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Does Increasing Haemoglobin At High Altitude Alone Cause A Rise In Coronary Artery Disease; A Prospective Study

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ABSTRACT

Objective: To study the effect of high altitude on haemoglobin concentration with coronary artery disease.
Study Design: Prospective longitudinal study.
Place and Duration of Study: Combined Military Hospital, Skardu Pakistan, from Jan to Dec 2018
Methodology: All individuals working at high altitudes diagnosed with coronary artery disease (CAD) were included. Haemoglobin concentration was measured by doing a complete blood picture.
Results: The total number of patients diagnosed with coronary artery disease in the study was 34 (all males). 16(47%) of the patients with coronary artery disease were evacuated from the height of 8000 to 13000 feet, 16(47%) from the height of 13001 to 18000 feet and 2(6%) patients were evacuated from the height of more than 18000 feet. The mean haemoglobin (Hb) of patients evacuated from the height of 8000 to 13000 feet was 15.7±1.4gm/dl; of patients evacuated from a height of 13001 to 18000 feet was 16.3±1.5gm/dl, and of patients evacuated from more than 18000 feet was 18.3±1.2gm/dl.
Conclusion: Persistent rise in haemoglobin was noted with increasing altitude. However, most of the patients with coronary artery disease were from a height of 13000 to 18000 feet.

Keywords: High altitude sickness, Coronary artery disease, Brain edema, Hemoglobin, Blood pressure, Skardu.

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INTRODUCTION

Coronary artery disease (CAD) is the leading cause of death worldwide, with about 80% to 86% of these deaths occurring in low and middle-income countries.[1] There is a substantial variation in the mortality rates according to gender, age, ethnicity, socio-economic status and geographical location.[2] Increasing incidence, regional variations, premature onset, poor management and greater mortality characterize CAD in South Asian countries.[3]

A height of more than 3000 meters is defined as a high altitude. The disease pattern at high altitudes differs from that of low altitudes.[4] The most feared event at high altitude is the increased risk of thromboembolic event. Thromboembolic events may be in the form of stroke, myocardial infarction, deep venous thrombosis, arterial thrombosis or pulmonary embolism.[5,6] An increased interest in high-altitude medicine has been noted in the recent era. At high altitudes, the risk of thromboembolic events is about 30-fold. Most of these thromboembolic events occur in young patients and those with no risk factors for such events.[7] In addition, people visiting a high altitude area are at risk of other diseases like acute mountain sickness, high altitude pulmonary oedema and high altitude cerebral oedema.[8]

Different mechanisms for thromboembolic events at high altitudes have been suggested, but the precise pathophysiology still needs to be well known. The main culprit at high altitudes is considered to be hypoxia.[9] In hypoxic conditions, tissue metabolism is compromised. It creates toxic radicals, which can cause tissue and cell death. Another metabolic change observed in the body due to hypoxia is a shift from oxidative metabolism to glycolysis to satisfy body energy needs.[10]

The rationale of our study was to determine whether a high altitude-associated increase in haemoglobin alone was responsible for coronary artery disease in people at high altitude. If not, it would pave the way for other risk factors responsible for coronary artery disease at high altitudes to be dug out.

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METHODOLOGY

The prospective longitudinal study was conducted at the Department of Medicine, Combined Military Hospital, Skardu, Pakistan from January to December 2018. Approval of the Hospital Ethical Committee was sought for the study.

Inclusion Criteria: All individuals deployed at high altitudes (at or more than 8000 feet) and diagnosed with coronary artery disease were included.

Exclusion Criteria: Any individual with a previous history of coronary artery disease or newly diagnosed coronary artery disease but with a height of less than 8000 feet were excluded.

All individuals posted to an area of high altitude are subjected to detailed physical examination and investigations. Investigations include a complete blood picture, ECG, chest x-ray, urine routine examination, blood sugar and lipid profile - patients with haemoglobin 15.5 gm/dl or more are not sent to high altitudes. Coronary artery disease was diagnosed by doing ECG and cardiac enzyme, i.e. CK MB and Trop T. If ETT or angiography were required, these patients were sent to the Armed Forces Institute of Cardiology (AFIC), Rawalpindi. The patients were managed by a senior medical specialist at the Combined Military Hospital Skardu or were referred to AFIC, Rawalpindi, for management. Height was divided into three categories: between 8000 and 13000 feet, between 13000 and 18000 feet and over 18000 feet.[11] Mean haemoglobin concentration of patients evacuated from each height category was determined.

Informed consent for blood sample collection and investigation was obtained from all study participants. Participants were informed of the results of the test.

Statistical Package for Social Sciences (SPSS) version 20.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Chi-square test and Anova test were applied to explore the inferential statistics. The *p*-value lower than or up to 0.05 was considered as significant.

RESULTS

The total number of patients diagnosed with coronary artery disease in the study was 34 (all males). 16(47%) of the patients with coronary artery disease were evacuated from a height of 8000 to 13000 feet, 16(47%) from a height of 13001 to 18000 feet and 2(6%) patients were evacuated from a height of more than 18000 feet. The mean haemoglobin (Hb) of patients evacuated from the height of 8000 to 13000 feet was 14.4±6.5 gm/dl; of patients evacuated from a height of 13001 to 18000 feet was 16.3±1.5 gm/dl and of patients evacuated from more than 18000 feet was 18.3±1.2 gm/dl. Patients with ages less than 30 years were 4(12%). In the age group 30 to 35 years and 36 to 40 years, there were 12(35%) each; in the age group 41 to 45 years, there were 5(15%); and in the age group 46 to 50, there were 1(2%) as given in the Table-I. A statistically significant increase in haemoglobin concentration was observed with increasing height (*p*-value less than 0.05). However, most of the patients with coronary artery disease had haemoglobin concentrations of less than 18 gm/dl.

DISCUSSION

Hypoxia increases the production of erythropoietin, resulting in secondary polycythemia.[11] At high altitudes, alteration in platelet function has been documented. Interaction between platelets and

Table-I: Characteristics of Patients with Coronary Artery Disease at various Levels of High Altitude (n=34)

Characteristics		Total	Height: 8000 – 13000 ft	Height: 13000 – 18000 ft	Height: > 18000 ft	*p*-value
Demographics						
Age Groups	< 30 years	4(12%)	-	4(12%)	-	0.568
	30 –35 years	12(35%)	6(17%)	4(12%)	2 (6%)	
	36 – 40 years	12(35%)	7(20%)	5(15%)	-	
	41 - 45 years	5(15%)	2(6%)	3 (9%)	-	
	46 - 50 years	1(3%)	1(3%)	-	-	
Pulse (/min)	Mean± SD	78±28	76±17	80±12	82±11	0.648
Systolic BP (mmHg)	Mean± SD	112±34	118±12	124±20	130±12	0.311
Diastolic BP (mmHg)	Mean± SD	76±26	78±18	82±11	82±14	0.594
Investigations						
Hb (g/dl)	Mean± SD	14.4±6.5	15.7±1.4	16.3±1.5	18.3±1.2	0.001
Coronary Artery Disease		34	16	16	2	0.199

endothelium is also impaired. All these mechanisms make the individuals living at high altitudes prone to thromboembolic events.[12] An increase in haemoglobin at high altitudes may be a protective phenomenon. Low oxygen pressure at high altitudes may result in serious cardiorespiratory events. This rise in haemoglobin compensates for the low oxygen tension by increasing the oxygen-carrying capacity.[13] However, this rise may not always be friendly and may result in some adverse events like cerebrovascular events, deep venous thrombosis and myocardial infarction. The main reason for such events is that with rising haemoglobin, the viscosity of blood is increased, which makes this individual at high altitudes to thrombotic events.[14] Exposure to a high-altitude environment increases the chance of cardiovascular diseases or has a beneficial effect, is debatable. The available literature has contradictory results. Even some studies have reported a decreased prevalence of obesity and diabetes mellitus in people living at high altitudes: both diseases increase the risk of cardiovascular diseases many fold.[15,16] In our study, although the concentration of haemoglobin increased with increasing altitude, a positive linear correlation was not found between increasing height and coronary artery diseases.

Our study found a linear relationship between haemoglobin concentration and high altitude. The mean haemoglobin (Hb) of patients evacuated from the height of 8000 to 13000 feet was 15.7±1.4 gm/dl; of patients evacuated from the height of 13001 to 18000 feet was 16.3±1.5 gm/dl and of patients evacuated from more than 18000 feet was 18.3±1.2 gm/dl with *p*-value less than 0.001. A similar trend was observed in a study by Chonchol *et al*., which reported an increase in haemoglobin concentration with increasing altitude. They also studied the effect of height on serum iron availability, hepcidin and erythroferrone. They observed that the serum erythroferrone increased with exposure to high altitude, increasing iron availability and suppressing hepicidin production. The overall effect was an increase in haemoglobin concentration with height. The mean haemoglobin concentration at sea level was 14.3±0.8 g/dL, which increased to 16.6±0.9 g/dl at exposure to high altitude.[17] León-Velarde *et al*. also studied the effect of height on haemoglobin concentration, red blood cell mass and hematocrit in men, women and children at different altitudes. They also observed a linear relation between haemoglobin concentration and hematocrit with height in all three populations.[18] Siques *et al*. studied the effect of high altitude on lipid profile and haemoglobin concentration in lowlanders exposed to high altitude for eight months. A statistically significant rise was observed in hematocrit and haemoglobin concentration with increasing height.[19]

Whether altitude has a protective or harmful effect on coronary artery disease is debatable. Different mechanisms have been claimed to protect against heart disease at high altitudes. A study found an inverse relation between altitude and leptin level. Similarly, it has been found that serum levels of HDL cholesterol increase with high altitude. These, in turn, decrease coronary artery disease incidence at high altitude.[20] Regarding hematocrit and coronary artery disease, a study found that both high and low hematocrit increased the chances of coronary artery disease.[21] However, our study could not establish a linear association between increasing haemoglobin and coronary heart disease.

LIMITATIONS OF STUDY

There were some limitations of this study. Most of the patients with coronary artery disease were evacuated from a height of 13000 to 18000 feet as compared to a height of more than 18000 feet. The reason may be that healthier individuals with younger ages are deployed at higher posts than older individuals.

CONCLUSION

This study observed an association between altitude and haemoglobin concentration. However, increasing haemoglobin concentration at high altitudes alone could not be responsible for coronary artery disease in deployed individuals.

Conflict of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

MQ & SAS: Data acquisition, critical review, approval of the final version to be published.

MZ & AL: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

QUA & SA: Conception, data analysis, drafting the manuscript, approval of the final version to be published.

Authors agree to be 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.

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