Relevance of Asymptomatic Electrocardiographic Abnormalities at High Altitude

Yatharth Dixit¹*, Dennis Abraham², Vishnu Prasad³

Abstract

Background: Cardiovascular diseases, especially coronary artery disease, are epidemic all over the world. Globally, CVD led to 17.5 million deaths in 2012. More than 75% of these deaths occurred in developing countries. India is a large and socioeconomically diverse country and is home to 17% of the world’s population. In India, more than 10.5 million deaths occur annually and it was reported that CVD led to 20.3% of these deaths in men and 16.9% of all deaths in women. The striking features of CVD epidemiology in India are high mortality rates, premature CAD, and increasing burden.

In the earlier days electrocardiogram (ECG) was used for identification of arrhythmias and conduction disturbances. This was followed by the realization that 12 lead ECG could be used for diagnosis of acute ischemic events. Resting and exercise ECGs were subsequently used to screen asymptomatic individuals for the presence of unsuspected disease. During the same time risk factors for atherosclerotic disease were recognized. This was followed by the development of risk-scoring profiles capable of classifying individuals (without prior CVD) into high-risk, intermediate-risk, and low-risk subgroups for CVD. One example of such a risk score is the widely validated Framingham Risk Score. This score takes into account the following factors - age, sex, smoking, systolic blood pressure, total cholesterol, high density lipoprotein (HDL), and whether the individual is on anti-hypertensives or not.

Regions above 1500 m are termed as High altitude (HA). Illnesses associated with HA are commonly observed above an altitude of 2500 m; therefore regions above 2500 m are considered as HA for all practical purposes. Upon ascent to HA, an individual’s body undergoes a series of adaptive changes to maintain normal performance in daily activities. This process is known as acclimatization. A recent estimate suggests that nearly 140 million people live at an altitude greater than 2500 m which includes the populations of South America, Central Asia, and Eastern Africa. These highlanders are chronically exposed to relative hypoxia, which has important consequences on the cardiovascular system.

One of the most important effects of prolonged stay in HA is pulmonary hypertension leading to right ventricular hypertrophy. The first direct measurement of increased pulmonary arterial pressure by cardiac catheterization was done in Peru (4540 m) in 1956. Penaloza et al. established the connection between chronic hypoxia and pulmonary hypertension for the first time in 1962. Since then numerous studies have confirmed this fact. This also propelled researchers to study the pattern of ECG abnormalities at HA. A study conducted by Rotta and Lopez on 120 healthy highlanders suggested four common patterns of ECG namely, (1) right ventricular hypertrophy, (2) suggestive of right ventricular hypertrophy (S1, S2, S3), (3) incomplete and complete heart block and (4) normal pattern. In another study conducted by Penaloza et al. in 13 healthy lowlanders who were temporarily taken to high altitude for four weeks, main changes seen in the ECG were clockwise rotation of axis.
The aim of the present study was to study the clinical profile of subjects with ECG abnormalities on ascent to HA and to identify the importance of ECG abnormalities in HA with relevance to CAD.

Material and Methods

The present study was conducted in a secondary care hospital having basic specialties and investigation facilities, located in the eastern sector of the country at an altitude of 2000 m. The study was carried out as a cross-sectional study over a period of one year (Nov 2017-Nov 2018). Study population consisted of all subjects meeting the eligibility criteria (healthy males between 20-60 years age, meeting the eligibility criteria (healthy population consisted of all subjects of the country at an altitude of 2000 m). The study was carried out as a cross-sectional study over a period of one year (Nov 2017-Nov 2018). Study population consisted of all subjects meeting the eligibility criteria (healthy males between 20-60 years age, meeting the ECG abnormality criteria on ascent to HA and no previous comorbidity). All subjects with past history of ECG abnormality and previous comorbidities like Hypertension, Type 2 Diabetes Mellitus, Cerebrovascular Accident etc were excluded from the study. Sample size was calculated to be 54 based on the formula:– (Za)² x p(1-p)/d²; where Za= 1.96 for 95% confidence interval, p= 0.036 proportion of asymptomatic subjects with ECG abnormality, d= acceptable deviation. Convenience sampling technique was used to select the study participants. Study protocol was approved by institutional ethics committee and performed in accordance with the Declaration of Helsinki. Informed written consent was obtained from all the participants before including them in the study.

Brief Procedure

All the study participants were transferred from Medical Establishments co-located with HA posts. All subjects more than 35 years of age were screened for ECG abnormality. All those who were detected to have ECG abnormality in HA were admitted to these Medical Establishments and subsequently transferred to our hospital located at a lower altitude (2000 m) for further evaluation. All subjects with ECG abnormality in HA were interviewed about family history of sudden death, consumption of tobacco and alcohol, continued exposure to certain drugs (beta blockers, calcium channel blockers), history of thyroid disorder and history of prior chronic illnesses. A complete physical examination was carried out including pulse, blood pressure, respiratory rate, temperature, height, weight, body-mass index, thyroid examination and complete systemic examination. 12 lead ECG was recorded by 12 channel Bionet ECG machine model No – 9108. All the study participants were then subjected to necessary haematological, biochemical and radiological investigations. Haematological investigations consisted of complete hemogram (to exclude polycythemia). Biochemical investigations included blood urea, serum creatinine and urine examination (to rule out kidney disease), serum potassium (to screen for electrolyte abnormality), thyroid profile (to screen for thyroid disorder) and liver function tests (to rule out liver disease). These subjects also underwent structural and functional study of the heart by 2D Echo and TMT. Those found to have a positive TMT underwent Coronary Angiography (CAG) and further risk stratification was subsequently carried out. A flow chart depicting the study procedure is shown in Figure 1.

Statistical analysis

The data was analysed using SPSS (Statistical Package for Social Sciences) version 22.0 software. Descriptive and inferential statistics were performed.

Results

A total of 54 subjects were included in the study. Mean age of the subjects was 40.6±3.7 years. Of these 51 (94.4%) subjects were detected to have ECG abnormality in the first stage of acclimatization. ECG abnormalities seen in HA are depicted in Table 1. Most common ECG abnormality was T wave inversion in inferiorly directed frontal plane leads seen in 16 (29.6%) subjects followed by T wave inversion in both inferiorly directed frontal plane leads and precordial leads noted in 13 (24%) subjects. Next most common ECG abnormality was T wave inversion in the precordial leads seen in 10 (18.5%) subjects. Other common abnormalities seen were Complete Right Bundle Branch Block (RBBB), Incomplete RBBB, ST depression in both frontal plane and precordial leads and Right Axis Deviation (RAD). Obesity was noted among 17 (31.5%) participants. and
54 (94.4%) subjects were found to have ECG abnormality in the first stage of acclimatization. This could be due to the effect of high altitude itself. This has been observed in a previous study in which 100% subjects developed ECG abnormality at HA. However they were directly inducted to an altitude of 4500 meter. It has also been observed that there is significant association between ECG abnormality and altitude. Odds ratio for abnormal ECG was found to increase significantly with every 1000 m increase in altitude.14 It was observed in the present study that the most common ECG abnormality was T wave inversion in inferiorly directed frontal plane leads. This was followed by T wave inversion in both inferiorly directed frontal plane leads and precordial leads. Another common abnormality seen was T wave inversion only in the precordial leads. These changes are likely due to overloading of the right ventricle because of changes in the pulmonary circulation and hypoxia. This finding is supported by previous studies conducted in HA.11, 12 However a recent study conducted on highlander natives of Nepal concluded that ECG abnormalities were present on both sides of the heart, on the left side of the heart for Mustang participants (Tibetan origin) and on the right side of the heart for Humla participants (Indo-Aryans).14 The principal finding of our study was that the majority of ECG abnormalities in high altitude are transient/ benign and do not suggest an increased risk of cardiovascular disease since only three out of 54 subjects turned out to be positive for inducible ischemia on TMT evaluation and none of them were found to have any abnormality on coronary angiogram. Study conducted by Aryal N et al. also concluded that HA populations of Humla and Mustang districts in Nepal had a prevalence of CHD comparable with that seen in low-altitude populations.14 It was also found that there is no association between ECG abnormality in HA in temporary residents and Framingham risk score since only one out of 54 subjects was found to be in high-risk category and only nine out of 54 subjects were found to be in the intermediate risk category. Only one out of these 10 subjects turned out to be positive for inducible ischemia on TMT but again had a normal coronary angiogram. This is in accordance with the latest US Preventive Services Task Force (USPSTF) recommendation which concluded that for asymptomatic adults at low risk of CVD events (individuals with a 10-year CVD event risk less than 10%), it is very unlikely that the information from resting or exercise ECG (beyond that obtained with conventional CVD risk factors) will result in a change in the patient’s risk category as assessed by the Framingham Risk Score.15 The authors have also observed that the majority of T wave inversions involving inferiorly directed frontal plane leads and right sided precordial leads reverted to normal within three to ten days of descent to a lower altitude. This observation is also supported by a previous study conducted on 202 healthy lowlanders inducted to HA, which concluded that ECG changes reverted to normal in 100% of individuals after descent to a lower altitude.16

### Conclusion

ECG abnormalities in high altitude are transient/ benign in nature and do not suggest an increased risk of cardiovascular disease whether evaluated by Framingham Risk Score or structural/ functional evaluation by 2D Echocardiography/ Treadmill Test.

### Acknowledgements

Authors would like to thank their spouses, teachers, colleagues, nursing staff and most importantly the patients who participated in the study.

### Declarations

Ethical approval

The study was approved by the Institutional Ethics Committee.

### References


### Table 1: Frequencies of ECG abnormalities in high altitude

<table>
<thead>
<tr>
<th>ECG abnormality</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>T wave inversion in limb leads</td>
<td>29.6%</td>
</tr>
<tr>
<td>T wave inversion in limb and precordial leads</td>
<td>24%</td>
</tr>
<tr>
<td>T wave inversion in precordial leads</td>
<td>18.5%</td>
</tr>
<tr>
<td>Complete RBBB</td>
<td>7.4%</td>
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<tr>
<td>Incomplete RBBB</td>
<td>3.7%</td>
</tr>
<tr>
<td>Right axis deviation</td>
<td>3.7%</td>
</tr>
<tr>
<td>ST depression and T wave inversion in limb leads</td>
<td>3.7%</td>
</tr>
<tr>
<td>ST depression and T wave inversion in limb and precordial leads</td>
<td>1.85%</td>
</tr>
<tr>
<td>Left bundle branch block</td>
<td>1.85%</td>
</tr>
<tr>
<td>Left ventricular hypertrophy</td>
<td>1.85%</td>
</tr>
<tr>
<td>Premature ventricular complexes</td>
<td>1.85%</td>
</tr>
<tr>
<td>Left anterior hemiblock</td>
<td>1.85%</td>
</tr>
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18 (33.3%) participants were noted to be consuming tobacco in some or the other form. Nearly 25 (46.3%) subjects had spent less than 30 days in HA (Figure 2). Out of 54 only three (5.5%) subjects were found to be positive for inducible ischemia on Treadmill Test. All the three subjects however turned out to have a normal coronary angiogram. Only two (3.6%) subjects had abnormal 2D Echocardiography out of which one (1.8%) subject was detected to have reduced ejection fraction and was finally diagnosed to have Coronary Artery Disease. Only one (1.8%) subject had high risk of general cardiovascular disease and nine (16.6%) subjects had intermediate risk of general cardiovascular disease according to Framingham Risk Score. Out of these 10 subjects also only one subject was found to be positive for inducible ischemia on TMT. However he also turned out to have a normal coronary angiogram.

### Discussion

The present study was an attempt to document ECG abnormalities on ascent to HA, in asymptomatic healthy individual without any previous ECG changes and correlation of these changes with CAD. All the subjects underwent ECG evaluation before ascent to high altitude. This allowed us to document ECG abnormality occurring on reaching HA which could not be attributed to preexisting illnesses. In our study mean age of the subjects was 40.6±3.7 years which could be attributed to the selection procedure itself since only asymptomatic individuals more than 35 years of age were included in the study. 54 (94.4%) subjects were found to have


