

# Electrocardiography in people living at high altitude of Nepal

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# **Electrocardiography in people living at high altitude of Nepal**

## **Objective**

The main objective of this study was to estimate the prevalence of coronary heart disease (CHD) of high altitude populations in Nepal determined by an electrocardiogram (ECG) recordings and a medical history.

## **Methods**

We carried out a cross-sectional survey of cardiovascular disease and risk factors among people living at four different altitude levels, all above 2800 m, in the Mustang and Humla districts of Nepal. 12-lead ECGs were recorded on 485 participants. ECG recordings were categorized as definitely abnormal, borderline or normal.

## **Results**

No participant had Q waves to suggest past Q-wave infarction. Overall 5.6% (95% CI 3.7 to 8.0) of participants gave a self-report of CHD. The prevalence of abnormal (or borderline abnormal) ECG was 19.6% (95% CI 16.1 to 23.4). The main abnormalities were: right axis deviation in 5.4% (95% CI 3.5 to 7.7), and left ventricular hypertrophy by voltage criteria in 3.5% (95% CI 2.0 to 5.5). ECG abnormalities were mainly on the left side of the heart for Mustang participants (Tibetan origin) and on the right side for Humla participants (Indo-Aryans). There was a moderate association between the probability of abnormal (or borderline abnormal) ECG and altitude when adjusted for potential confounding variables in a multivariate logistic model; with an odds ratio for association per 1000 m elevation of altitude of 2.83 (95% CI 1.07 to 7.45),  $P=0.03$ .

## **Conclusion**

Electrocardiographic evidence suggests that although high altitude populations do not have a high prevalence of CHD, abnormal ECG findings increase by altitude and risk pattern varies by ethnicity.

## **Main Text**

### **Introduction**

More than 140 million people in the world, comprising 2% of the global population, live permanently at high altitude (HA), defined as at greater than 2500 m<sup>1</sup>. The Himalayan mountains of Asia, Andean mountains of South America, and Ethiopian summits of northeast Africa are the major geographical locations of HA populations<sup>1</sup>.

The positive and negative effects induced by living at HA, and chronic hypobaric hypoxia, on cardiovascular health, are uncertain. Increased angiogenesis and structural vascular changes caused by HA may reduce blood pressure (BP) and promote cardio-metabolic efficiency. However, erythrocytosis (from chronically low inspired oxygen concentrations) and pulmonary hypertension (HT) amongst those living at HA may be risk factors for adverse cardiovascular events<sup>2</sup>. The largest HA populations, Tibetans and Andeans, exhibit different patterns of adaptation and physiological responses to environmental hypoxia<sup>3</sup>. Past research shows that genetic factors account for some variance in levels of physiological adaptation of HA populations<sup>4</sup>. These factors, in association with different lifestyle practices of HA populations, may contribute to research findings that the different HA populations have different risk for cardiovascular events. Despite more than five decades of research on cardiovascular health at HA the impact of hypoxia on cardiovascular health is still uncertain.

In Nepal, nearly 2 million people permanently live in mountain areas, representing 7% of the national population<sup>5</sup>. Those with Tibetan ancestry are the dominant ethnic HA population in Nepal, for example Sherpa, Thakali, Tibetan Gurung, Lama.

There may be a relationship between usual resident altitude and cardiovascular health in Nepalese HA populations because of hypoxia induced physiological responses. In addition, Tibetan related populations are known to have a high prevalence of HT which may raise their risk of coronary heart disease (CHD). There has been no research published on prevalence of CHD among HA populations in Nepal. The main purpose of this study was to investigate the prevalence of CHD, determined by a medical history and an electrocardiogram (ECG) recording, of people living at different levels of HA in Nepal.

## **Methods**

This was a cross-sectional study.

### *Study sample*

Sixteen, out of 75 districts of Nepal, are classified as 'mountain ecological' regions. Two mountainous districts (Mustang and Humla) were selected for sampling based on past documentation of geography, altitude, population and ethnicity; and the feasibility of conduct for the study. The selected study areas were Jomsom (2800 m), Jharkot (3270 m) and Muktinath (3620 m) of the Mustang district, and Simikot (2890 m) of the Humla district. In Mustang, the population is predominantly of Tibetan ancestry and that of the Humla district is mainly Indo-Aryan. Both districts are close to the border with China and are heavily influenced by Tibetan culture. Life expectancy at birth is 64.1 years in Mustang and 65.0 years in Humla. Both are lower than the national figure of 68.8 years<sup>6</sup>.

As a group Tibetans migrated to high mountains of Nepal some 500 years ago. Tibeto-Burman is their native language and they practice Buddhism. Indo-Aryans migrated to Nepal some 2000 years ago, speak Nepalese language, and majority of them are Hindu {Eagle, 2000 #4910}. Tibetans and Indo-Aryans are distinctive by appearance, language, and name.

Inclusion criteria for participation were age 30 years and above and the ability to speak and understand the Nepalese language. Exclusion criteria were inability or unwillingness to provide written or verbal consent, inability to speak or hear properly, and pregnancy.

### *Sampling process*

Sampling was carried out in two stages. In the first stage, three study areas of Mustang and one study area of Humla were selected on the basis of altitude levels, population density and logistical support to undertake the study. In the second stage, a list of households was developed, and a unique number was assigned to each of them. Household numbers were randomly selected with the help of the computer based randomization technique. All eligible family members of the randomly selected households were considered. If none of the household members were eligible or agreed to take part in the study, a household in the close proximity was selected.

The desired sample size within each district was calculated to be around 250 individuals<sup>7</sup>. This gave a margin of error for a proportion based on anticipated prevalence of HT of around 25% of plus or minus 5% after adjusting for the design effect and expected non-response rate of 10%.

### *Data collection procedures*

The questionnaires administration and blood pressure measurements were carried out at the house of the selected participants. Practically it was not feasible to undertake blood sample testing, ECG recordings and bio-physical measurements in individual houses so a local community hall was used as the measurement facility. Participants were requested to come for these measurements at a time suitable for them. Glycated Hemoglobin (HbA1c) and lipid profiles were measured using Cobas b 101 device (Roche Diagnostics). A small amount of capillary whole blood was taken by single finger-prick and processed into the device. A 12 lead ECG was recorded using a portable Edan SE-600 instrument. Participants were requested to remove clothing from the chest, lie supine with arms at their sides and legs uncrossed. Oily, sweaty or clammy skin was wiped with alcohol swabs. Qualified female nurses recorded the ECG, however, they were standardised on performing ECGs.

Data was collected during June-August (summer) 2014 in Mustang district and March-May (spring) 2015 in Humla district. The ambient temperature was between 25 to 31 degree Celsius in Mustang and around 15 degree Celsius in Humla on most of study days.

### *Definitions*

The prevalence of CHD was defined as the presence of pathological Q waves in the ECG (Table 1) or self-report of personal history of CHD (previous event of MI or chest pain from heart disease (angina)). ECG recordings were categorized as definitely abnormal (e.g. showing evidence of previous myocardial infarction (MI)), borderline (e.g. non-specific T-wave inversion) or normal after review by a cardiologist (SM) using standard widely accepted criteria. The commonly used Sokolow-Lyon index<sup>8</sup> and Romhilt-Estes score<sup>9</sup> were used for the diagnosis of left ventricular hypertrophy (LVH). The ten-year risk of fatal or non-fatal cardiovascular events (MI or stroke) was calculated using a validated risk prediction chart designed by the World Health Organization (WHO) and the International Society of Hypertension (ISH) for WHO region of South-East Asia, sub region D<sup>10</sup>.

**Table 1: Definition of pathological Q waves**

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- Any Q-wave in leads  $V_2$ - $V_3 \geq 0.02$  s or QS complex in leads  $V_2$  and  $V_3$
  - Q-wave  $\geq 30$  ms and  $\geq 0.1$  mV deep or QS complex in leads I, II, aVL, aVF or  $V_4$ - $V_6$  in any 2 leads of a contiguous lead grouping (I, aVL,  $V_6$ ;  $V_4$ - $V_6$ ; II, III, and aVF)
  - R-wave  $\geq 40$  ms in  $V_1$ - $V_2$  and  $R/S \geq 1$  with a concordant positive T-wave in the absence of a conduction defect
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Thygesen, K., Alpert, J. S., Jaffe, A. S., Simoons, M. L., Chaitman, B. R., & White, H. D. (2012). Third universal definition of myocardial infarction. *Circulation*, 126(16), 2020-2035.

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### *Statistical methods*

Simple data description is by mean, standard deviation (SD), frequency counts, and proportions expressed as percentages. Comparison of age by altitude level was by the Kruskal-Wallis test and Chi-square test of independence was used for the subgroup comparisons by sex and ethnicity. The Clopper-Pearson method was used to estimate an exact confidence interval for a single proportion. Logistic regression was used to estimate the association between an abnormal (or borderline abnormal) ECG and altitude. Altitude was treated as a continuous variable in the multivariate model which also included the variables age, sex, systolic blood pressure (SBP), total cholesterol (TC) to high-density lipoprotein-cholesterol (HDL) ratio, glycated hemoglobin (HbA1c) and standard drink units (SDUs) of alcohol intake. The strength of the associations was considered as strong, moderate, and weak at the significance level of  $P < 0.01$ ,  $P = 0.01$  to  $0.05$ , and  $P = 0.06$  to  $0.10$  respectively. Stata version 12 was used for data analysis. Analysis was performed for completed ECG recordings only and thus there were no missing points.

This study was approved by the ethical review board of Nepal Health Research Council (NHRC) and the University of Otago, Human Ethics Committee.

### **Results**

A total population of study areas was 2576, of which study participants were selected from 1587 potential eligible participants aged 30 years or more. The study participants comprised a total of 521 HA residents at three altitude levels; 2800 m (N=165), 3270 m (N=61) and 3620 m (N=44) of the Mustang district and 2890 m (N=251) of the Humla district. More than 70% participants in Mustang and Humla were Tibetans and Indo-Aryans respectively. Particular ethnic groups amongst Tibetans were: Thakali, Tibetan Gurung and Lama; and for Indo-Aryans: Brahmin, Chhetri, and Dalit. Thirty six (6.9%) participants with completed questionnaires and BP measurements did not turn up for ECG recordings and bio-chemical tests. ECG reports were available for 485 participants. The overall non-response rate was 3.4%. The most

common reason for non-participation was unwillingness to provide blood sample due to the cultural belief of becoming sick. Participants are described in Table 2.

**Table 2: Description of study participants by altitude level**

	Mustang			Humla	P value
	2800 m	3270 m	3620 m	2890 m	
	(N=165)	(N=61)	(N=44)	(N=251)	
<b>Continuous variables</b>	<b>Mean (SD)</b>				
Age	50.3 (13.7)	55.4 (13.2)	48.3 (12.5)	42.9 (11.0)	<0.001
Average walk time/day (minute)	53.0 (44.8)	95.6 (79.9)	73.2 (53.0)	89.4 (89.6)	<0.001
<b>Categorical variables</b>					
	N/165* (%)	N/61* (%)	N/44* (%)	N/251* (%)	
Sex					0.47
Male	80 (48.5)	29 (47.5)	19 (43.2)	103 (41.0)	
Female	85 (51.5)	32 (52.5)	25 (56.8)	148 (59.0)	
Education					<0.001
No formal education/illiterate	67 (40.6)	41 (67.2)	29 (65.9)	168 (66.9)	
Less than primary	45 (27.3)	19 (31.1)	6 (13.6)	18 (7.2)	
Primary level completed	25 (15.1)	0 (0)	4 (9.1)	20 (8.0)	
Secondary level completed	28 (17.0)	1 (1.6)	5 (11.4)	45 (17.9)	
Occupation					<0.001
Govt. or nov-govt. employee	25 (15.1)	1 (1.6)	7 (15.9)	39 (15.5)	
Self-employed	86 (52.1)	6 (9.8)	14 (31.8)	21 (8.4)	
Agriculture/daily waged labour	41 (24.8)	39 (63.9)	21 (47.7)	135 (53.8)	
Unemployed/retired/homemaker	13 (7.9)	15 (24.6)	2 (4.5)	56 (22.3)	
Ethnicity					<0.001
Tibetan	132(80.0)	58 (95.1)	37 (84.1)	82 (32.7)	
Indo-Aryans	33 (20.0)	3 (4.9)	7 (15.9)	169 (67.3)	
High altitude residence					<0.001
For lifetime	148 (89.7)	59 (96.7)	38 (86.4)	246 (98.0)	
>10 years	17 (10.3)	2 (3.3)	6 (13.6)	2 (0.8)	
5 to 10 years	0 (0)	0 (0)	0 (0)	3 (1.2)	
Current smoker	17 (10.3)	2 (3.3)	4 (9.1)	97 (38.6)	<0.001
Current drinker	84 (50.9)	39 (63.9)	20 (45.4)	123 (49.0)	0.17
Hypertension or medication	76 (46.1)	25 (40.9)	24 (54.5)	73 (29.1)	<0.001
Overweight or obesity	81/143 (56.6)	16/60 (26.7)	21 (47.7)	52/251 (20.7)	<0.001
High TC/HDL ratio or medication	34/139 (24.0)	3/54 (5.6)	11/37(29.7)	46/167 (27.5)	<0.01
Diabetes or medication	15/142 (10.6)	2/61 (3.3)	6 (13.6)	6/172 (3.5)	0.01

\*Except where indicated; hypertension,  $\geq 140/90$  mmHg; overweight, body mass index  $\geq 25$  kg/m<sup>2</sup>; obesity, body mass index  $\geq 30$  kg/m<sup>2</sup>; high TC/HDL ratio,  $\geq 5.0$ ; diabetes, glycated hemoglobin (HbA1c)  $\geq 48$  mmol/mol.



More than a quarter of the study participants at the altitude of 2800 m, 3270 m and 3620 m were aged 60 years or more. There was evidence of a difference in age at the different altitude levels; Kruskal-Wallis test Chi-square (3 DF) 59.1,  $P < 0.01$ . Women comprised a greater proportion than men at all levels of altitude and overall 55.7% of study participants were women but there was no evidence this proportion was different by altitude level; Chi-square (3 DF) 2.5,  $P = 0.47$ . Most of the participants were illiterate or had no formal education and reported being born and living at HA for most of their lives. By self-report about half of the participants at all altitude stated they were current consumers of alcohol.

#### *Electrocardiographic analysis*

Arrhythmias: Three participants had *isolated ectopic beats* on their 12-lead ECGs; one atrial, one junctional and one ventricular. Four participants had clear evidence of *pre-excitation* of the ventricles (Wolff-Parkinson-White syndrome). Four participants showed prolonged atrioventricular (AV) nodal conduction (first degree AV block) with PR intervals varying between 205 and 286 msec (normal up to 200msec). One participant had left bundle branch block (LBBB) and six had right bundle branch block (RBBB) (three each complete and incomplete). Two participants, a man and a woman, had prolonged QT intervals; 470 and 490 msec.

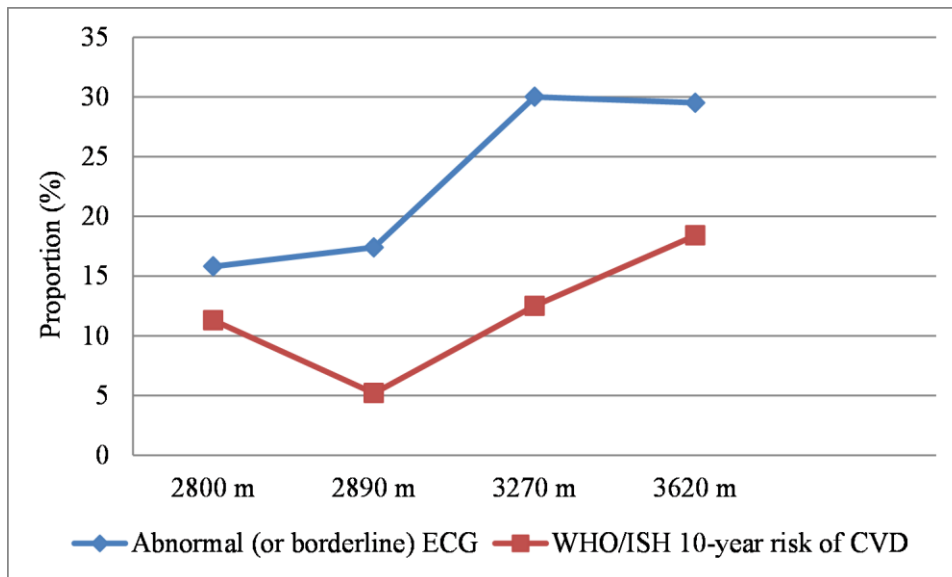
Morphological abnormalities: Two participants had tall peaked P waves suggesting right atrial hypertrophy. Three participants showed extreme axis deviation (arm lead electrode positions all verified as correct) with QRS axes between  $+185^\circ$  and  $+237^\circ$  suggesting possible congenital abnormalities and/or pulmonary hypertension. Twenty-six other participants showed right axis deviation (RAD), with QRS axes between  $92^\circ$  and  $143^\circ$ , of which two had right ventricular hypertrophy (RVH). Four others had left axis deviation (LAD), with QRS axes between  $-34^\circ$  and  $-85^\circ$ . No participant had Q waves to suggest past Q-wave MI. Thirteen had inverted T waves outside the accepted normal leads (III, aVR, V1), nine of these were of doubtful significance as they were in the antero-septal precordial leads V1 to V4. Two had inverted T waves in inferior leads (II, III and aVF) and two in aVL alone. Seventeen participants met Sokolow-Lyon criteria for LVH, with the largest S in V1 or V2 plus the largest R in V5 or V6 greater than 3.5mV, but only one of these met the stricter definition of Romhilt and Estes (six points), three others were borderline (four points). Two additional participants had down-sloping ST segments with no other cause but suggestive of hypertrophy.

Overall, none of the participants showed a definite electrocardiographic evidence of CHD. Overall 27/485, 5.6% (95% confidence interval [CI] 3.7 to 8.0), of the participants gave a self-report of a history of CHD confirmed by a medical doctor. The prevalence of CHD according was 17/212 (8.0%) in men and 10/273 (3.7%) in women, Chi-square (1 DF) 4.3,  $P = 0.04$ . Altogether 95/485, 19.6% (95% CI 16.1 to

23.4), of the participants had an abnormal (or borderline abnormal) ECG. The main abnormalities were: RAD in 26/485, 5.4% (95% CI 3.5 to 7.7) and LVH by voltage criteria in 17/485, 3.5% (95% CI 2 to 5.5). Of 26 participants with RAD, 16 (61.5%) were men and 13 (50%) were from the age-group 30-39 years. Among 17 participants with LVH, 11 (64.7%) were women, 12 (70.6%) were aged 50 years or more, and 11 (70.6%) were hypertensive or on anti-hypertensive treatment.

Participants resident living in the Mustang district at altitudes of 2800 m, 3270 m and 3620 m mostly had abnormalities on the left side of the heart. For Humla participants at 2890 m the main reasons for the abnormality were mostly on the right side. For example, Mustang participants had 15/243 (6.2%) ECG findings of LVH, LAD, or LBBB; compared to 7/242 (2.9%) Humla participants; Chi-square (1 DF) 3.01, P=0.08. In Humla, 21/242 (8.7%) ECG reports had RAD, RBBB, or right atrial hypertrophy; compared to 13/243 (5.3%) in the Mustang participants; Chi-square (1 DF) 2.06, P=0.15.

Figure 1 shows the proportions of participants with abnormal (or borderline abnormal) ECG and with WHO/ISH 10-year risk of fatal or non-fatal cardiovascular events (MI or stroke) of greater than 10% by altitude level. More than one-fourth of the participants at 3270 m (30%) and 3620 m (29.5%) had an abnormal (or borderline abnormal) ECG; nearly two-fold higher than those living at 2800 m (15.8%) and 2890 m (17.4%). Residents at higher altitudes of 3270 m and 3620 m were also more likely to have a predicted greater than 10% risk of a fatal or non-fatal major cardiovascular event over the next 10 years.



**Figure 1: Proportions of abnormal (or borderline) ECG and WHO/International Society of Hypertension 10-year risk of fatal or non-fatal cardiovascular disease (CVD) events by >10% at each altitude level.**

There was a moderate association between the probability of an abnormal (or borderline abnormal) ECG and altitude when adjusted for potential confounding variables in a multivariate logistic model (Table 3). There were 99 missing data points in multivariate model and there were no statistically significant differences between ECG reports (abnormal or normal) and data status (missing or not missing).

**Table 3: Estimates of the odds ratio for abnormal or borderline ECG by altitude in a multivariate logistic model and associations for confounding variables**

<b>Variables and Comparison</b>	<b>Odds ratio (95% CI)</b>	<b>P value</b>
Altitude (per 1000 m higher)	2.83 (1.07 to 7.45)	0.03
Systolic blood pressure (per 10 mmHg higher)	1.25 (1.08 to 1.44)	0.002
TC to HDL ratio (per unit ratio higher)	0.93 (0.75 to 1.15)	0.49
HbA1c (per mmol/mol higher)	1.02 (0.99 to 1.05)	0.49
Smoke tobacco (yes compared to no)	1.69 (0.97 to 2.94)	0.06
Age (per decade older)	1.14 (0.91 to 1.43)	0.24
Sex (men compared to women)	1.69 (0.97 to 2.94)	0.06

## **Discussion**

The prevalence of CHD in this HA population is estimated to be 5.6%. This is based on personal history alone as no participant had ECG evidence of past Q-wave MI. The prevalence was higher in men. The prevalence of an abnormal (or borderline abnormal) ECG was between 16 and 30% in different HA areas sampled for this study from Nepal. After adjusting for the important confounding variables the odds of having an abnormal (or borderline abnormal) ECG increased five-fold for every 1000 m increment in altitude. This association was particularly strong for men. RAD and LVH were the most common abnormalities.

Our result is strikingly similar to available evidence derived from ECG recordings at low altitude of Nepal, China, and Asia; and close to that of rural areas of South Asian countries. Electrocardiographic evidence for CHD at the population level is sparse in Nepal to allow comparisons for our study results. Based on ECG and documented medical history, only one population-based sample survey has been reported at low altitude of Nepal and amongst men only documented the prevalence of CHD at 5.7%<sup>11</sup>. A systematic review of global studies of CHD prevalence based on ECG reports or documented medical history in adults and including publications through to 2014 estimated the prevalence of CHD in Asia at 5.8%, between 5.6% and 5.9% in rural China, between 1.4% to 4.6% in rural areas of India, 3.4% in rural area of Bangladesh, and 5.1% in urban Pakistan<sup>12</sup>. Although there have been few population-based studies

on CHD in HA populations living at 2500 m or more worldwide, our findings are consistent with the majority of hospital-based reports<sup>13 14</sup> but in contrast to few others<sup>15 16</sup>. The most recent systematic analysis of the burden of disease in Chinese provinces showed that the age-standardized mortality rate from CHD in Tibet (average altitude of 4500 m from sea level) was significantly lower in men but similar in women when compared with those living at lower altitudes<sup>17</sup>. The prevalence of ECG abnormalities in this study was also lower when compared with other ECG based studies in HA natives<sup>18-20</sup>. It should be noted that studies reporting markedly higher prevalence were conducted in higher levels of altitude compared to our study and this may partly explain the differences.

A review of the English language literature on ECG recordings at different levels of altitude above 2500 m identified no studies. Thus our finding of significant association between abnormal (or borderline) ECG and altitude is difficult to compare with other studies. However, one study did report increasing rates of RAD with increasing levels of altitude in HA setting<sup>21</sup>. In our study, there was a positive relationship between SBP and altitude in a multivariate model adjusting for potential confounders. This relationship may explain the increased prevalence of an abnormal (or borderline) ECG with increasing levels of altitude. For example, more than two-thirds of the participants with LVH were hypertensive or on treatment. There are important differences in the prevalence of overweight or obesity, diabetes, and walking time by altitude level which may be attributed to urban (2800 m and 3620 m) and rural (2890 m and 3270 m) residential settings. The main reason behind low prevalence of current smoker in Tibetan dominant study areas is cultural non-preference to tobacco smoking.

The low prevalence of CHD in the study reported here may have several possible explanations. The reasons proposed for possible cardioprotection in HA residents includes activation of a transcription-modulator hypoxia inducible factor (HIF-1) which induces the expression of multiple genes with cardioprotective properties<sup>22</sup>. High levels of vitamin D due to an exponential increase in ultraviolet B (UVB) light at HA<sup>23</sup>, improvement in coronary vasculature through increased number of branches and peripheral vessels<sup>24</sup>, increased levels of physical fitness and low level of air pollution<sup>25</sup> could also provide cardioprotection. A 'healthy individuals effect' is an alternative explanation to these findings from non-experimental studies of illness at HA because sick people often migrate to LA for better treatment<sup>26</sup>.

It is plausible that the CHD related risk pattern at HA is also ethnicity specific due to varying degree of adaptation, physiological response, lifestyle and genetic factors. Contrasting cardiopulmonary responses to HA exposure among the largest HA populations; Tibetans, Andeans, and Aymaras have been documented<sup>27</sup>. The finding in this study that abnormal or borderline abnormal ECG recordings on the left side of the heart were more prevalent among those of the Tibetan ethnicity (Mustang district) whereas

right sided abnormalities were more frequent in Humla district with majority of Indo-Aryan participants, may reflect this phenomena. The ECG abnormalities suggesting right heart abnormalities may reflect increased pulmonary vascular resistance; well reported at greater level among HA dwellers less adapted with hypoxia such as Andeans or North Americans<sup>19 28</sup> but at lower level in those with high degree of adaptation such as Tibetans<sup>29</sup>. The high prevalence of RAD in our study, particularly in Humla participants, also suggests a possible early indication of pulmonary HT or RVH. A previous report suggested RAD could be up to four times more prevalent at HA compared to sea level presumably correlating with differences in pulmonary artery pressure<sup>30</sup>.

As far as we are aware, this is the only study which has provided detailed information on CHD health and comprehensively assessed cardiovascular risk among HA natives in Nepal. Limitations of this study included possible bias due to the purposive selection of the study areas on the basis of altitude levels, population density and logistical convenience. Validity of the self-report of CHD is also questionable particularly due to the poor literacy rate of the participants. Reported prevalence might not reflect true incidence due to the 'healthy individual effect'. Difference in temperature in Mustang and Humla districts during data collection period may confound observed association. There were possible confounding variables which are commonly relevant for CHD. There might be other unmeasured confounding variables particularly related to the HA populations.

In conclusion, our findings based on personal history and ECG recordings suggest that HA populations of this study area had a prevalence of CHD comparable to that seen in low altitude populations. However, we demonstrated moderate evidence of an association between participants having an abnormal (or borderline abnormal) ECG and altitude in our HA populations in Nepal. The risk pattern may vary by ethnicity; increased pulmonary vasoconstriction reflected by RAD in Indo-Aryans (Humla district) and HT induced LVH in participants of Mustang with Tibetan ancestry. Clinicians should be aware of differential effects of HA living on cardiovascular health by ethnicity. More useful epidemiology may depend on better information infrastructure in the relevant population (e.g. improvement in registration of births, deaths and marriages). Directly comparable data compilation from residents living at low and high altitudes would add clarity to attribution of health status to altitude *per se*.

### **1. What is already known about this subject?**

The balance of risks and benefits for cardiovascular health in permanent residents of high altitude is uncertain. Different patterns of adaptation and physiological responses against hypobaric hypoxia as well as different lifestyle practices of high altitude populations probably contribute.

### **2. What does this study add?**

This is first ECG-based study examining evidence of coronary heart disease in high altitude populations of Nepal. The prevalence of coronary heart disease in high altitude populations may be comparable with those from low altitude residents. However, ECG abnormalities may increase by altitude and the risk pattern may vary by ethnicity; mostly on the right side of the heart in Indo-Aryans and on the left side in Tibetans.

### **3. How might this impact on clinical practice?**

Clinicians should be aware of differential effects of high altitude living on cardiovascular health by ethnicity.

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**Author's Contribution:** All authors contributed to study design. NA collected the data, performed statistical analysis and prepared the first draft of the manuscript. YKDB helped with data collection and MW helped with the statistical analysis. SM reviewed and interpreted the ECG reports. All authors contributed intellectually to the revision of the article and approved the final version.

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