HDL, and LDL, there are significant differences among groups (p-values < 0.05). For BIL and Creatinine, there are no significant differences among groups (p-values > 0.05) as shown in Table-III.

Significant differences in ALT, AST, ALP, BUN, TGs, HDL, and LDL levels among groups suggest potential influences of altitude on these biomarkers. The lack of significant differences in BIL and Creatinine may indicate that altitude may not have a substantial impact on these parameters.

Table-I: Mean and standard deviation of parameters.

Variable	Mean± Standard Deviation
Age (years)	46.49±10.71
Altitude (meters)	2018.67±210.91
ALT (U/L)	44±16.0
AST (U/L)	42±17.0
ALP (U/L)	75±17.7
Bilirubin (mg/dl)	0.91±0.60
Creatinine (mg/dl)	0.79±0.11
BUN (mg/dl)	12.88±3.59
CHOL (mmo/L)	160±78.54
TGs (mmo/L)	116±104.8
HDL (mmo/L)	34±5.18
LDL (mmo/L)	97±18.50
CHOL (mmo/L)	160±78.54
TGs (mmo/L)	116±104.8
HDL (mmo/L)	34±5.18
LDL (mmo/L)	97±18.50

Table-II: Pearson's correlation between ALT, AST and altitude.

Parameter	Altitude	P-value
ALT	-0.227	0.005
AST	-0.212	0.009

Table-III: ANOVA showing significant differences among groups-based Altitude level.

Parameter	F-value	p-value
ALT	3.876	.001
AST	3.690	.001
ALP	2.922	.007
Bilirubin	.971	.455
Creatinine	.561	.786
BUN	2.989	.006
Cholesterol	1.885	.076
Triglycerides	2.938	.007
HDL	3.211	.003
LDL	2.504	.019

DISCUSSION

Our study involved 150 participants with demographics providing a diverse and representative sample, allowing for a comprehensive exploration of the impact of high altitude on various physiological parameters. The mean values of liver function tests (LFTs) revealed intriguing insights. ALT and AST levels were negatively correlated with altitude, demonstrating significant negative correlations (-0.227, $p = 0.005$ for ALT; -0.212, $p = 0.009$ for AST) The ANOVA results indicated significant differences in ALT, AST, and ALP among groups based on altitude levels (p-values < 0.05) [10]. ALT and AST, known markers of hepatocellular damage, displayed higher levels at lower altitudes. This supports the notion that liver function is influenced by changes in altitude, potentially due to variations in oxygen availability and environmental stressors. Unlike liver function tests, creatinine and blood urea nitrogen (BUN) levels did not show significant differences among altitude groups (p-values > 0.05) This suggests that altitude may not substantially impact renal function parameters in the studied population. These results are consistent with the study by Sawka *et al*. [11], which emphasized the adaptability of blood volume to environmental stresses. The study also explored the lipid profiles of participants at different altitudes. Significant differences were observed in total cholesterol (CHOL), triglycerides (TGs), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) among altitude groups (p-values < 0.05) [12]. The elevated levels of CHOL and TGs at higher altitudes may indicate an adaptive response to the lower oxygen availability. The shifts in HDL and LDL levels further underscore the complex interplay between altitude exposure and cardiovascular health. These results are in line with studies by Ward and Milledge [13], which acknowledged Griffith Pugh's pioneering work on Everest and its implications for understanding altitude physiology.

These findings contribute to the broader field of altitude medicine, shedding light on the adaptability of the human body to hypobaric conditions. As altitude-related activities and travel become more prevalent, understanding these physiological adaptations becomes increasingly important for both medical practitioners and individuals exposed to high altitudes [14]. Further research, building upon the foundations laid by studies referenced in this discussion, will continue to unravel the complexities of high-altitude physiology. The significant correlations and differences observed in LFTs, renal function tests, and lipid profiles underscore the intricate relationship between altitude exposure and physiological adaptations [15]. These findings have practical implications for individuals residing at high altitudes, such as mountain climbers and residents of high-altitude regions.

Moreover, it is essential to consider the implications of high altitude on other physiological systems beyond those directly measured in this study. For instance, research has shown that high-altitude exposure can lead to alterations in pulmonary circulation, contributing to conditions such as high-altitude pulmonary hypertension [16]. This highlights the importance of investigating not only hepatic and renal function but also cardiopulmonary dynamics in individuals exposed to hypobaric conditions. Additionally, the effects of chronic hypoxia on oxygen transport mechanisms warrant further investigation, as they play a crucial role in the body's adaptation to high altitude [17].

Furthermore, the impact of hypoxia on oxidative stress and cellular metabolism cannot be overlooked. Studies have demonstrated an association between hypoxic environments and increased oxidative stress, which may contribute to various physiological changes observed at high altitudes [18]. Understanding the mechanisms underlying these processes is essential for developing targeted interventions to mitigate the adverse effects of altitude exposure.

In addition to physiological adaptations, it is crucial to consider the psychological and cognitive effects of high-altitude exposure. Research has shown that prolonged stays at high altitude can lead to cognitive impairments

and mood disturbances, known as acute mountain sickness (AMS) [18]. These symptoms can significantly impact individuals' quality of life and performance, particularly in demanding environments such as mountain climbing expeditions or high-altitude workplaces.

Moreover, the role of genetics in mediating individual responses to high-altitude environments merits further investigation. Studies have identified genetic variants associated with improved oxygenation and reduced susceptibility to altitude-related illnesses in certain populations, highlighting the importance of genetic factors in altitude adaptation [19].

In summary, our study contributes to the growing body of literature on altitude medicine by providing insights into the physiological adaptations of the liver, kidneys, and cardiovascular system to high-altitude exposure. However, further research is needed to elucidate the comprehensive effects of altitude on human physiology, including pulmonary circulation, oxygen transport, oxidative stress, cognitive function, and genetic predispositions. By expanding our understanding of these complex interactions, we can better support individuals living and working in high-altitude environments and optimize their health and performance.

CONCLUSION

In conclusion, this study shows the negative correlations between altitude and ALT, AST, coupled with significant differences in these biomarkers, suggest that altitude plays a role in influencing liver function. Additionally, the lack of significant differences in BIL and Creatinine indicates a potential resilience of renal function to altitude changes. The alterations in lipid profiles highlight the multifaceted nature of altitude's impact on cardiovascular health.

LIMITATIONS

However, it's crucial to acknowledge the limitations of the study. The cross-sectional design limits the establishment of causation, and confounding variables, such as lifestyle factors and pre-existing health conditions, may influence the observed outcomes. Future longitudinal studies and controlled experiments could provide deeper insights into the causal relationships between altitude and physiological parameters.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHORS CONTRIBUTION

Mustajab Alam: Conception, data collection, formal analysis, investigation and resources, accountable for all aspects of the work

Hunain Habib: Drafting the manuscript and interpretation of the work, accountable for all aspects of the work

Naveed Asif: Drafting, designing the study content, review writing, accountable for all aspects of the work

Bushra Anwar: Results analysis, review of writing, accountable for all aspects of the work

Tahir Asad: Data collection, analysis, investigation, accountable for all aspects of the work

Khizar Hameed: Review writing and editing**,** accountable for all aspects of the work

REFERENCES

1. Lala V, Zubair M, Minter DA. Liver Function Tests. [Updated 2023 Jul 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482489/
2. Cornelius CE. Liver function tests in the differential diagnosis of hepatotoxicity. In Hepatotoxicology 2020 Jan 16 (pp. 181-213). CRC Press.
3. Arshad AR, Islam F, Qayyum M. Renal vein thrombosis at high altitude. Pak Armed Forces Med J. 2021; 71(Suppl-1): S283-85. DOI:https://doi.org/10.51253/pafmj.v71iSuppl-1.2444
4. Naeije R, Huez S, Lamotte M, Retailleau K, Neupane S, Abramowicz D, *et al*. Pulmonary artery pressure limits exercise capacity at high altitude. Eur Respir J. 2010; 36(5): 1049-55. DOI: https://doi.org/10.1183/09031936.00024410
5. He L, Jiang Y, Su H, Li J, Cheng X. Vascular endothelial function assessed by postischemic diastolic blood pressure is associated with acclimatization and acute mountain sickness. High Alt Med Biol. 2016; 17(1): 11-5.

DOI: https://doi.org/10.1089/ham.2015.0070
6. Vats P, Ray K, Majumadar D, Amitabh, Joseph DA, Bayen S, *et al*. Changes in cardiovascular functions, lipid profile, and body composition at high altitude in two different ethnic groups. High Alt Med Biol. 2013; 14(1): 45-52. DOI: https://doi.org/10.1089/ham.2012.1071
7. Ortiz-Prado E, Portilla D, Mosquera-Moscoso J, Simbaña-Rivera K, Duta D, Ochoa I, *et al*. Hematological parameters, lipid profile, and cardiovascular risk analysis among genotype-controlled indigenous Kiwcha men and women living at low and high altitudes. Front Physiol. 2021: 1769. DOI: https://doi.org/10.3389%2Ffphys.2021.749006
8. Aryal N, Weatherall M, Bhatta YK, Mann S. Lipid profiles, glycated hemoglobin, and diabetes in people living at high altitude in Nepal. Int J Environ Res Pub Health. 2017; 14(9): 1041. DOI: https://doi.org/10.3390/ijerph14091041
9. Naeije R, Chesler N. Pulmonary circulation at exercise. Compr Physiol. 2015; 5(1): 655-78. DOI: https://doi.org/10.1002%2Fcphy.c100091
10. Sawka MN, Convertino VA, Eichner ER, Schnieder SM, Young AJ. Blood volume: importance and adaptations to exercise training, environmental stresses, and trauma/sickness. Med Sci Sports Exerc. 2000; 32(2): 332-48. DOI: https://doi.org/10.1097/00005768-200002000-00012
11. Appenzeller O, Martignoni E. The autonomic nervous system and hypoxia: mountain medicine. J Auton Nerv Sys. 1996; 57(1-2): 1-12. DOI: https://doi.org/10.1016/0165-1838(95)00093-3
12. Ward MP, Milledge JS. Griffith pugh, pioneer everest physiologist. High Alt Med Biol. 2002; 3(1): 77-87. DOI: https://doi.org/10.1089/152702902753639595
13. Winslow RM, Samaja M, West JB. Red cell function at extreme altitude on Mount Everest. J Appl Physiol. 1984; 56(5), 1097-1103. DOI: https://doi.org/10.1152/jappl.1984.56.1.109
14. Zhao Y, Wang X, Noviana M, Hou M. Nitric oxide in red blood cell adaptation to hypoxia. Acta Biochim Biophys Sin. 2018; 50(7): 621-34. DOI: https://doi.org/10.1093/abbs/gmy055
15. Brito J, Siques P, Pena E. Long-term chronic intermittent hypoxia: A particular form of chronic high-altitude pulmonary hypertension. Pulm Circ. 2020; 10(1_suppl): 5-12. DOI: https://doi.org/10.1177%2F2045894020934625
16. Bärtsch P, Swenson ER. Acute high-altitude illnesses. New Eng J Med. 2013;. 368(24). 2294-302. DOI: https://doi.org/10.1056/nejmcp1214870
17. Mallet RT, Burtscher J, Pialoux V, Pasha Q, Ahmad Y, Millet GP, *et al*. Molecular mechanisms of high-altitude acclimatization. Int J Mol Sci. 2023; 24(2): 1698. DOI: https://doi.org/10.3390%2Fijms24021698
18. Beall CM. Two routes to functional adaptation: Tibetan and Andean high-altitude natives. Proc Natl Acad Sci USA. 2007; 104 (suppl 1): 8655-60. DOI: https://doi.org/10.1073/pnas.0701985104
19. Sample size calculator. (2023, July 08). Retrieved from [https://www.calculator.net/sample-size-calculator.html]