Prevalence and determinants of diabetes mellitus in high altitude: A cross sectional study in mountainous region of Nepal

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ABSTRACT

Background: There had been many studies depicting variations in the prevalence of diabetes mellitus in Nepal ranging from 1.4% to 19%. However, the pooled prevalence was found to be 8.4%. There are only few studies done till date in our part of the world to study the actual prevalence and determinants of Type 2 Diabetes Mellitus (DM-2) in people residing in mountains. **Aims and Objectives:** This study was conducted with to estimate the prevalence and determinants of diabetes mellitus among the high-altitude population in Jomsom district of Nepal. **Materials and Methods:** A cross sectional study was carried out in Jomsom district of Nepal, at an altitude of 2743 meters on 4th and 5th of June, 2017 . A detailed history from the participants of their past medical illness including diabetes mellitus and hypertension was taken. In addition, blood sugar level, blood pressure, anthropometric variables like weight, height, BMI, Waist, Hip, Waist/hip ratio were documented after the verbal consent of the participants. **Results:** A total of 617 local residents of Jomsom were enrolled in the study. The mean age of study population was 44.4 ± 17.6 years with female to male ratio being 1.15:1 (53.5% vs 46.5% male). The prevalence of diabetes mellitus was found to be 5.2%, which was significantly lower than the overall prevalence of diabetes in the Nepalese population which is 8.4%. Male population was found to have higher prevalence of diabetes in our study. Higher BMI and waist/hip ratio were also associated with increased incidence of diabetes mellitus. This study revealed that compared with individuals with a normal BMI, individuals who were overweight or obese were more likely to be diagnosed with DM-2 (OR [95%CI]: ranging from 4.33 [0.96–19.46] for overweight adults to 7.76 [1.76–34.13] for adults in Obesity. **Conclusion:** The overall prevalence of diabetes mellitus is lower among the individuals residing in higher altitude compared to the general population although the other determinants are comparable.

Key words: Diabetes mellitus; BMI; High altitude population; Waist/hip ratio

INTRODUCTION

Nepal has significant geographic diversity with large area in northern belt covered by mountains. There are human settlements of various ethnic groups in high altitude areas above 3000 meters above sea level.[1] However, there are very few studies conducted on the prevalence and determinants of diabetes mellitus in the people who reside in high altitude of Nepal.

A total of 6.7% of Nepalese population reside in mountains whereas globally only about 2% of the population reside at an altitude of 2500 meters or more.[2]In the recent decades, diabetes mellitus has been a significant burden to health

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care system throughout the world and its prevalence is increasing in countries of all economic levels.

The actual effect of hypoxic and hypobaric condition in the glucose metabolism is still uncertain. However, there are many hypotheses proposed. Hypoxia results in a preference for glucose utilization and decreases uptake of free fatty acids because of oxygen-deficient adaptation.[3] Also, the inhibition of gluconeogenesis in hepatocytes in intermittent hypoxia leading to smaller hepatic glucose output can be an important factor for decreased blood glucose profile in inhabitants of high altitude of Nepal.[4] Moreover, it can also be correlated with the reduced basal insulin level,[4] increased physical activity and dietary pattern in natives residing in mountains of Nepal.

We aim to study the prevalence of diabetes mellitus andits determinants including various anthropometric measurements and blood pressure in people residing in high altitude region of Nepal.

MATERIALS AND METHODS

A descriptive cross sectional study was carried out in 4th and 5th June of 2017 at Jomsom of Mustang district of Nepal which is situated at an altitude of 2743 meters from sea level. A routine cardiac screening camp of Shahid Gangalal National Heart Center was conducted and a total of 617 adults of more than 18 years of age were screened.

Adults of either sex, who were the permanent resident at the given place, were enrolled in the study. They were explained about the purpose of study and the methods used. Informed verbal consent was taken assuring full confidentiality. The details of the patients which include sex, age, height, weight, blood pressure, BMI, waist and hip circumference were measured and recorded in a predesigned data collection form.

Fasting Blood Glucose (FBG) and Two-hour postprandial Blood glucose (2-h BG) were measured in 550 adults while only Random blood glucose (RBS) was taken in another 67 adults as they visited in non fasting state. Blood Glucose was measured using capillary blood via glucometer. As it was logistically not possible to measure blood glucose via venous blood in all participants in that set up we used capillary measurement of blood glucose. However, in the initial few participants blood sample was taken for venous blood glucose in addition to capillary blood glucose for cross verification which also revealed that there is not much difference between venous blood and capillary blood glucose level.

Various studies done previously showed strong positive correlation between capillary glucose and venous plasma glucose[5]. Hence capillary glucose measurement can be used as alternative to venous glucose in resource limited situations for screening of diabetes mellitus[5].

The diagnosis of diabetes was made as per the American diabetes association (ADA) diagnostic criteria for diabetes mellitus, 2015 where adults with FPG ≥126 mg/dl OR 2-h PG ≥200 mg/dL OR the RBS of ≥200 mg/dl with classicsymptoms were diagnosed with diabetes mellitus[6]. In addition, patients already diagnosed with diabetes mellitus and on treatment(oral hypoglycemics and/or insulin) were also included in the study as diabetic population group.

However, it was not feasible to take blood samples for glycated hemoglobin (HBA1c) and performrepeat test of blood glucose profile for final confirmation due to logistic reasons.

Statistical analysis was performed with statistical software (SPSS-22.0 for windows).Results were analyzed using appropriate statistical methods. P-value was calculated under the predetermined level of significance (0.05) and Confidence interval (CI) of 95% was constructed. Results were expressed in percentage, mean and standard deviation. Ethical clearance was taken from Institutional Review Committee of Shahid Gangalal National Heart Center, Nepal.

RESULTS

A total of 617 people were screened in the camp, which included 287(46.5%) male and 330(53.5%) female. The mean age of the study population was 44.4±17.6 years and the mean age of male participants was 44.7±17.8 years and the mean age of female was 44.3±17.5years. Various anthropometric measurements are enlisted in Table 1.

There were 32(5.2%) subjects who were diagnosed with T2DM. Average age of subjects with T2DM was 64.75±8.7768 years. The mean age of male subjects with T2DM was 64.7±9.7 years and mean age of female subjects with T2DM was 64.8±6.4 years.

Table 1: Anthropometric measurements (N=617)

	Minimum	Maximum	Mean	Standard deviation
Height (cm)	108	180	156.40	8.90
Weight (Kg)	32	110	62.251	11.44
BMI (kg/m²)	14.23	50.59	25.46	4.28
Waist (cm)	48	130	86.73	10.58
Hip (cm)	49	166	92.71	9.47
Waist/hip ratio	0.47	1.63	0.93	0.07

T2DM was 3.11 times higher in male as compared to female at 95%CI (p value:0. 003) as shown in Table 2.

T2DM was 14.286 times higher in hypertensive subjects as compared to non-hypertensive at 95%CI (p value<0. 001) as shown in Table 3.

This study revealed that compared with individuals with a normal BMI, individuals who were overweight or obese were more likely to be diagnosed with DM-2 (OR [95%CI]: ranging from 4.33 [0.96–19.46] for overweight adults to 7.76 [1.76–34.13] for adults in Obesity as shown in Table 4.

Waist/Hip ratio was also significantly high in subjects with T2DM at 95%CI as shown in Table 5.

Alcohol consumption was present in 29.3% of the subjects whereas cigarette smoking was present in 15.9%. Likewise, tobacco consumption was present in 8.3%.

DISCUSSION

Diabetes mellitus is a leading cause of death worldwide with the estimated global prevalence of around 6.4% and is anticipated to increase up to 7.7% by 2030.[7] In Nepal the estimated pooled prevalence of diabetes mellitus is around 8.4% with the prevalence in urban and rural populations of the country being 8.1% and 1.0% respectively.[8] However, a study done by Sharma et al revealed the overall prevalence of diabetes in Nepalese population to be 6.3%.[9]

There are limited studies regarding the prevalence and determinants of diabetes mellitus in high altitude population in our part of the world. Analysis of the results revealed the overall prevalence of diabetes in inhabitants of high altitude of Nepal to be 5.2%. This is less than the previous 2 studies on overall prevalence of diabetes in Nepalese population. This clearly demonstrates the lower prevalence of diabetes mellitus in the people living in high altitude than in low altitude in Nepal. Although the actual cause of decreased blood sugar profile in inhabitants of high altitude is not clearly understood there are various hypotheses for the same. There are numerous reports suggesting the beneficial effects of living at high altitude on glucose homeostasis. In addition, residents of high altitude also shows better glucose tolerance compared to those living in sea level.[10] This could probably be due to hypoxia induced decreased gluconeogenesis, reduced hepatic glucose output.

Hypoxia also favors the rate of glycolysis and higher glucose uptake to enter the glycolytic pathway or glucose oxidization to generate the ATP can contribute to lower blood glucose profile in high altitude. Moreover there is important beneficial effect of prolonged hypoxia on insulin sensitivity and decreased prevalence of obesity in high altitude which can be another factor for decreased

Table 2: Sex distribution of study population (N=617)

| | | T2DM | | Total | OR (95%CI) | p-value |
		Present	Not present			
Sex	Male	23	264	287	3.11(1.41-6.85)	0.003
	Female	9	321	330		
Total		32	585	617		

Table 3: Association and hypertension with diabetes mellitus (N=617)

| | | T2DM | | Total | OR (95%CI) | p-value |
		Present	Not present			
HTN	Present	25	117	142	14.28 (6.03-33.83)	<0.001
	Not Present	7	468	475		
Total		32	585	617		

Table 4: Association of BMI categories with T2DM

| | | T2DM | | Total | Prevalence of DM (%) | Odds ratio (OR) |
		Not present	Present			
BMI category	Underweight	17	0	17		
	Normal	158	2	160	1.25	
	Overweight	237	13	250	5.2	4.33(P = 0.05)
	Obese	173	17	190	8.95	7.76(P = 0.006)
Total		585	32	617		

Table 5: Association of Waist/Hip ratio with T2DM

T2DM	Number	Mean Waist/Hip ratio	Std. deviation	p-value
Not Present	585	0.93	0.07	<0.001
Present	32	1.00	0.11	

prevalence of diabetes in people living there.[11] There are other possible mechanisms by which hypoxic environment in highlands may stimulate glucose uptake. One important mechanism is stimulation of glucose uptake by promoting GLUT4 translocation via AMPK-dependent pathway.[11] Also at the cellular level, hypoxia inhibits oxidative phosphorylation and stimulates oxygen signaling pathway through the hypoxia-inducible factor-1 alpha (HIF-1 alpha).[12]

The result of our study is nearly comparable to the results of the study done in similar geographical region of Nepal by Aryal et al where Overall, 6.9% of participants residing in high altitude had diabetes or were on hypoglycaemic treatment.[3] Another study done by Woolcott et al in United States also revealed that diabetes was substantially less prevalent in high-altitude counties compared to low altitude counties (6.4% [5.4-7.3] and 9.1% [7.8-10.5]).[10]

The study revealed male population had higher prevalence of diabetes mellitus in comparison with the female group (OR 3.11(1.41-6.85), P=0.003). This finding is similar to the study by Kapil et al[13] inhigh-altitude region of rural Uttarakhand, India where 14.6%; males (5.2%) and females (9.4%) were found to have diabetes.

The findings of our study were in contrary to the results obtained from systematic review by Gyawali et al[8] where female gender were found to have higher prevalence of diabetes in Nepalese general population. Also, in study by Gillett M et al,[14] Shera AS et al[15] and Satman I et al,[16] positive association of diabetes with female gender was observed.

The odds of having diabetes in hypertensive patient were higher compared to non hypertensive patients OR- 14.286 CI (6.032-33.836). The risk factors of both hypertension and diabetes are common and thereby such association could be observed. Similarly, diabetes predisposes to accelerated atherosclerosis, which can result in hypertension on the long run.

T2DM was also significantly associated with increased BMI. The prevalence of diabetes in normal BMI group was 1.25%, in overweight group 5.2% and in obese group was 8.95%. The people with diabetes had increased waist hip ratio compared to non diabetic population. The mean waist hip ratio in diabetic population was 1.00 +/-0.118, compared to non diabetic group 0.931+/-0.065. This consolidates the fact that even in high altitude, increased BMI and waist/hip ratio can be risk factors to develop diabetes mellitus.

CONCLUSION

The prevalence of diabetes in higher altitude of Nepal was lower compared to the general population. Male sex had higher prevalence of diabetes compared to the female population which was just opposite to that of the national data. BMI and waist hip ratio were also a significant risk factors for diabetes in high altitude. Odds of having diabetes in hypertensive patients were higher than in non hypertensive.

Limitation of the study
Blood glucose was measured by capillary blood rather than by venous blood as it was logistically not possible although initial few participants blood was taken both for venous blood glucose and capillary blood glucose for cross verification. HbA1c measurement could not be done due to lack of proper logistics.

The prevalence of diabetes in people with the above risk factors was not evaluated. Thus, these may serve as confounding bias in the study. Lipid profile and age group distribution were also not considered in the study.

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