HIGH ALTITUDE MEDICINE & BIOLOGY
Volume 12, Number 1, 2011

DOI: 10.1089/ham.2010.1050

# Lipid Profile and Its Association with Risk Factors for Coronary Heart Disease in the Highlanders of Lhasa, Tibet

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## Abstract

Sherpa, Lhamo Y., Deji, Hein Stigum, Virasakdi Chongsuvivatwong, Ouzhu Luobu, Dag S. Thelle, Per Nafstad, and Espen Bjertness. Lipid profile and its association with risk factors for coronary heart disease in highlanders of Lhasa, Tibet. *High Alt. Med.* Biol. 12:57–63, 2011.—The aim of this study was to determine the prevalence of abnormal lipid levels and its association with selected coronary heart disease (CHD) risk factors in the Tibetan population living at 3660 meters above sea level in Lhasa, Tibet. Three hundred seventy one randomly selected male and female, aged 30 to 70 yr took part in the study. Based on the National Cholesterol Education Programme (NCED) adult treatment panel ATP-III 2004 criteria, the age-adjusted prevalence of hypertriglyceridemia was 12.0%; high triglycerides (TG), 33.4%; high low-density lipoprotein cholesterol (LDL-C), 4.8%; and low high-density lipoprotein cholesterol (HDL-C); 24.3%. After adjusting for age, sex, smoking, alcohol, physical activity, diet, hemoglobin (Hb) concentration, and systolic and diastolic blood pressure (BP), an increase in waist-to-hip ratio (WHR) by 0.1 unit was associated with a statistically significant increase in TG, total cholesterol (TC) and LDL-C by 0.25 mmol/L, 0.24 mmol/L, and 0.18 mmol/L, respectively. Female gender increased HDL-C by 0.18 mmol/L when compared with males. Age-adjusted prevalences of Framingham CHD risk score for males and females were 16.3% and 0.6%, respectively. This study demonstrated a high prevalence of hypertriglyceridemia in males, a higher prevalence of low HDL-C in females, and a high hypercholesterolemia prevalence in both genders. However, further longitudinal studies assessing CHD risk factors in high altitude natives are required.

**Key Words:** Tibetans; lipid profile; highlanders; heart disease; obesity

## Introduction

Together with elevated blood pressure, obesity, and diabetes mellitus, dyslipidemia is a component of the metabolic syndrome and associated with increased coronary heart disease (CHD) risk (Lehto et al., 1997; Sarwar et al., 2007). There are clear patterns that show how the different lipid components are linked to CHD risk factors, such as elevated blood pressure, smoking, low physical activity, obesity, and unhealthy food habits (Freedman et al., 1986; Craig et al., 1989; Bonaa et al., 1991; Neuhouser et al., 2002; Mohanna et al., 2006; de Campos et al., 2010). These patterns are well established in both high- and low-income populations living at low altitude, but studies from high altitude populations are scarce. Worldwide, approximately 140 million people live throughout their lives at altitudes >2500 m above sea level, and more than 17 million live above 3500 m (Huddleston et al., 2003). Most of these high altitude populations are poor, and they will be at various levels of economic development, disease transition, and urbanization. Biological adaptation to tough climate and hypobaric hypoxia and genes selected to allow metabolic efficiency (Hancock et al., 2008),may have influenced how CHD risk factors are related to each other at high altitudes (de Koning et al., 2008; Hancock et al., 2008).

The aims of the present study were to estimate the prevalence of abnormal lipid levels (high- and low-density lipoprotein

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cholesterol, triglycerides, and total cholesterol) in 30- to 70-yr-old male and female Tibetans living at an altitude of 3660 m above sea level and to investigate the relationship between blood lipids and selected CHD risk factors. Based on the findings, we estimated the 10-yr coronary heart disease risk for this population using the Framingham risk score.

## Materials and Methods

### *Study population*

All the study participants were of Tibetan descent and lived in a Lhasa municipality, Tibet Autonomous Region (TAR), located at an altitude of 3660 m above sea level. Some of these urban participants still practice traditional agriculture and animal husbandry. However, as a result of economic development and marked lifestyle heterogeneity, economic inequality has emerged in this community, with some individuals involved in wage-earning employment and others completely dependent on subsistence activities. The staple diet of an ordinary Tibetan in Tibet is yak meat, mutton, barley, flour, and dried cheese. The main beverage is brick tea flavored with butter and salt.

The present cross-sectional study was conducted in Cheng Guan district, Lhasa municipality from September through December 2006. The temperature during the data- collection period ranged from 7° to 10°C. Four resident committees were randomly selected out of 28 from the Cheng Guan district. A list of individuals residing in the selected resident areas was obtained from the registration office of the residence committee. Out of 1457 men and women in the list (480 men and 977 women), aged between 30 to 70 yr, 537 (219 men and 318 women) were randomly selected and invited to participate in the survey. Individuals mentally or physically unfit to undergo the study were excluded before informed consent was signed.

### *Data collection*

A personal invitation letter was sent to the subjects 3 days before the study to explain the objectives of the study and provide information about attending place, time, and procedures. Data collectors included a team of trained teachers, a physician, and laboratory personnel from Tibet University Medical College. The participants were asked to come to one of the houses of the residential committee after night fasting for 8 to 12 h abstaining from any alcohol intake the previous night. Data collection included an interview questionnaire adapted from the WHO MONICA project. Some of the questions were modified according to local conditions. Further, a clinical examination, including BP measurement and WHR, was performed. Finally, venous blood was drawn for the measurement of blood lipids (TG, TC, LDL-C, and HDL-C), and capillary blood was drawn for the measurement of hemoglobin Hb concentration. BP was measured 3 times on the right arm using a standard mercury sphygmomanometer after at least 5 min rest in a sitting position. Waist circumference was measured at the midpoint between the lower costal margin and superior iliac crest after exhaling. Hip girth was measured at the point where the buttocks extended the maximum. WHR was calculated by dividing waist circumference by hip girth. A 10-mL venous blood extraction was made with sterilized syringes and slowly transferred into glass tubes without anticoagulants. Blood samples were clotted at room temperature. They were sent to a clinical laboratory in Lhasa and centrifuged at 2000 rpm for 15 min within 2 h the same morning. The serum thus obtained was analyzed on the same day for TG, TC, LDL-C, and HDL-C using an automatic biochemistry analyzer (Hitachi, 7060, Tokyo, Japan). TG and TC concentrations were determined enzymatically using GPO-PAP and COD-CE-PAP methods, respectively. Concentrations of HDL-C and LDL-C were measured by direct method. The reagents were obtained from Sichuan Maker Biotechnology Co. Ltd., Chengdu, China. For quality control, duplicate serum samples were stored at $-80^{\circ}$c and later airlifted on Dry Ice to a reference laboratory (Central Clinical laboratory of Fu Wai hospital, Beijing, China). Hb concentration was measured with capillary blood from a finger using a portable Hb spectrophotometer (HemoCue Hb 201 analyzer, HemoCue, Angelholm, Sweden). The machine was calibrated each morning with a standard liquid.

### *Variables*

Lipid profile was defined according to the criteria contained in the report of the National Cholesterol Education Programme (NCEP) Adult Treatment Panel (ATP)-III (Grundy et al., 2004), which defines lipid profile as follows: TG: $\geq$1.69 mmol/L; borderline high TC: 5.17–6.19 mmol/L; high TC: $\geq$6.20 mmol/L; high LDL-C: 4.13–4.90 mmol/L; very high LDL-C: $\geq$4.91 mmol/L; low HDL-C: $<$1.03 mmol/L in men and $<$1.28 mmol/L in women. Abdominal obesity was defined at WHR $>$0.95 in males and WHR $>$0.8 in females. Blood pressure was analyzed following the MONICA standard (Hense et al., 1995). An average of second and third BP measurements was used for analysis, rejecting the first. Alcohol consumption was defined as "yes" if a person drank alcohol regularly for at least 5 days a week; otherwise, "no." Smoking was classified as "yes" if a person smoked daily or occasionally over the past year; otherwise, "no." Physical activity was established using the criteria of Ford and colleagues (1991) by adding up activity at home and at work, time spent walking other than leisure and work, and time spent in leisure activities. Global physical activity (WHO, 2009) was calculated by multiplying the metabolic equivalent of tasks (Mets) of each activity by the number of hours per week and by the individual's weight in kilograms; it was expressed in kcal/week. A dietary questionnaire was developed on the basis of food habits practiced each day over a period of least 1 month. Subjects were also classified into having a "healthy diet" if the diet included fruits, fresh vegetables, and white meat each day; "unhealthy" if the diet included red meat, full-fat milk, and no fruits and vegetables each day; and "moderately healthy" if the diet alternated between healthy and unhealthy. CHD risk was calculated using Framingham CHD risk scores (Wilson et al., 1998). Sex-specific prediction algorithms accounted for age, blood pressure, cigarette smoking, and levels of HDL-C and LDL-C. Subjects were defined as at no CHD risk when they had $<$10% risk in 10 yr. Those having 10% risk in 10 yr were defined as having a CHD risk (moderate to elevated).

### *Statistical analysis*

Data were analyzed using R 2.9.2. (R Development Core Team, 2009). The prevalence of abnormal lipid values were age-adjusted to the WHO world standard population (Ahmad et al., 2001). Means and standard deviation of each serum

lipid were computed and displayed with breakdown by demographic and behavioral characteristics. Student *t* test and one-way analysis of variance were used to test the initial difference among the subgroups. Linear regression was then used to investigate the association between selected lipid variables (TG, TC, LDL-C, and HDL-C) and explanatory variables adjusted with one another (i.e., age, gender, smoking, alcohol consumption, physical activity, systolic blood pressure (SBP), diastolic blood pressure (DBP), Hb, diet, and obesity. The estimates and 95% confidence interval (CI) of the coefficients were displayed. A $p$ value of $\leq 0.05$ or 95% CI was considered statistically significant. Sample size calculation was based on a prevalence study of hypertension in Lhasa (Zaxi et al., 2003). For a confidence interval of 95%, an estimated prevalence of hypertension was 40% with a delta of $\pm 0.04$; the estimated sample size was 537 subjects. However, as a result of nonrespondents in our study the final sample size was 371.

## Results

Three hundred seventy-one subjects (69%) participated. The main reason for non-participation was fear of venepuncture. The mean ages of males and females in the study were 47.8 and 48, respectively.

### *Blood lipids*

Table 1 shows the prevalence of abnormal lipid values in males, females, total, and total standardized to the WHO world standard population. The crude prevalence of hypertriglyceridemia was higher in males (18.8%) than in females (8.3%), while the prevalence of hypercholesterolemia was high in both genders (31.0% in males and 32.3% in females, respectively). The prevalence of low HDL-C was high at 24.3% and higher among females than males.

Table 2 shows the crude mean values of TG, TC, LDL-C, and HDL-C by selected CHD risk factors. Mean TC and LDL-C increased significantly with increasing age, whereas mean TG was higher in males than females and increased in those having higher Hb levels. However, this trend was erratic for TC. Except for HDL-C, mean values of TG, TC, and LDL-C were higher among those with abnormal WHR. Mean values of TG, TC, LDL-C, and HDL-C standardized to WHO world standard population was not different from the crude values (results not shown).

Table 3 displays adjusted coefficients from linear regression analyses of TG, TC, LDL-C, and HDL-C by selected CHD risk factors. A slight increment in TC and LDL-C was noted with age and DBP. However, an inverse association occurred with SBP. A small but significant association was also seen between TG and Hb. The largest increase in TG, TC, and LDL was noted with WHR. An increase in WHR by 1 unit was associated with an increase in TG by 2.55 mmol/L, in TC by 2.37 mmol/L, and in LDL-C by 1.85 mmol/L, respectively. Female gender was the only factor associated with HDL-C, increasing it by 0.18 mmol/L when compared with males.

### *Framingham risk score*

The overall prevalence of moderate and higher (i.e., $\geq 10$ %) 10-yr CHD risk among men and women between 30 and 69 yr of age was 20.1% and 0.9%, respectively. However, after age adjustment to the WHO world standard population, the estimates for men and women were 16.3% and 0.6% respectively.

## Discussion

This cross-sectional study is the first to report the prevalence of abnormal lipid distribution in the Tibetan population of TAR. The main findings were a high prevalence of hypertriglyceridemia in males, a higher prevalence of low HDL-C in females, and a high hypercholesterolemia prevalence in both genders. In spite of the observed association between TG, TC, and LDL-C with age, Hb, DBP, and SBP, the age-related changes were minimal. The most profound increase in TG, TC, and LDL-C was noteworthy for increased units of WHR. The prevalence of CHD risk based on the Framingham risk score adjusted to WHO standard world population was high among men and low in women.

Results from two high altitude populations support our findings of a high prevalence of hypercholesterolemia and low HDL-C. Mohanna and colleagues (2006) determined a

Table 1. Crude Prevalence of Abnormal Serum Lipid Values[a] in 30- to 70-Year-old Tibetans by Gender; Totals Adjusted to the WHO World Standard Population

| *Serum lipids* (n = *371*) | *Male* (n = *139*) n *(%)* | *Female* (n = *232*) n *(%)* | *Total* (n = *371*) n *(%)* | *Total adjusted* (n = *371*) *% (95% CI)* |
|---|---|---|---|---|
| Total cholesterol (mmol/L) | | | | |
| Borderline high (5.17–6.19) | 31 (23.3) | 60 (26.2) | 91 (24.5) | 27.78 (18.6, 37) |
| High (≥6.20) | 10 (7.5) | 14 (6.1) | 24 (6.5) | 5.6 (−3.6, 14.7) |
| Hypercholesterolemia (total) | 41 (30.8) | 74 (32.3) | 115 (31.0) | 33.52 (24.8, 42.1) |
| High density lipoprotein (mmol/L) | | | | |
| Low HDL-C (<1.03 in men Low HDL-C (<1.28 in women) | 21 (15.1) | 62 (26.7) | 83 (22.4) | 24.34 (15.1, 33.5) |
| Low density lipoprotein (mmol/L) | | | | |
| High LDL-C (4.13–4.90) | 9 (6.8) | 5 (2.2) | 14 (3.9) | 3.72 (−6.1,13.5) |
| Very high LDL-C (≥4.91) | 2 (1.5) | 2 (0.9) | 4 (1.1) | 1.03 (−8.7, 10.7) |
| Triglycerides (mmol/L) | | | | |
| Hypertriglyceridemia (≥1.69) | 25 (18.8) | 19 (8.3) | 44 (12.2) | 11.97 (2.3, 21.5) |

[a]National Cholesterol Education Programme (NCEP) adult treatment panel (ATP)-III criteria (Grundy et al., 2004).
CI, confidence interval.

Table 2. Crude Mean Values of Triglycerides (TG), Total Cholesterol (TC), Low-Density Lipoprotein Cholesterol (LDL-C), and High-Density Lipoprotein Cholesterol (HDL-C) in 30- to 70-Year-Old Tibetans by Selected Coronary Heart Disease Risk Factors

| | | *TG* | | *TC* | | *LDL-C* | | *HDL-C* | |
|---|---|---|---|---|---|---|---|---|---|
| | n = *371* | *Means (SD)* | p *value* | *Means (SD)* | p *value* | *Means (SD)* | p *value* | *Means (SD)* | p *value* |
| *Variable:* | | *1.1 (0.6)* | | *4.7 (1)* | | *2.8 (0.7)* | | *1.5 (0.4)* | |
| Age (yr) | | | 0.08 | | 0.001 | | 0.04 | | 0.55 |
| 30–39 | 99 | 1.5 (0.5) | | 4.39 (0.9) | | 2.64 (0.7) | | 1.44 (0.5) | |
| 40–50 | 125 | 1.20 (0.6) | | 4.75 (1) | | 2.84 (0.7) | | 1.46 (0.4) | |
| 51–60 | 81 | 1.6 (0.4) | | 4.86 (0.8) | | 2.91 (0.6) | | 1.51 (0.5) | |
| 61–70 | 66 | 1.24 (0.8) | | 5.10 (1.3) | | 3.6 (0.9) | | 1.52 (0.5) | |
| Gender | | | 0.001[g] | | 0.69 | | 0.275 | | 0.108 |
| Male | 139 | 1.27 (0.6) | | 4.71 (1.1) | | 2.9 (0.8) | | 1.43 (0.5) | |
| Female | 232 | 1.06 (0.5) | | 4.75 (1) | | 2.81 (0.7) | | 1.50 (0.4) | |
| Smoking | | | 0.33 | | 0.459 | | 0.626 | | 0.696 |
| Yes | 90 | 1.19 (0.5) | | 4.67 (1.1) | | 2.81 (0.9) | | 1.49 (0.5) | |
| No | 281 | 1.12 (0.6) | | 4.76 (1) | | 2.85 (0.7) | | 1.47 (0.4) | |
| Alcohol | | | 0.773 | | 0.28 | | 0.213 | | 0.105 |
| Yes | 164 | 1.14 (0.5) | | 4.67 (1) | | 2.78 (0.7) | | 1.52 (0.5) | |
| No | 207 | 1.13 (0.6) | | 4.79 (1.1) | | 2.88 (0.8) | | 1.44 (0.4) | |
| PA[a] (kcal/wk) | | | 0.288 | | 0.26 | | 0.35 | | 0.452 |
| <2000 | 241 | 1.11 (0.5) | | 4.69 (1) | | 2.81 (0.7) | | 1.45 (0.5) | |
| ≥2000 | 130 | 1.18 (0.7) | | 4.82 (1) | | 2.89 (0.8) | | 1.49 (0.4) | |
| SBP[b] ≥140 (mmHg) | | | 0.563 | | 0.88 | | 0.1 | | 0.221 |
| Yes | 60 | 1.09 (0.7) | | 4.72 (0.8) | | 2.69 (0.6) | | 1.54 (0.5) | |
| No | 311 | 1.14 (0.6) | | 4.74 (1.1) | | 2.87 (0.8) | | 1.46 (0.4) | |
| DBP[c] ≥90 (mmHg) | | | 0.833 | | 0.80 | | 0.23 | | 0.514 |
| Yes | 59 | 1.15 (0.7) | | 4.71 (0.8) | | 2.73 (0.6) | | 1.51 (0.5) | |
| No | 312 | 1.13 (0.6) | | 4.74 (1.1) | | 2.86 (0.8) | | 1.47 (0.4) | |
| Hb[d] (mg/dL) | | | 0.045[g] | | 0.009[g] | | 0.386 | | 0.843 |
| 6–12 | 27 | 0.95 (0.4) | | 4.31 (1) | | 2.72 (0.8) | | 1.49 (0.4) | |
| 12.1–18 | 301 | 1.13 (0.6) | | 4.81 (1) | | 2.86 (0.7) | | 1.47 (0.4) | |
| 18.1–25 | 41 | 1.31 (0.7) | | 4.44 (1.1) | | 2.72 (0.7) | | 1.51 (0.6) | |
| Diet | | | 0.398 | | 0.18 | | 0.058 | | 0.931 |
| Healthy | 97 | 1.44 (0.6) | | 4.63 (1) | | 2.79 (0.7) | | 1.46 (0.5) | |
| Mod H[e] | 160 | 1.15 (0.5) | | 4.85 (1.1) | | 2.94 (0.8) | | 1.48 (0.4) | |
| Unhealthy | 114 | 1.17 (0.6) | | 4.67 (0.9) | | 2.73 (0.7) | | 1.48 (0.4) | |
| WHR[f] (unit) | | | 0.013[g] | | 0.002[g] | | 0.02[g] | | 0.101 |
| Yes | 200 | 1.20 (0.6) | | 4.89 (1) | | 2.92 (0.8) | | 1.51 (0.5) | |
| No | 171 | 1.05 (0.5) | | 4.55 (1) | | 2.74 (0.7) | | 1.43 (0.4) | |

[a]Physical activity; [b]systolic blood pressure; [c]diastolic blood pressure; [d]hemoglobin; [e]moderately healthy; [f]waist-to-hip ratio >0.95 in males and >0.8 in females.

hypercholesterolemia prevalence of 34.3% and a prevalence of low HDL-C at 30.4% in high altitude men and women of Peru (4100 m). Likewise, Santos and collegues (2001) from Northern Chile (2000 to 4500 m) report a prevalence of hypercholesterolemia at 36.8% for men and 37.4% in women and low HDL-C at 26.3% for men and 24.4% in women, respectively. However, in contrast to our findings, the prevalence of hypertriglyceridemia in Peru was considerably higher at 53.9% (Mohanna et al., 2006). A very high overweight–obese prevalence (74.2%) and abnormal waist circumference (77.4%) among Peruvians when compared with Tibetans possibly explains the difference in TG. Nevertheless, it should be noted that Tibetans are undergoing an epidemiological transition (Xu et al., 2008), which may influence health behaviors and finally health changes at population level.

Mean TG and TC levels in Tibetans was slightly lower compared with other high altitude permanent residents (Temte, 1996; Santos et al., 2001; Baibas et al., 2005; Mohanna et al., 2006). However, mean LDL-C and HDL-C levels were slightly higher. These disparities can be owing to ethnic differences (de Koning et al., 2008; Zhang et al., 2010) and behavioral risk factors such as smoking (Freedman et al., 1986; Craig et al., 1989) and obesity (Mohanna et al., 2006).

Studies in animals and humans have consistently shown an association between serum iron concentration, TG, and TC (Bottiger and Carlson, 1972; Choi et al., 2001). Concentration of red blood cells was affected by cholesterol synthesis or its mobilization from tissue to plasma. Cholesterol, triglycerides, and Hb values were also influenced by changes in plasma volume (Bottiger at al., 1972; Choi et al., 2001). In a study by Salonen and colleagues (1992), high body iron stores were related to CHD. Higher mean TG and TC with increasing Hb level in our study may be explained by a higher serum iron concentration, which is considered a risk factor for myocardial infarction (Salonen et al., 1992; Morrison et al., 1994). However, Tibetans rarely exhibit higher Hb levels (Wu at al., 2005), possibly for being the oldest natives living at high altitudes and having a genetic

Table 3. Adjusted[a] Coefficients (Coeff.) from Linear Regression Analyses of the Association between Triglycerides (TG), Total Cholesterol (TC), Low-Density Lipoprotein Cholesterol (LDL-C), and High-Density Lipoprotein Cholesterol (HDL-C) with Selected Coronary Heart Disease Risk Factors in 30- to 70-Year-Old Tibetans, $N = 371$

| | *TG* | *TC* | *LDL* | *HDL* |
|---|---|---|---|---|
| *Variables* | *Coeff. (95% CI)* | *Coeff. (95% CI)* | *Coeff. (95% CI)* | *Coeff. (95% CI)* |
| Expected values[b] | 0.93 (0.17, 1.68) | 4.05 (2.49, 5.6) | 2.60 (1.34, 3.85) | 1.22 (0.35, 2.08) |
| Age | | | | |
| per year | 0.001 (−0.004, 0.007) | 0.02 (0.01, 0.03)* | 0.01 (0.007,0.022)* | 0.003 (−0.0008, 0.008) |
| Gender | | | | |
| Female | 0.05 (−0.13, 0.23) | 0.29 (−0.04, 0.62) | −0.04 (−0.28, 0.20) | 0.18 (0.04, 0.33)* |
| Smoking | | | | |
| Yes | −0.02 (−0.19, 0.15) | 0.19 (−0.12, 0.51) | 0.03 (−0.20, 0.26) | 0.13 (−0.01, 0.27) |
| Alcohol | | | | |
| Yes | 0.03 (−0.08, 0.15) | 0.07 (−0.14, 0.28) | 0.07 (−0.08, 0.23) | −0.08 (−0.18, 0.01) |
| PA[c] (kcal/week) | 0.03 (−0.012, 0.07) | 0.006 (−0.07, 0.08) | −0.01 (−0.06, 0.04) | −0.01 (−0.05, 0.02) |
| SBP[d]/(mmHg) | −0.001 (−0.007, 0.003) | −0.012 (−0.02,-0.002)* | −0.01 (−0.02, −0.003)* | 0.001 (−0.002, 0.006) |
| DBP[5] (mmHg) | 0.00007 (−0.008, 0.008) | 0.02 (0.005, 0.034)[i] | 0.01 (0.001, 0.02)[i] | −0.0006 (−0.005, 0.007) |
| Hb[f]/(mg/dL) | 0.03 (0.0004, 0.06)* | 0.003 (−0.05, 0.05) | −0.02 (−0.06, 0.01) | −0.002 (−0.02, 0.03) |
| Diet | | | | |
| Mod.H.[g] | 0.04 (−0.09, 0.19) | 0.12 (−0.13, 0.38) | 0.10 (−0.08, 0.28) | −0.005 (−0.11, 0.12) |
| Unhealthy | 0.01 (−0.14, 0.16) | −0.06 (−0.33, 0.21) | −0.12 (−0.32, 0.08) | −0.002 (−0.12, 0.13) |
| WHR[h] (unit) | 2.55 (1.65, 3.44)* | 2.37 (0.8, 3.97)* | 1.85 (0.67, 3.02)* | 0.27 (−0.44,0.98) |

CI, confidence interval.

[a]Adjusted to age, gender, smoking, alcohol; [b]at age 35; gender, male; smoking, no; alcohol, no; PA = 2000 kcal/week; SBP = 120 mmHg; DBP = 90 mmHg; Hb = 15 mg/dL; WHR = 0.7 unit; [c]physical activity; [d]systolic blood pressure; [e]diastolic blood pressure; [f]hemoglobin and diet; [g]moderately healthy; [h]waist-to-hip ratio.

*$p \leq 0.05$.

predisposition (Simonson et al., 2010). Nonetheless, this finding may be of importance for other high altitude natives exhibiting polycythemia.

This study also found an association between blood pressure and TC and LDL. There was an inverse association with SBP, but a positive one for DBP (Bonaa et al., 1991). Differences in blood pressure with a significantly higher DBP among high altitude natives and no difference in SBP between low and high altitude natives have been reported (Smith, 1999). Hypoxia and cold temperature increase plasma catecholamines (Moncloa et al., 1965). Because catecholamines are likely to be involved in the development of atherosclerosis, it seems paradoxical to find the inverse relation between SBP with TC and LDL-C. However, lower oxygen tension decreases the effects of catecholamine with regard to their hypertensive action (Surtshin et al., 1948; Vanloo et al., 1948). The reduction in TC and LDL-C may be the direct effect of lipolysis stimulation by catecholamines (Okuda at al., 1966).

The massive economic transition in the TAR, from traditional ways of living to modern lifestyle may have brought changes in diet and a lower physical activity pattern that contributes to a sedentary life-style and obesity. It is well known that an energy expenditure of ≥2000 kcal/week is considered a cardioprotective threshold (Pate et al., 1995). However, in our study, 65% of people had energy expenditure of less than 2000 kcal/week. Increase in abdominal obesity with age has been demonstrated for Peruvian highlanders and has also been reported in Tibetans (Medina-Lezama et al., 2007; Sherpa et al., 2010). Prospective studies have shown that abdominal obesity, particularly with a higher WHR, is associated with a higher risk for CVD and CHD (de Koning et al., 2007; Canoy, 2008), independently of body mass index (BMI), as well as other classic cardiovascular risk factors, even among nonobese individuals (BMI<30 kg/m$^2$) (Canoy et al., 2007). Our study supports this view, because an as increase in WHR increased TG, TC, and LDL-C. Except for female gender, none of the other components of the CHD risk factors predicted high HDL-C. Large waist circumference is a crude indicator of visceral fat mass. Increased visceral fat in obesity releases excess free fatty acids into the portal vein (Nielsen et al., 2004). According to portal theory, continuous exposure of the liver to elevated free fatty acid concentration leads to peripheral and hepatic insulin resistance, impaired insulin secretion, and development of atherogenic dyslipidemia (Björntorp et al., 1990).

In the present study, there were more nonresponders in the younger age group in men. Because blood lipids, obesity, and CHD risk increases with increasing age, higher CHD risk in men in our study may be confined to men in older age groups. We also did not have any data on dietary lipid and carbohydrate intake. Therefore, differences in food habits were sought by asking for the frequency of individual food items to work as a proxy indicator of food pattern. To account for differences in lipid levels that may occur owing to changes in temperature, data were also analyzed adjusted for temperature using retrograde historic weather information (Climate-Lhasa, weather, 2001) during the data-collection month and year. However, we did not find any difference even after adjusting for temperature. Analyses of blood samples were quality controlled by analyses of 40 duplicate samples at the reference laboratory in Beijing, Central Clinical Laboratory of FuWai Hospital. We found a higher mean TC level and lower LDL-C level with no difference in TG and HDL-C levels when compared with the reference laboratory. Since duplicate serum samples were airlifted to Beijing after a period of 4 months following the

data-collection period, it is likely that these differences may have occurred owing to variation in the storage method (Rehak and Chiang, 1988) and or storage time (Shih et al., 2000). The response rate of our study was relatively low (69%), which could have introduced power diminution to the study. The random sample selection of 537 invitees from the 1457 eligible in the list resulted in a skewed sex distribution, in favor of more women. It was not possible to explain this. However, due to a higher response rate among women than men, the final sample, consisting of 139 men and 232 women, reflects fairly well the sex distribution in the population under study, with a slight predomination of women. It is a general finding that association measures in cross-sectional epidemiological studies are robust, even though the response is low and skewed (Sogaard et al., 2004). This study included only known CHD risk factors, but it is possible that there may be other unknown potential confounders that may explain the variation in lipid profile in populations living at high altitudes. The Framingham risk score was validated for an Asian population (Berger et al., 2010); however, validation among high altitude populations is lacking. Moreover, the incidence and prevalence of coronary disease is not available for the Tibetan population. The very low CHD risk in females in our study may be owing to the inability of the Framingham risk score measurement to capture all the other unknown risks in a high altitude population. Finally, the absence of longitudinal studies in high altitude populations on CHD risk factors makes it difficult to assess the significance of other variables.

## Conclusion

This study demonstrated a high prevalence of hypertriglyceridemia in males, a higher prevalence of low HDL-C in females, and a high hypercholesterolemia prevalence in both genders. WHR is associated with an increase in TG, TC, and LDL-C and supports the view that abdominal obesity may be an important cardiovascular risk factor. This study emphasizes the role of HDL-C, which may avert the CHD risk in females. Further studies with longitudinal data are needed to assess the risk factors for CHD in high altitude populations.

## Acknowledgments

We appreciate the support and cooperation of the community leaders in Lhasa, Tibet, and the field workers from Tibet University Medical College. The study was funded by the Network for University Cooperation Tibet–Norway, University of Oslo.

## Disclosures

The authors have no conflicts of interest or financial ties to disclose.

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Received August 1, 2010;
accepted in final form November 1, 2010.