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Effect of Altitude on Metabolic Syndrome

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ABSTRACT

Background: Metabolic syndrome is a constellation of overweight/obesity, hypertension, and disturbances in lipid and carbohydrate metabolism. Hypoxic and hypobaric conditions of high altitude alter the use of energy producing metabolic fuels which may secondarily affect lipid and blood glucose concentrations. Thus, this study aims to assess prevalence and risk factors of the metabolic syndrome in high and low altitude inhabitants of Nepal.

Methods: A hospital based descriptive cross-sectional study was carried out including 58 individuals from high altitude and 58 individuals from low altitude attending Manmohan Memorial Teaching Hospital, Kathmandu. Anthropometric measurements and blood pressure were recorded and blood samples were obtained for laboratory analysis. The samples were analyzed for fasting glucose, triglycerides, total cholesterol, high density lipoprotein cholesterol and low density lipoprotein cholesterol as per the standard guidelines.

Results: Among the study group, 31.8% of high altitude and 68.2% of low altitude are found to have metabolic syndrome according to National Cholesterol Education Program Adult Treatment PlanIII and 35.5% of high altitude and 64.5% of low altitude are found to have metabolic syndrome according to HJSS criteria. The most prevalent defining components were low high density lipoprotein cholesterol (38.8%), high triglyceride (36.2%), elevated fasting blood sugar (33.6%) and Hypertension (34.4%). Among the lifestyle factors, alcohol consumption, unhealthy diet and physical inactivity were found to be an independent risk factors for MetS.

Conclusions: High altitude inhabitants have significantly lower metabolic syndrome than that of low altitude inhabitants because of less physical activities in their work and sedentary. Thus, encouragement of food habit, healthy lifestyle, and timely health screening and monitoring help in prevention of metabolic syndrome.

Keywords: Altitude; diabetes mellitus; early diagnosis; metabolic syndrome; prevention.

INTRODUCTION

Metabolic syndrome (MetS) is a disturbance in carbohydrate and lipid metabolism due to obesity, diabetes, insulin resistance, dyslipidemia, and hypertension.[1, 2] MetS have arisen as a public health concern due to elevation in obesity and sedentary lifestyles: early identification and diagnosis is crucial for reducing MetS.[3]

High altitude residents are typically subjected to mild to moderate hypoxia from birth, resulting in a series of adaptive changes such as lower blood glucose, higher insulin sensitivity, greater hyperglycemic hormone secretion, and caloric expenditure.[4] In the absence of adequate oxygen, either energy production from oxidative metabolism is reduced, or accumulation of reactive oxidative intermediates resulting cell death.[5] In addition, high-altitude populations may have a different lifestyle than that of low altitude like environmental exposure varying occupations, diet, and cultural habits. Thus, we designed our study to investigate the altitude-dependent prevalence of metabolic syndrome and their associated risk factors.

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METHODS

This descriptive cross-sectional study was performed at Manmohan Memorial Teaching Hospital, Kathmandu, Nepal. Diversity of landscape of Nepal is divided into five major regions including Terai (60-300m), Siwalik Hills (700-1500m), Middle mountain (100-2700m), High mountain (2700-4000m) and High Himalayas (4000-8848m) [6]. A total of 116 adult individuals residing habitable high altitude (above 1500m) and low altitude (below 700m) were included in the study. All participants included in the study provided written, informed consent, and all lifestyle variables needed for the study were collected using a standard questionnaire.

Individual who had history of or clinical evidence of the following: ascites, cirrhosis, obstructive liver disease, and chronic renal failure, metabolic diseases, and those who were pregnant or had given birth in the past year were excluded from the study.

A standard questionnaire was used to record each person's anthropometric, demographic, and clinical baseline information. Height and weight was measured by using a wall scale meter with barefoot and a standard digital weighing machine[7]. Body mass index (BMI) was determined in kilograms per square meter (kg/m^2), with 25 kg/m^2 being the cut-off value for a normal BMI; the National Institute of Health (NIH) recommended that 25–29.9 kg/m^2 be classified as overweight and 30 kg/m^2 as obese[8]. The measurement of waist circumference was taken halfway between the superior border of the iliac crest and the lower rib. A sphygmomanometer was used to measure the blood pressure [7]. Further, the presence of MetS was determined based on diagnostic criteria provided by the NCEP ATP III 2004 and Harmonized Joint Scientific Statement 2009.

Venous blood was drawn after an 8–12 hour fast, and the serum was separated for biochemical examination. In accordance with the guidelines supplied by the manufacturer of the reagent (Agappe Diagnostics Switzerland GmbH), fasting blood samples were drawn to examine for glucose (FBG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C).

All the data were collected and analyzed by SPSS version 20 (IBM corporation, Armonk, NY, USA). The mean comparison of baseline characteristics between the male and female populations was analyzed using the Independent Sample t-test. Categorical variables were presented as numbers and compared using chi-square test. Further, Logistic regression analysis was carried out to evaluate the risk factors associated with metabolic syndrome. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Among total of 116 individuals enrolled in the study, 50 were males (43.1%) and 66 were females (56.9%). Inhabitants of high altitude in the study were 50%, while those of low altitude of 50%, with ages (mean ± SD) of 52.50 ± 14.69 years and 50.16 ±13.18 years respectively (Table 1).

As shown in Table 2, anthropometric and biochemical variable between high and low altitude is compared. Fasting plasma glucose was significantly higher in low altitude population (123.12 ± 52.34 mg/dl) than high altitude (103.93 ± 37.20 mg/dl) (p= 0.025). However, HDL-C was significantly lower among low altitude (40.47±7.83 mg/dl) compared to high altitude population (44.95±6.57 mg/dl) (p= 0.001).

Table 3 depicts about the lifestyle habit in high and low altitude inhabitants. Alcohol consumption (p=0.04), consumption of fast food (p=0.03), rigorous physical activity (p=0.01), moderate activity (p=0.040), and daily walking were significantly associated between high and low altitude population.

The prevalence of MetS was found to be significantly higher among population of low altitude based on hypertriglyceridemia, hyperglycemia, systolic, and diastolic blood pressure using both HJSS and NCEP ATP III criteria (Table 4). Nearly two-third individuals in low altitude population were significantly presenting MetS (Figure 1).

Furthermore, different risk factors were assessed for MetS in our study population in table 5. Among all variables, alcohol consumption (OR = 2.64, 95% CI: 1.23-5.65), lesser intake of green vegetables and fruits in diet (OR = 4.518, 95% CI: 1.23-5.65), and lesser extent to rigorous physical activity (OR = 2.865, 95% CI: 1.247-6.580) were found to be the risk factors associated with MetS.

Table 1. Distribution of demographic variables of study population.

Variables	Groups	Frequency(n)	Percent
Age	20-45 45-65 Above 65	34 61 21	29.3% 52.6% 18.1%
Sex	Male Female	50 66	43.1% 56.9%
Altitude	High Low	58 58	50.0% 50.0%

Table 2. Comparison of anthropometric and biochemical variables among high and low altitude inhabitants.

Parameter	High Altitude(n=58) (mean + SD)	Low Altitude(n=58) (mean + SD)	*p*-value
BMI	25.27 ± 4.56	25.06 ± 3.86	0.79
W.C.	92.22 ± 10.10	92.05 ± 9.00	0.92
SBP	120.86 ± 14.78	121.38 ± 14.4	0.84
DBP	79.66 ± 10.29	78.10 ± 10.50	0.42
TG	159.83 ± 88.68	190.38 ± 114.39	0.11
TC	180.61 ± 52.63	182.21 ± 61.72	0.88
HDL-C	44.95 ± 6.57	40.47 ± 7.83	**0.001**
LDL-C	103.7 ± 51.96	103.6 ± 52.00	0.99
FBG	103.93 ± 37.20	123.13 ± 52.34	**0.025**

WC= Waist circumference; BMI= Body mass index; SBP= Systolic Blood Pressure; DBP= Diastolic Blood Pressure; TG=Triglycerides; TC= Total cholesterol; HDL-C= High density lipoprotein cholesterol; LDL-C= Low density lipoprotein cholesterol; FBG= Fasting Blood Glucose

Table 3. Lifestyle habits between High and Low altitude inhabitants.

Categorical variables	Groups	Total	High	Low	*p*-value
Alcohol consumption	Occasionally 2-4 times a month 2-4 times a week 3or more times a week Never	24(20.7%) 12(10.3%) 6(5.2%) 9(7.8%) 65(56.0%)	17(29.3%) 5(8.6%) 5(8.6%) 4(6.9%) 27(46.6%)	7(12.1) 7(12.1%) 1(1.7%) 5(8.6%) 38(65.5%)	**0.04**
Smoking	Weekly Daily >3times a day Never	2(1.7%) 9(7.8%) 11(9.5%) 94(81.0%)	2(3.4%) 5(8.6%) 4(6.9%) 47(81.0%)	0(0%) 4(6.9%) 7(12.1%) 47(81.0%)	0.4
Inclusion of green vegetables and fruits	Daily >3 days a week weekly	49(42.2%) 63(54.3%) 4(3.4%)	28(48.3%) 28(48.3%) 2(3.4%)	21(36.2%) 35(60.3%) 2(3.4%)	0.4
Consumption of Red meat and full fat milk	Daily >3 days a week Weekly Monthly never	1(9%) 10(8.6%) 49(42.2%) 40(34.5%) 16(13.8%)	0(0%) 5(8.6%) 21(36.2%) 21(36.2%) 10(17.2%)	1(1.7%) 5(8.6%) 21(36.2%) 21(36.2%) 10(17.2%)	0.5
Consumption of fast foods	Daily >3 days a week Weekly Never	16(13.8%) 23(19.8%) 44(37.9%) 33(28.4%)	7(12.1%) 11(19.0%) 29(50.0%) 11(19.0%)	9(15.5%) 12(20.7%) 15(25.9%) 22(37.9%)	**0.03**
Physical activity Rigorous	Yes No	34(29.3%) 82(70.7%)	23(39.7%) 35(60.3%)	11(19.0%) 47(81.0%)	**0.01**
Moderate	Yes No	92(79.3%) 24(20.7%)	50(86.2%) 8(13.8%)	42(72.4%) 16(27.6%)	**0.04**
Daily walking	Yes No	103(88.8%) 13(11.2%)	55(94.8%) 3(5.2%)	48(82.8%) 10(17.2%)	**0.03**

Table 4. Distribution of Metabolic syndrome in different groups.

	Groups	NCEP ATP III(MetS)	*p* value	HJSS (MetS)	*p* value
Altitude	High Low	36.4% 62.3%	**0.005**	38.2% 61.8%	**0.003**
Age	Below 45 45-65 Above 65	21.8% 58.2% 20.0%	0.24	25.0% 55.9% 19.1%	0.47
Sex	Male Female	54.5% 45.5%	0.05	51.6% 48.4%	**0.04**
Cholesterol	Desirable Cholesterol Borderline Cholesterol High Cholesterol	70.9% 16.4% 12.7%	0.68	67.6% 20.6% 11.8%	0.54
Triglyceride	<169.9 mg/dl >170.1 mg/dl	38.2% 61.8%	**0.000**	44.1% 55.9%	**0.000**
HDL	<29.9 mg/dl 30 - 70 mg/dl	5.5% 94.5%	0.56	2.1% 97.9%	0.40
Glucose	<69.9 mg/dl 70 - 110 mg/dl >110.1 mg/dl	0% 43.6% 56.4%	**0.000**	0% 51.5% 48.5%	**0.000**
Systolic	80-120mmhg 121-139mmhg 140-159mmhg >160 mmhg	45.5% 18.2% 32.7% 3.6%	**0.000**	50.0% 20.6% 26.5% 2.9%	**0.000**
Diastolic	60-80mmhg 81-89mmhg 90-99mmhg >100 mmhg	47.3% 30.9% 9.1% 12.7%	**0.001**	52.9% 29.4% 7.4% 10.3%	**0.003**

Table 5. Risk factor associated with Mets.

Lifestyle		Percentage	OR (95%CI)	*p*-value
Habit of alcohol consumption	Yes No	66.7% 43.1%	2.64 (1.23-5.65)	**0.012**
Habit of smoking	Yes No	54.5% 53.2%	0.947 (0.373-2.405)	0.90
Daily inclusion of green vegetables and fruits in diet	Yes No	32.7% 68.7%	4.518 (2.052- 9.947)	**<0.001**
Physical activity **Rigorous**	Yes No	35.3% 61.0%	2.865 (1.247-6.580)	**0.013**
Moderate	Yes No	48.9% 70.8%	2.537 (0.961-6.694)	0.06
Daily walking	Yes No	51.5% 69.2%	2.123 (0.615-7.332)	0.234

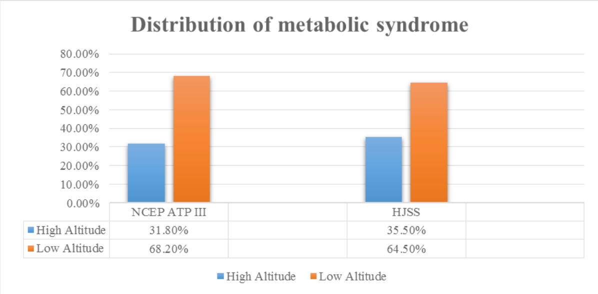

Figure 1. Distribution of Mets from NCEP ATP III and HJSS criteria among study populations of high and low altitude of Nepal.

DISCUSSION

The rate of non-communicable diseases (NCDs) is an alarming increase in low and middle income countries which results in 4 out of 5 deaths.[9] MetS the constellation of overweight/obesity, hypertension, and disturbances in lipid and carbohydrate metabolism has become one of the major public health burdens, the world is facing which affects 20-25% of world's adult population.[1,10] It leads to the risk of diabetes and cardiovascular disease (CVD); both are emerging as global epidemics. Urbanization, obesity, and physical inactivity are all contributing to the global epidemiological and nutritional changes that are resulting in an increase cardio-metabolic disorder. [9]

In our study, 68.2% of low altitude and 31.8% of high altitude inhabitants were predicted of MetS as reported by the NCEP ATP III criteria; similarly, 64.5% of low altitude and 35.5% of high altitude inhabitants were estimated as MetS as reported by HJSS criteria. The most prevalent defining components were low HDL-C (38.8%), high triglyceride (36.2%), elevated FBS (33.6%) and hypertension (34.4%). In contrast to our study, the prevalence of MetS in the findings by Baracco et al was found to be 24.2% at high altitude and 22.1% at low altitude and the difference is not statistically significant.[11] This might be due to differences in lifestyles choices and dietary habits of different continent.

Our findings suggest significantly higher level of fasting plasma glucose in low altitude than high altitude population. Similar to our study, high altitude residents had a lower glycemic profile (50.6 ± 3.7 mg/dl) than sea level residents (73.4 ± 4.0 mg/dl) ($p \leq 0.001$) in the study performed by Oscar Castillo.[12] The main causes for lower glycemia may be increased utilization of glucose as a metabolic substrate,[13-15] lower socio-economic status of high altitude residents, higher insulin sensitivity compared to low altitude residents,[16] anti-diabetic properties of plants and crops produced in high altitude,[17] and cold ambient temperature affecting glucose metabolism during shivering.[18]

In companion to our study, High density lipoprotein cholesterol concentration is significantly increased among the population living at a higher altitude in the study performed in Spain by S Dominguez Coello.[19] At higher altitudes, body adjusts to transient altitude hypoxemic situation leading to hepatic lipid oxidation resulting in increased HDL concentration.[20] Short-term exposure to high altitude caused a sudden improvement in reverse cholesterol transport, which likely led to greater catabolism of triglyceride-rich lipoproteins as well as an increase in HDL levels.[21]

Among 116 participants in our study, only 42.2% included green vegetables and fruits in their daily diet. It has been reported, that vegetables and fruits are mainly responsible for the protection against hypertension and cardiovascular diseases. Moreover, antioxidants present in vegetables and fruits inactivate the effects of free radicals and lipid peroxidation, that could affect arterial stiffness.[22]

In our study, Alcohol consumption, unhealthy diet and physical inactivity were found to be an independent risk factor for MetS. Alcohol consumptions and unhealthy diet prone to the risk of development of hypertension, obesity, hyperglycemia, and hypertriglyceridemia.[23] Previous findings suggest that engaging in moderate-to vigorous physical activity mitigate the risk of metabolic syndrome.[24]

The prevalence of MetS in our study (Figure 1) indicates that there is a need of health screening measures in identification of at-risk adults and implementation of proper targeted interventional development. However, the study time frame and sample size limits the study and this study was limited to only hospital patients, community based sampling was not done. Hence, there is a need for further altitude based research in Nepal to obtain valuable data regarding the prevalence of MetS that can be useful for future healthcare planning and policy formulation.

CONCLUSIONS

In this study, 31.8% of high altitude and 68.2% of Low altitude are found to have metabolic syndrome according to NCEP ATPIII and 35.5% of high altitude and 64.5% of low altitude are found to have metabolic syndrome according to HJSS criteria. High altitude inhabitants have significantly lower metabolic syndrome than that of low altitude inhabitants may be due to less physical activities in their work in low altitude inhabitants. Life style interventions are associated with high metabolic risk. Moreover, environmental factors including atmospheric temperature and pressure may affect the metabolic status. Encouragement of food habit, healthy lifestyle, and timely health screening and monitoring will help in prevention of metabolic syndrome and associated cardiovascular mortality.

CONFLICT OF INTEREST

There is nothing to be declared.

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