GLYCEMIC STATUS AND ASSOCIATED RISK FACTORS IN HIGH ALTITUDE POPULATION

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF

Doctor of Philosophy in Zoology

By

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DEDICATED

TO

MY PARENTS, BROTHER, SUPPORTING WIFE AND CHILDREN
Summary
SUMMARY

The objective of this study was to investigate glycemic status and its relationship with risk factors in high altitude population. The study was conducted on 1168 subjects. Among these, 973 (495 males and 478 females) were high altitude subjects and 195 subjects were lowlander (90 male and 95 female). The study was conducted at two higher altitude ranges, one between 1200 to 1800 meter altitude and the second range 1801 to 3000 meter height. The control study for comparison was done at lowland (almost sea level). The glycemic status and associated risk factors were determined in relation to high altitude in the selected districts of Azad Jammu and Kashmir, namely, Muzaffarabad, Bagh, Rawalakot, Pallandri and lowland of district Narowal (Punjab). The inhabitants of that populated area were mostly native. The subjects were studied for fasting blood glucose level, BMI, total cholesterol, triglyceride, blood pressure, aging twenty to above sixty years. A reasonable number of diabetic subjects with age >40 were also included in this study.

In the present study, above mentioned parameters were specifically compared between lowland, moderate and comparatively high altitude subjects.

In a comparison of the data of the subjects inhabiting high altitude with low land, there is a significant decrease in body mass index, fasting blood glucose, blood pressure, cholesterol, triglyceride, and pulse rate whereas there is a significant increase in hematocrit at moderate and comparatively high altitude.

This comparison showed that at high altitude, the major risk factors including BMI, cholesterol, triglyceride and blood pressure are significantly lowered as compared to low land subjects.
In the population at moderate altitude, at an altitude of 1801 to 3000 meter, gender comparison was done. There was a non-significant difference in fasting blood glucose, body mass index, cholesterol and blood pressure whereas a significant difference was observed in hematocrit, triglyceride and pulse rate. In second category of comparatively high altitude (>1800 meter), there was a non-significant difference in blood pressure, cholesterol, and triglyceride whereas a significant difference was found in body mass index, fasting blood glucose, hematocrit, and pulse rate in male and female subjects.

When compared in both the population categories of higher altitudes, a non-significant difference was observed in diastolic blood pressure and cholesterol and a significant difference in body mass index, fasting blood glucose, systolic blood pressure, hematocrit, triglyceride and pulse rate.

Lowered levels of fasting blood glucose, BMI, total cholesterol, triglyceride, blood pressure in the present study are considered to be due to the active life style, low lipid diet and less tension. Relative hypoxic and hypobaric conditions also play an important role in low blood pressure and increased hematocrit.

Social/life style factors such as marital status, exercise and dietary habits, may be related to overweight/obesity in both gender at high altitude.

The present results of the comparisons are in accordance with the literature available.
Acknowledgements
ACKNOWLEDGEMENTS

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(ABDUL QAYYUM NAYYER)
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<tr>
<td>AMS</td>
<td>Acute Mountain Sickness</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
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<tr>
<td>BP</td>
<td>Blood Pressure</td>
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<tr>
<td>°C</td>
<td>Centigrade</td>
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<tr>
<td>CAD</td>
<td>Coronary Artery Disorder</td>
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<tr>
<td>FBG</td>
<td>Fasting Blood Glucose</td>
</tr>
<tr>
<td>GCT</td>
<td>Glucose, Cholesterol and Triglyceride</td>
</tr>
<tr>
<td>GH</td>
<td>Growth Hormone</td>
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<tr>
<td>GLUT-1</td>
<td>Glucose Transporter-1</td>
</tr>
<tr>
<td>GTD</td>
<td>Glucose Tolerance Disorder</td>
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<tr>
<td>HA</td>
<td>High-Altitude</td>
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<tr>
<td>HACE</td>
<td>High Altitude Cerebral Edema</td>
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<td>HAPE</td>
<td>High Altitude Pulmonary Edema</td>
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<tr>
<td>Hct</td>
<td>Hematocrit</td>
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<tr>
<td>HDL</td>
<td>High Density Lipoprotein</td>
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<tr>
<td>HDL-C</td>
<td>High Density Lipoprotein-Cholesterol</td>
</tr>
<tr>
<td>HGP</td>
<td>Hepatic Glucose Production</td>
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<tr>
<td>HL</td>
<td>High Lander</td>
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<tr>
<td>HLA</td>
<td>Human Leucocyte Antigen</td>
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<tr>
<td>IDDM</td>
<td>Insulin Dependent Diabetes Mellitus</td>
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<tr>
<td>kg/m²</td>
<td>Kilogram per Meter Square</td>
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<tr>
<td>LDL</td>
<td>Low Density Lipoprotein</td>
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<tr>
<td>LDL-C</td>
<td>Low Density Lipoprotein-Cholesterol</td>
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<tr>
<td>LL</td>
<td>Low Lander</td>
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<tr>
<td>m</td>
<td>Meter</td>
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<tr>
<td>m²</td>
<td>Meter Square</td>
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<tr>
<td>min</td>
<td>Minute</td>
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<tr>
<td>mg/dl</td>
<td>Milligram per Deciliter</td>
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<td>mmHg</td>
<td>Millimeter Mercury</td>
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<td>mmol/l</td>
<td>Millimole per Liter</td>
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<td>PDE</td>
<td>Phosphodiesterase- E</td>
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<td>Parathyroid Hormone</td>
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<td>RBC</td>
<td>Red Blood Cells</td>
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<td>rpm</td>
<td>Revolution per Minute</td>
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<td>SL</td>
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<tr>
<td>T3</td>
<td>Tri-iodothyronine</td>
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<tr>
<td>T4</td>
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<tr>
<td>TSH</td>
<td>Thyroid Stimulating Hormone</td>
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<td>VLDL</td>
<td>Very Low Density Lipoprotein</td>
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<tr>
<td>WHO</td>
<td>World Health Organization</td>
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<td>&gt;</td>
<td>Greater than</td>
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<td>≥</td>
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Introduction
INTRODUCTION

Sustainability of an organism is dependent upon its ability to maintain its energy flow. The major constituents required for energy metabolism are carbohydrates and lipids. In human beings, glucose which is the primary source of energy available is maintained in a narrow range of 70 – 110 mg/dl normally. This normoglycemia is the result of innumerable mechanisms working at biochemical, molecular, cellular and tissue level. The failure of any mechanism results in altered glycemic level and it is indicative of clinical manifestations in the subjects.

The inavailability of insulin or its failure to implement action of glucose transport into the cell for energy generation results in glycemic changes, particularly excessive glycemia and it is indicative of diabetes mellitus.

It is well agreed that an ecosystem is like a super-organism and an individual is the inseparable component of this setup. This relationship is so strong that several genetic dependent functions cannot be separated from its environment, as genetic expression may be dependent on environmental trigger. This interdependence is now well accepted in all biochemical, molecular, genetic and physiological mechanisms. This interrelationship is the result of organismic adaptation in the changing environment.

Historically, human being had been a hunter which accompanied considerable activity, therefore, its physiological and metabolic setup has been adapted to this life style. The social developments have rendered humans, inactive in life style. Furthermore, increase in food productivity has substantially increased caloric consumption. Such changes have been affecting the metabolic setup to new adjustments and these alterations have been appearing in the clinical manifestations.
One of the principle target is the primary energy component, the glucose and its regulation.

It is regularly forewarned by various quarters that present day life style is increasing the incidence of diabetes mellitus at alarming rate.

Diabetes mellitus has been divided into two groups, insulin-dependent diabetes mellitus (type-1 diabetes mellitus) and non-insulin dependent diabetes mellitus (type-2 diabetes mellitus). Type-1 diabetes mellitus is a familial disease but the precise mode of inheritance is not known. Hence the disease is described as being multi-factorial where genetic and environmental factors play their role (Alberti and Zimmet, 1998). There is no association of type-2 diabetes with HLA (human leukocyte antigen) as in type-1 diabetes mellitus (Bell et al., 1983).

The maintenance of a blood glucose level is mainly regulated by the balanced production of insulin (Walter and Israel, 1994). High altitude dwellers are less sensitive to insulin compared with sea level (Braun et al., 2001).

Type-2 diabetes mellitus generally develops gradually and the subject remains unaware of its development until serious crisis appear. The present day life style is contributing in failure of glycemic regulation with the consequent risk of cardiovascular nature, which is one of the major concerns, regarding type-2 diabetes.

The cardiovascular abnormalities include microvascular, macrovascular and neuropathic diseases. The microvascular abnormalities are diabetic retinopathy and diabetic nephropathy resulting in blindness and renal failure respectively. The macrovascular abnormalities are due to accelerated atherosclerosis with increased incidence of stroke and myocardial infarction. Neuropathic abnormalities (diabetic neuropathy) involving autonomic nervous system and peripheral nerves, when combined with vascular changes, results in limb amputation (Ganong, 2001).
The term “high altitude” does not have any precise definition. Arbitrarily an altitude of more than 3000 meters has been taken as high altitude, however, some “high altitude research stations” were established at level of 1260 meters in Jujuy in Argentinias (Heath, 1979). As this is the altitude (>3000 m) after which most of the sea level residents start showing sign and symptoms like Acute Mountain Sickness (AMS), High Altitude Pulmonary Edema (HAPE), High Altitude Cerebral Edema (HACE) associated with altitude ascent due to hypoxia (Sawhney, 1991).

Hypoxia results in physiological polycythemia at high altitude (Zubieta et al., 2006). Polycythemia is a compensatory mechanism to sustain O₂ delivery during life at high altitude in which there is an increased production of erythropoietin that results in an increase in total number of red blood cells. It occurs in individuals living at high altitudes chronically at low oxygen level.

Significant proportion of the world population lives in mountainous area, like Sub-Himalayan region of Pakistan. The natives of this area have obligatory active life. They also manage in comparatively hypoxic (low oxygen) conditions. No doubt, this population has adapted these conditions, therefore, these populations would/may have specific pattern of glycemic regulation and consequently the incidence of diabetes and accompanied cardiovascular complication, may be different from sedentary urbanized population.

The comparison of the mechanisms in the glycemic regulation including the associative risk in the population at high altitude in comparison to the low land may provide information at biochemical, molecular and physiological levels which could be of importance in the management of associated diseases in the ever-expanding urban population (Castillo et al., 2007)
The North-Western Sub-Himalayan region is naturally, a unique highland ecosystem incomparable to any other part in the world. The state of Azad Jammu and Kashmir lies between longitude 73°-75° and latitude 33°-36°. Its topography is mainly hilly and mountainous with valleys and stretches of plains. The maximum temperature in summer is about 40°C and in the winter season it drops about up to -13°C (Bates, 1991).

The area is full of natural beauty with thick forests of Deodar, Kail, Fir, Spruce and Cheer. The climate is sub-tropical highland type with an average annual rainfall of 1300 mm. The major crops are maize, wheat and rice while the minor crops include grams, pulses, oil-seeds and vegetables. The most important fruits are apples, pears, apricots, walnuts and plums. The texture of present population is composed of races claiming their descent from Semitic, Mongloid, Aryans, Persians, Turks & Arabs (Bates, 1991).

Thus the present investigation was planned to study glycemic regulation and associative mechanisms at biochemical, molecular and physiological targets among the North-Western Himalayan highland while comparing it with low land population. So the proposed study would prove to be of an additional significance.

The objectives of present study were to monitor the glycemic status and associated lipid and vascular targets in the populations inhabiting higher altitudes and compare with those as lowlanders. This provides the information on physiological adaptations at higher altitude compare to lowland dwellers. The implications of lifestyle changes leading to glycemic and lipids anomalies and causing diabetes and cardiovascular complications to be compared in different altitude living to assess the advantages and disadvantages of higher altitude living compare to lowland living.
Review of Literature
REVIEW OF LITERATURE

Glycemia is the concentration of glucose in blood. Glucose is, no doubt, indispensable for the human body and is an absolute requirement for human life. Under normal conditions, almost all of the energy used by brain cells is supplied by glucose derived from blood (Guyton, 2000). Its excess (hyperglycemia) or deficiency (hypoglycemia) in blood causes different problems. The most important upset in glucose regulation is diabetes mellitus (Vallace-Owen, 1975).

Diabetes mellitus consists of sub-groups of disorders that currently afflict 15 million Americans (Sheerwood, 2001) with the number expected to rise to 23 millions by 2025. Diabetes is the sixth leading cause of death by disease in USA (195,000 diabetic-related deaths annually). It is estimated that 5-7% of the U.S population has this disease (Ganong, 2001). According to WHO report (2002), Pakistan which ranked nowhere in 1995 among the top 10 countries where diabetes was common has now attained the position first in the list with 15 millions diabetic patients. Diabetes is the leading cause of blindness, kidney failure and limb amputation (McArdle, 2007).

Diabetes mellitus may appear as silently as a cat or storm in like an enraged bull (Clement and Bell, 1985). The incidence of the disease is almost similar in most of the parts of the world. Efforts are being made to improve the situation all over the world, particularly in developed countries. According to a survey conducted on children in U.K, there is an improvement in services provided to the patients of diabetes but serious deficiencies still remains (Jefferson et al., 2003).

National Diabetes Data Group of the National Institute of Health proposed a classification that divided diabetes into two main types, insulin-dependent and non-insulin-dependent diabetes that differed in their pattern of inheritance, insulin response and origin (Bennett, 1983) but this classification is proved unsatisfactory. In
1997 an International Committee of Diabetologists with the endorsement of American Diabetes Association (ADA) and World Health Organization (WHO) retained term type-1 and type-2 diabetes (Greenspan, 2001; Mc Ardle, 2007).

Type-2 diabetes mellitus is a familial disease but the precise mode of inheritance is not known. Hence the disease is described as being multi-factorial with genetic and environmental factors playing a part. There is no association of type-2 diabetes with HLA as is in type-1 diabetes mellitus (Bell et al., 1983). A study of identical twins revealed that genetic factors have contributed in diabetes mellitus. These twins have the same genetic make up so if one identical twin develops diabetes and the conditions really are inherited, then the other twin should develop it within a few years (O’Riordan et al., 1988). The concordance rate among identical twins is over 97% (Barnett et al., 1981). Studies of human leukocyte antigen (HLA) markers have indicated that there is a relationship between these antigenic determinants and type-1 diabetes. The class II antigens DR3 and DR4 are associated with the increased risk of developing insulin deficient diabetes (O’Riordan et al., 1988).

Over the past four decades, there has been an increase in the prevalence of overweight and obesity in adults across all genders, ages, and racial/ethnic groups (Ichinohe et al., 2004). The negative effects of obesity on both the individual and society are serious and multi-dimensional. Obesity is a risk factor for many health problems, including coronary heart disease, certain forms of cancer, type 2 diabetes, hypertension, dislipidemia, stroke, gall bladder diseases, osteoarthritis, sleep apnea, and gout and is associated with increases in all-cause mortality (Cataldo, 1999).

Obesity is caused by a combination of increased caloric intake and decreased caloric expenditure resulting in a state of “positive” energy balance (Miller, 1999). Sedentary life style is among the risk factors for significant diseases. Regular physical
activity prevents or limits weight gain and gain in body mass index (Kyle et al., 2001).

In a study conducted by Moor et al., (2001) showed that people with type-1 diabetes can participate in extreme altitude mountaineering. However there are significant risks associated with this activity including hypoglycemia, ketoacidosis and retinal hemorrhage.

Life style changes reduced the incidence of diabetes in persons at high risks and it was also found that life style intervention was more effective than metformin (Bo-Abbas et al., 2002).

Exercise is a key component in the management of type-2 diabetes. It is beneficial for both glucose uptake mechanisms and the antilipolytic effects of insulin (Balasubramanyam, 1999). Lee et al., (2003) studied the improving effect of hiking at high altitudes. He concluded that glucose tolerance appears to be influenced by the geographic environment. He suggested that high altitude living conditions and activities may possibly be developed as potential natural medicines for the prevention and treatment of type-2 diabetes in the future. The beneficial effects of exercise in these patients are related to an improvement in cardiovascular fitness and insulin resistance. Dr. M. Cizmic and colleague from the Institute of Medical Research Belgrade, Yugoslavia looked at the relationship between the improvement in aerobic capacity and the degree of improvement in insulin sensitivity after short-term physical training in patients with type-2 diabetes.

It has been revealed that exercise was associated with dynamic changes in the cellular contents of the insulin-stimulated glucose transporter in muscle. Glut-4 increases over the first year and decline back to baseline during second years (Balasubramanyam, 1999).
Diabetes is the most common cause of blindness in the older population. Macular degeneration and cataracts are the common cause of loss of vision in the elderly and seem to be even more common in diabetes (M.M.W.R., 1996).

The epidemic of type-2 diabetes and impaired glucose tolerance is one of the main causes of morbidity and mortality worldwide (Saltiel and Kahn, 2001) and environmental factors also play an important role in it. It is suggested that high altitude living conditions and activities may possibly be developed potential medicine for the prevention and treatment of type-2 diabetes mellitus in the future (Lee et al., 2003). In another study conducted by Larsen et al., 1977, it was found that exposure to altitude hypoxia elicits changes in glucose homeostasis with increase in glucose and insulin concentration within first few days at altitude. He concluded that insulin action decreases markedly in response to two days altitude hypoxia, but improves with more prolonged exposure. Enzo et al., (2004) established that individuals with low insulin sensitivity and low insulin response had a sevenfold higher risk of diabetes.

In north-east United States, over the last 30 years, there has been a tripling of type-1 diabetes in children under the age of 15. In three studies in Japan, Israel and Canada emigrants assume a risk of type-1 diabetes closer to that of their destination country than of their country of origin (Rewers et al., 1987). Type-1 or IDDM is primarily the result of pancreatic β-cell destruction and is associated with a variety of immune phenomena, directly involved in β-cell killing (Dahlquist, 1993).

The maintenance of a blood glucose level within a narrow limit (3.0 to 5.0 mmol/l or 55 to 90 mg/dl in the fasting subjects) is an important homeostatic mechanism (Walter and Israel, 1994). The blood glucose level is mainly regulated by
two principal hormonal factors, insulin and glucagon and these are counter-regulatory in action (Karam and Forsham, 1994).

In the two types of diabetes, obesity is present in most of the people with type-2. Hypertension is also common in people with type-2 diabetes. Although we do not know all reasons why hypertension is very common in diabetics, it is believed that it is the increase of blood insulin that promotes hypertension by affecting key check points in the body. Increased blood insulin makes blood vessels widen (vasodilate) and this widening of the blood vessels affect the sympathetic nervous system that increases blood pressure directly or indirectly by making the kidney retain salt. Another way the increase in blood insulin can lead to increased blood pressure is by promoting atherosclerosis which hardens the blood vessels (Levetan, 2001).

Hormones play a vital role in body metabolism. In an experiment on women, conducted by Braun et al., (2000) at higher altitude, it was explained that decreased carbohydrate utilization may be due to relative abundance of estrogen and progesterone. Sawhney et al., (1991) conducted an experiment on euglycemic men and monitored concentration of glucose, lactic acid, free fatty acid, insulin, cortisol and growth hormone in blood of human at high altitude and found a significant increase in cortisol concentration after arrival at high altitude. There was no appreciable change in growth hormone and free fatty acid during the sojourn at high altitude. Blood lactic acid concentration decreased significantly and plasma insulin and growth hormone was higher in acclimated lowlander and high altitude natives than the values of sojourn at sea level. All these results indicated that at high altitude glucose values were high for the insulin concentration observed and might have been due to increased secretion of growth hormone by pituitary gland.
Stepanova et al., (1989) also observed increased level of blood cortisol in relative insulin insufficiency in migrants moving to high altitude. In an experiment on rat with alloxan diabetes, Tikhonova et al., (1987,1988) observed a decrease in insulin and glucagon concentration in blood of rats within fourteen days of maintaining at high altitude and a steadily decrease when adapted to high altitude.

In a study conducted on glucose metabolism in pregnancy by Krampf, et al., (2001), there was no significant difference between levels of C-peptide and beta cells function at high altitude and sea level, however fasting concentration of glucose, insulin and pro-insulin were significantly lower at high altitude than that at sea level.

Blum et al., (1979) in an experiment on cattle during treadmill exercise at high altitude observed that concentration of epinephrine and nor-epinephrine as well as parathyroid hormone increased within minutes. Elevated parathyroid hormone levels were probably caused by sympathetic stimulation.

Stock et al., (1978) concluded a study on fed and fasted human subjects and found that T₃, T₄ and TSH correlated with free fatty acids and exercise at high altitude caused greatest increase in circulatory levels.

Sutton and Garmendia (1977) found that in acute exposure to altitude exercise produced a marked rise of glucose, cortisol and growth hormone and fall in the insulin content of plasma. High altitude dwellers showed no significant changes in somatostatin, meanwhile an important elevation of cortisol occurred. Urdanivia et al., (1975) found that peak cortisol level occurred earlier in high altitude than in man living at sea level.

Insulin is a major anabolic hormone (Kahn and Halbane,1997). It is the dominant glucose lowering hormone (Service,1983) It suppresses endogenous glucose production and stimulates glucose utilization thereby lowering the plasma glucose
concentration. It is secreted into hepatic portal circulation and has important action on liver as well as on peripheral tissues. However a relative or absolute deficiency of insulin (Truglia and Olefsky, 1985) or its failure to implement its action of glucose transport into the cells for energy generation results in glycemic changes particularly hyperglycemia and it is indicative of the disease diabetes mellitus (Volk and Arquilla, 1985) and associated cardiovascular diseases (Heptinstall, 1974, Stout et al., 1975, Vracko, 1982, Craighead, 1988). Enzo et al., (2004) also reported that individual with low sensitivity and low insulin response had a sevenfold higher risk of diabetes. In a study conducted by Andrea et al., (2001), it was found that physical activity is negatively associated with insulin concentrations both in the Pima Indians, who tend to overweight, and in Mauritians who are leaner. These findings suggest a beneficial role of activity on insulin sensitivity that is separate from any influence of activity on body composition. If the population is insulin resistant, as reported in 2002 in Bethesda, it is a key in the cause for the diabetes mellitus.

Few studies have revealed that Mexican-Americans of both gender and all ages demonstrated greater levels of insulin resistance when compared to Non-Hispanic white population. In this report it is also suggested that genetic factors could explain the higher prevalence of insulin resistance in Hispanic population group. A lower Insulin resistance is observed in Mexican-Americans, regardless of behavioral and metabolic factors (Bethesda, 2002).

Insulin secretion was greater in response to altitude exposure. The data suggest that there is a transition from reduced to increased sensitivity to insulin as individuals acclimatize to hypoxia. There are many mechanisms that could potentially explain the transition but the most probable involve a change in tissue glucose uptake and/or
hepatic glucose production (HGP) as a result of the direct or indirect effects of one or more of counter-regulatory hormones (Lindgarde et al, 2004).

High altitude residence is well known to modify body chemistry and hormone status. (Savourey et al., 1998). High altitude dwellers are less sensitive to insulin compared with sea level (Braun et al., 2001). Balasubramanyam (1991), after an experiment, suggested that the activity of PDE-3 is increased by regular exercise that perhaps reflex a greater sensitivity to insulin.

Glucagon is secreted by alpha cells of islets of Langerhans. It is released whenever the blood glucose level drops below 4.5 mmol/l (80 mg/dl) and its main action is stimulating the liver to break down glycogen into glucose (glycogenolysis), which is released in the blood. In the adipose tissue, lipolysis is stimulated. It is evident that glucagon opposes the action of insulin (Fehling, 1970). Influence of the physical exercise at high altitude on endocrine function was studied by Sutton and Garmendia (1977). They concluded that the exposure to altitude provoked a rise in glucagon concentration directly proportional to the time of exposition to altitude.

Epinephrine which increases muscle glycogenolysis and hepatic glucose output raises glucose concentrations. Epinephrine increases sharply on short-term altitude exposure. Epinephrine promotes glycogenolysis and lipolysis (Crampes, 1991). It inhibits insulin secretion and insulin-mediated uptake of glucose by peripheral tissues. Epinephrine is not normally essential in combating hypoglycemia but it can assume a critical role when glucagon secretion is deficient. Both glucagon and epinephrine are most important in the acute short term regulation of blood glucose level.

Cortisol is secreted under stress. In the liver it deaminates and provides ideal substrates for conversion into glucose. Cortisol and growth hormone are less
important in the short-term maintenance of blood glucose concentration, rather they play role in the long-term management of glucose metabolism (Guyton, 2000).

BMI is a simple numeric measure of a person’s “fatness” or “thinness”, allowing health professional to discuss over/under-weight problems more objectively with their patients. It is meant to be used as a simple means of classifying sedentary (physically inactive) individuals with an average body composition. (World Health Organization, 2002)

A BMI nearing 15kg/m² is usually used as an indicator for starvation and the health risks involved. A BMI < 14.5kg/m² is an informal criterion for the diagnosis of anorexia nervosa. A BMI below 18.5kg/m² indicates underweight, 18.5 – 24.9kg/m² is normal range, 25-29.9 is overweight, and a BMI of ≥ 30 indicates obesity. There are some limitations to BMI such that the index is based solely on height and weight. (Cataldo, 1999).

BMI is also related to blood pressure. According to Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC VII) high blood pressure, hypertension affects about 50 million Americans and one billion people world wide. According to this report, the relationship between blood pressure and risk of cardiovascular disease/events is continuous, consistent, and independent of other risk factors. The committee comments “the higher” the blood pressure, the greater the chances of heart attack, heart failure, stroke and kidney diseases. In traditional or in under-developed society, the association of overweight with maternity and nurturing makes obesity culturally acceptable in contrast to western developed countries (Enzi, 1994).

The relationship between glycemic index and glycemic load was determined by using data obtained during 1988-1994 and presented in Third National Health and
The relationship between glycemic index and glycemic load was determined by using data obtained during 1988-1994 and presented in Third National Health and Nutrition, Examination Survey, it was found that high dietary glycemic index and high glycemic load are associated with a lower concentration of plasma HDL-C (Earl et al., 2001). In another study, a positive association was found between BMI and glycemic index and a measure of glycemic response was associated with ingesting different types of carbohydrates, but not with daily carbohydrate intake. The results suggested a relationship between the type of carbohydrate and body weight (Yunsheng et al., 2005).

A high prevalence of hypercholesterolemia and hypertriglyceridemia in both genders was observed at high altitude of Lima, Peru by Mohanna et al., (2006) It was also observed that regular exercise affective in reducing levels of triglyceride-rich VLDL. In a study conducted at high altitude by Mohanna et al., (2006) it was found that high BMI have a high prevalence of hypercholesterolemia (34.3%) and hypertriglyceridemia (53.9%) in both genders at high altitude which are the risk factors for cardiovascular diseases and coronary heart disease. Must et al., (1999) reported increased prevalent ratios by increasing severity of overweight and obesity for several health conditions, including high blood pressure. They also found higher prevalence ratios for cholesterol among overweight and obese men and women than among normal weight person.

It is known that residents at high altitude (HA) have a lower basal glycemia than residents at sea level (SL). However, whether such a difference is maintained throughout the full day remains unknown. Glucose profile at high altitude was lower throughout the glucose monitoring than that at sea level (mean profile: 50.6 +/- 3.7 and 73.4 +/- 4.0 mg/dl respectively; p < 0.001). In conclusion, high altitude
natives resident have a lower blood glucose profile than sea level residents throughout 12-h continuous monitoring. At high altitude due to low oxygen level, glucose consumption is ultimately low. In different studies conducted on rats by McClelland et al., (1998) and Vats et al., (1999) and on women by Braun et al., (2000), results showed that exposure to high altitude caused alteration in metabolic process in carbohydrates. In women, unlike in men, exposure to high altitude, caused decreased utilization of carbohydrates (Braun et al., 2000) and in rats (McClelland, 1998), relative contribution of total carbohydrates, circulatory glucose and muscle glycogen did not increase after high altitude acclimation because the oxygen-saving advantage of carbohydrate is out-weighed by limited carbohydrate stores. Relative exercise intensity was the major determinant by metabolic fuel selection at high altitude as well as at sea level.

Glycemia in mammals is maintained according to its environmental needs. Studies on rats under hypoxic, hypobaric condition showed hypoglycemia (Singh et al., 1997) but a mild hyperglycemia during chronic exposure to hypoxia (Singh and Selvamurthy, 1993).

The metabolism of glucose in mammalian heart is 25-50% more oxygen efficient than the metabolism of free fatty acids. It was concluded that an elevated glucose preference was a true metabolic adaptation in human, adapted over generation to chronic hypoxia (Holden et al; 1995).

By the stimulation of adenylate cyclase by β-adrenergic like epinephrine, phosphorylase in the liver and skeletal muscle is activated. The consequence of this activation is a rise in the blood glucose and lactate level (Brook et al.,1991). In an experiment conducted by Yoshino (1987), it was found that blood glucose was not changed by adrenergic blockade, Prazosin and propranolol showed no effect on
glycolytic metabolites in plasma in fed rats at high altitude. However, blood glucose of fed rat was increased by α-1 blockade during severe hypoxia. Glucose homeostasis remained unchanged in rats adapted to high altitude (Tikhonova et al., 1987). However, an experiment conducted on rats with alloxan diabetes at high altitude hypoxic conditions, indicated an activation of cellular glycolysis, an increase in 2,3, diphosphoglyceric acid level in erythrocytes (Tikhonova and Kuchuk, 1988).

In an experiment on women at high altitude, blood glucose response was lower as compared with the sea level. It was possibly due to greater suppression of hepatic glucose production or stimulation of peripheral glucose uptake by insulin (Braun et al., 1998). Stepanova et al., (1989) conducted an experiment on human and concluded a high frequency of glucose tolerance disorder (GTD) in migrants. This GTD is associated with an increased level of blood cortisol in relative insulin insufficiency.

In an experiment to study glucose tolerance of lowlanders during prolonged stay at high altitude and among high altitude natives, Srivastava et al., (1975), found that the tolerance curve of Ladakki is similar to that of lowlanders but showed sharper blood glucose decline rate.

In a study on rats exposed to hypoxic stress, three fold increase in liver glycogen and slight increase in muscle glycogen was determined (Vats et al., 1999). During exercise active skeletal muscle is predominant site for glucose disposal at higher altitude but not the sole source of blood lactate during exercise (Brook et al., 1991). Plasma lactate and pyruvate were increased more markedly in fed rats than in fasted rats exposed to higher altitude. The increase in plasma lactate and pyruvate was enhanced and inhibited by α-1 adrenergic antagonists, prazosin and the β-blocker propranolol respectively (Yoshino et al., 1987).
In an experiment to determine a relationship between uphill running performance at altitude and blood metabolic level, it was found that lactate concentration was elevated in the blood of fast runner. It suggested that an anaerobic metabolism can contribute to total energy production during prolonged exercise at high attitude. Increased exercise-arterial lactate concentration response on arrival at high altitude and subsequent decrease with acclimatization are due to change in blood lactate appearance (Brook et al., 1992).

Vats et al., (1999) in an experiment on rats subjected to hypoxic stress showed rise in blood hemoglobin and plasma proteins in response to acclimatization. These results suggested no dramatic changes in levels of proteins in muscle and liver.

In an experiment conducted on male albino rats, which were fed on glutamate it was indicated that activity of glutamate may possibly ameliorate hypoxia-induced oxidative stress (Kumar et al., 1999).

In a study conducted by Young et al., (1987) on human, it was found that post-exercise plasma ammonia concentration was decreased with altitude acclimatization, when compared with ammonia concentration following exercise performed at the same relative intensity at sea level. The decrease in ammonia accumulation may contribute to enhanced endurance performance and altered substrate utilization will exercise following acclimatization to altitude.

Kumar et al., (1999) in an experiment on male albino rats found urea level remained elevated on glutamate supplementation under hypoxic condition. He also found that high altitude stress led to lipid per-oxidation and free radical formation, which resulted in cell membrane damage in organs and tissue and associated diseases.

At high altitude hypoxic conditions, enzyme levels also change. Vats et al., (1999) studying rats exposed to hypoxic stress showed no change in glycogen
synthetase. However there was an increase in glutaminase activity in liver and muscle. Kumar et al., (1999) found serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) levels elevated in glutamate fed albino rats.

According to Wang et al., (2007) there is a relationship between the polymorphism of gene of glucose transporter-1(GLUT-1) and the human body adaptation to high altitude hypoxia environment. He hypothesized that GLUT-1G + 22999T may be associated with the adaptation to high altitude hypoxia.

In different studies conducted it was found that rats exposed to hypoxic stress showed decrease in food intake (Singh et al., 1997; Vat, 1999) and water intake (Singh and Selvamurthy, 1993, Singh et al., 1997) and also 28-30% decrease in body weight (Singh and Selvamurthy, 1993; Singh et al., 1997) during continuous and also chronic exposure to hypoxia.

A study on relation of glycemia and hematocrit during high altitude acclimatization was conducted by Di Tano et al., (1981) and to observe if, subsequently to an increase of hematocrit, glycemia should become lower. From observed results, this relation was not found. High hemoglobin can occur due to long disease, living at high altitude, or excessive bone marrow production of blood cells (Di Tano et al., 1981)

Hemoglobin increase with increasing altitude and this increase in hemoglobin concentration leads to an increased atherosclerotic process (Wu et al., 2005). Hematocrit is significantly related to the incidence of CVD including CAD, myocardial infarction, angina pectoris.
to hypocapnia, are also impaired. The reason for these apparently abnormal cerebrovascular responses is unknown, but one possibility is that they may be related to the high hematocrit, as Andean (Goenz et al., 1993), who are both hypoxic and polycythemic, have impaired cardiovascular responses to changes in oxygen and carbon dioxide levels, whereas Tibetans, who are also hypoxic, but less polycythemic, have apparently normal responses.

It is concluded that high altitude native did not display any sign of great sympathoadrenergic activation during chronic hypoxia and that the exercise-induced hormonal changes remained unaffected by acute inhalation of a normoxic gas mixture (Favier et al., 1996).

A Peruvian study reported that the prevalence of hypertension at high altitude was lower than in a low altitude population (Wolff et al., 1994). A study in Central Asia also agreed with the Peruvian study. It demonstrated that hypertension was more prevalent at lower altitude than at high altitude (Fiori et al., 2000). A Russian study on high altitude also reported that hypertension was significantly higher among residence in low altitude region compared with residents in high altitude region (Mirrakhimov et al., 1985).

In an experiment conducted by Smith (1999) on Sherpa men in Nepal, data showed that obese men (>30 kg/m²) were 8.6-9.1 times more likely to have elevated B.P. Higher altitude dwellers usually have lower B.P (Liu, 1990). Elevated blood pressure appeared to be associated with elevated BMI (Smith, 1999). Gesang et al., (2002) in a study observed a significant association between the D- allele of the ACE gene and hypertension. Among the 17 European countries, Greece had the highest percentage (26.7%) of its population in the obese category and Italy and Netherlands the lowest (White and Cash, 2004). In Bulgaria 62.6% of men and 55.5%
of women has increased BMI. The percentage of men with BMI exceeding 25-29.9 kg/m² dominated in the age group 35-44 years. In this age group 20% had a BMI above 30 (Vassilevsky and Voukov, 2003). African-Americans had larger BMIs and were consuming more fat than the females. These results are in agreement with previous investigations (Winkleby et al., 1999), Huang et al., 2002, Post et al., 2001). It is suggested that the increased adiposity among the African-Americans males may be a function of increased energy intake. In particular the wsextremization of dietary style is a major factor, as exemplified by fast rising sale of high caloric drinks or fast food in non-Western nations (Enzi, 1994).

Here are some limitations to BMI such that the index is based solely on height and weight. Individual who have significant lean tissue or skeletal mass may reveal high BMI values, yet have a lower risk for obesity. However, BMI is an imprecise measurement of fatness (Roubenoff et al., 1995).

In a study, it has been reported that high altitude acclimation alone greatly stimulate lipolysis (Grant et al., 2001). Hypoxia results in adipose lipolysis and muscle or liver glycogenolysis. An increase in the blood concentrations of free fatty acids and/or ketones could be at least partially responsible for the exaggerated blood glucose response observed in response to hypoxia (Braun et al., 2001). Colder temperatures produce an increase break down of triglycerides in muscles and adipose tissues (Vallerand and Jacobs, 1990). Ferezou et al., (1988) proved that level of triglyceride decreased, suggesting that hypoxia induced lipolysis of plasma triglycerides. Triglycerides are a form of fat in the bloodstream. People with high triglycerides often have high total cholesterol, a high LDL (bad) cholesterol and low HDL (good) cholesterol level. Many people with heart diseases also have high triglyceride levels. Several clinical studies have shown that people with above normal
triglyceride levels (greater than or equal to 200 mg/dl) have an increased risk of heart disease. People with diabetes or who are obese are also likely to have high triglycerides.

High triglycerides in the blood are often seen in overweight people. Even, people who are not overweight may have stores of fat in their arteries as a result of insulin resistance. These triglycerides in the blood are the direct result of carbohydrates from the diet being converted by insulin. These triglycerides do not come directly from dietary fats. They are made in the liver from any excess sugars, which have not been used for energy (Avins and Neuhaus, 2000).

According to another report of daily University Science News, high altitude works against development of fat cells. Training, at high altitude, where oxygen levels are lower, enhances body fat reduction (Giaccia, 2002).

Glisezinski et al., (1999) in a study to examine the effect of prolonged hypoxia on adipose tissue lipolysis, in relation to the weight loss, usually observed at high altitude, concluded that prolonged exposure to hypobaric hypoxia led to a potent reduction in lipid mobilization through a decrease in the efficiency of β-adrenergic, GH and PTH. The main finding of the studies indicated that decreased BMI in both men and women significantly decreased cholesterol and triglyceride in women and a significant correlation between glucose and BMI were observed. Increased BMI is an independent risk factor for numerous cardiovascular diseases. The proportion of obesity in women was very high and there was a big gender difference. In Europe and America, there is a small difference in obesity prevalence between men and women, as is the case in South Pacific countries, in contrast with Jamaica. The same tendency as found in Jamicans is seen only in Africa and in U.S.A blacks (Ichinohe et al., 2004). The association observed between cholesterol and physical activity in men,
only during walking, could be explained by the fact that in this case there was an energy expenditure (>2000 kcal/week), which is considered as the accepted cardioprotective threshold.

A sedentary life style is among the risk factors for significant diseases. Regular physical activity prevents or limits weight gain, and gain in body mass index (Kyle et al., 2001). Due to mountainous topography, the subjects are generally doing hard physical work. Regular exercise exerts a potent influence to control body weight and improves sensitivity to insulin (Stamler, 1991). Physical activity has been shown to be neuroprotective in many neurodegenerative and neuromuscular diseases (Clement and Bell, 1985).

Not everything benefits equally from exercise. There is tremendous variation in individual response to training where most people will see a moderate increase in endurance form aerobic exercises, some individuals will be benefited as much as double their oxygen uptake, while others will never get any benefit at all, from the exercise (Christensen, 2004)

Aerobic exercise reduces blood pressure in both hypertensive and normotensive persons. An increase in aerobic physical activity should be considered an important component of lifestyle modification for prevention and treatment of high blood pressure (Duncan, 1985).

Prolonged high altitude exposure significantly reduces lean body mass and body fat with the magnitude elevation. In addition to depressed appetite and food intake during high altitude exposure, intestinal absorption efficiency decrease, compound the difficulty in mountaineering. The basal metabolic rate also increases significantly upon arrival at altitude which further affects the tendency-lose weight. (Rose, 1988)
Obesity is caused by a combination of increased caloric intake and decreased caloric expenditure resulting in a state of “positive” energy balance (Miller, 1999). Obesity multiplies the risk of developing hypertension about fourfold in men and threefold in women (National Audit Office; 2001). In England, the proportion categorized as obese are about one in five men and one in four women (Joint Health Surveys Unit; 2004 and Health Survey for England; 2003). Levels of obesity are much lower in Pakistani, Indians, Chinese, and Bangladeshi men and higher in Black Caribbean and Pakistani women (Joint Health Surveys Unit; 2000).

High altitude pulmonary edema is a life threatening form of non-cardiogenic pulmonary edema, that occurs in otherwise healthy mountainous at altitude above 2500 meters (8202 feet). However some cases have been reported at lower altitudes (between 1500-2500m in highly vulnerable subjects), although what makes some people susceptible to HAPE remains the cause of death, related to high altitude exposure with a high mortality in absence of emergency treatment (Wikipedia, 2008).

A lower mortality from coronary heart disease has been observed in populations living in areas of high altitude. However, the effect of living at high altitudes in itself is difficult to quantify, as there are other variables that must be taken into account such as genetic factors, diet and physical activity. There is a strong and direct relationship between excess weight and hypertension (Kornitzer et al., 1999). Cardiovascular diseases due to high-density lipoprotein cholesterol also change with changing altitude. In a study it has been shown that high density lipoproteins cholesterol level are linearly and significantly increased when living at high altitude. This fact should be taken into account when comparing cardiovascular risk in populations living at different altitudes (Domínguez et al., 2000).
In a study it is reported that total cholesterol decreased with increasing altitude whereas high-density lipoprotein cholesterol (HDL-C) increased (Sharma, 1990), however the Central Asia study reported that the serum lipid level did not differ between population in low and high altitude areas (Fiori et al., 2000). A study that was conducted on Tibetans demonstrated lower serum lipid level with a low incidence of CAD with high altitude living (Fujimota et al., 1989). A Venezuelan study reported that men and women living at high altitude had significantly lower plasma total cholesterol and low-density lipoprotein cholesterol (LDL-C) levels and slightly lower HDL-C levels than those at lower altitudes (De Mendoza et al., 1979).

In a report from a hospital at high altitude in Saudi Arabia where 124 patients were admitted with proved acute myocardial infarction, there were 116 men (94%) and the major risk factor were diabetes and hypercholesterolemia (Ashouri et al., 1994).

Al-Tahan et al., (1998) and Jha et al., (2002) found that the frequency of thrombotic stroke at high altitude was higher than at low altitude. High frequency of thrombotic stroke was explained by increased hematocrit which might have caused this in conjunction with other factors such as hypertension and ischemic heart disease.

The literature presents a clear picture of association of highlanders active life and hypoxic and hypobaric conditions with incidence of diabetes mellitus and cardiovascular risks. The present study will be a useful contribution in this regard.
Materials & Methods
MATERIALS AND METHODS

a) Subjects

A significant number of high altitude and lowlanders natives of various hilly districts of Azad Jammu & Kashmir and plain area of Punjab were studied. All subjects in investigation participated in a familiar way. During studies subjects were informed about the experimental procedure and they filled their questionnaire.

b) Questionnaire

A comprehensive questionnaire was designed according to the objectives of the study. Questionnaires were administrated to 1168 subjects, 973 of whom were native of moderate and high altitude where as 195 were lowlanders. The questionnaires were filled on spot. In included information regarding different parameters given in experimental design.

c) Experimental Design

For survey and sampling, District Health Officer, Director Population Welfare Programme, Physicians at the selected area and Cardiologist at Combined Military Hospitals, Forest officials, Agriculture Officers, college principals and staff, social and political workers were contacted and a detailed plan and programme of work at different location in each selected district was discussed approximately a week before data collection and blood sampling.

A physician/dispenser/nursing staff accompanied the researcher to the selected area one-two day before the date of data collection. By a messenger, the population of that area was requested for overnight fasting for at least ten hours and motivated for blood test and its sampling on the spot.
Study area was divided into three categories. Category A, consists of area which is plain at low land. Category B, consists of area with moderate altitude ranging from 12,00 to 18,00 meters and category C consists of area with high altitude ranging from 1801-3000 meter.

The study included the data concerning the levels of glucose, BMI, blood pressure, total cholesterol, triglyceride, hematocrit, pulse. Data was collected at the residences/ dispensary/ hospital. Personal profile was also taken from subjects.

Weight was measured by Bathroom scale Tanita and their height was measured by wall tape, eyes looking straight ahead. Glucose estimation was done for every subject. However total cholesterol, triglyceride, hematocrit was done on volunteers.

d) Blood Sampling

Before estimation of glucose, cholesterol, triglyceride, the fingertip was sterilized with methylated spirit and then lancet pen was used to obtain a full drop of blood. Blood sample was obtained from antecubital vein for the estimation of hematocrit. Blood for hematocrit was collected in heparinized capillary tubes which were, later on, centrifuged at 3000 rpm for 15 minutes for the separation of plasma and cells. Later, the percentage of plasma and cells was recorded.

Glycemic status of the subjects was assessed with glucometer.

Cholesterol and triglyceride estimation was done by GCT Meter (Made Accutrend, Roche Company, Japan).

i) Glucose Estimation

Glucose reflectance meter (glucometer) was used to measure the glucose level and recorded on the questionnaires. In area category A, 195 and from B and C area
category at least 400 male and female individuals were investigated. These individuals were mostly 40 + years.

ii) Hematocrit

Hematocrit is the percent volume of whole blood that is occupied by red blood cells. It is determined by centrifuging the blood in special hematocrit capillary tubes. Hematocrit was determined by puncturing the finger with a sterile lancet and a drop of blood was obtained. First drop of blood was wiped off and the second drop was allowed to accumulate. Red circled end of heparinized capillary tube was touched to the drop. Tube was held in a horizontal position and blood was allowed to enter until the tube was one half to three fourth full. One end of the tube was sealed by pushing it into a tablet of sealing compound and rotating it to form a plug. The capillary tubes were placed in centrifuge machine bound tightly with glass test with the plug end to the outside and centrifuged for four minutes. After four minutes height of RBC column was measured in millimeter. The ratio of red blood cells with plasma level determined the hematocrit of the subjects. The formula of hematocrit determination is:

$$\text{Hct} \% = \frac{\text{Height of red cells (mm)}}{\text{Height of red cells + plasma}} \times 100$$

e) Altitude Measurement

To measure the altitude, Pocket Altimeter / Barometer Model 7030 was used. This is an aneroid-type altimeter that indicates the altitude of the position converted from the air pressure that goes lower as we climb up and goes higher as we go down.

f) Data Collection

Fasting blood glucose, total cholesterol and triglyceride were measured in samples obtained from the antecubital vein between 8:00 a.m. and 10:00 a.m. after an overnight period of fasting for 10-14 hours.
Five ml of blood was obtained after overnight fast by venipuncture from all participants who attended at the health centre as requested. Individuals were also weighed, measured, and asked to answer a questionnaire regarding smoking habits, physical activity, diet, and medical history. Blood pressure of the subjects was measured in a seated position, employing a mercury sphygmomanometer.

**g) Data Classification**

**i) Glycemia**

Glycemia was classified according to WHO criteria (1999) and found that fasting blood glucose level <110mg/dl is considered normal, 110-126 mg/dl, as impaired glucose tolerance and more than 126 mg/dl as diabetic.

**ii) BMI**

The BMI was calculated as weight in kg divided by height in m². In 1998, the U.S National Institutes of Health brought U.S definitions into line with World Health Organization guidelines. Adults whose BMI is between 18.5 kg/m² and 22.9 kg/m² have a low risk of developing heart disease and other health problems such as diabetes.

The US National Heart, Lung and Blood Institute (1998) uses the body mass index to classify obesity.

<table>
<thead>
<tr>
<th>CATEGORIES</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anorexic</td>
<td>&lt; 14.5 kg/m²</td>
</tr>
<tr>
<td>Underweight</td>
<td>14.6-18.4 kg/m²</td>
</tr>
<tr>
<td>Normal</td>
<td>18.5-24.9 kg/m²</td>
</tr>
<tr>
<td>Over-weight</td>
<td>25.0-29.9 kg/m²</td>
</tr>
<tr>
<td>Obesity 1</td>
<td>30.0-34.9 kg/m²</td>
</tr>
<tr>
<td>Obesity 2</td>
<td>35.0-39.9 kg/m²</td>
</tr>
<tr>
<td>Obesity 3</td>
<td>≥40 kg/m²</td>
</tr>
</tbody>
</table>
The weight excess or deficiency may, in part, be accounted for body fat (Adipose tissue). Although other factors such as muscularity also affects BMI significantly. The statistical spread is usually described in broad category: The CDC and the WHO record a BMI of less than 18.5 as underweight and may indicate malnutrition, an eating disorder, or other health problems, while a BMI greater than 25 is considered overweight and above 30 is considered obese (Jeukendrup et al., 2005).

iii) Cholesterol

The recommended values from the National Cholesterol Education Program are as follow (McArdle, 2001)

<table>
<thead>
<tr>
<th>Category</th>
<th>Total Cholesterol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desirable</td>
<td>&lt;200mg/dl</td>
</tr>
<tr>
<td>Borderline</td>
<td>200-239 mg/dl</td>
</tr>
<tr>
<td>Abnormal</td>
<td>&gt;240 ml/dl</td>
</tr>
</tbody>
</table>

iv) Triglyceride

The American Heart Association has set guidelines for triglyceride levels.

<table>
<thead>
<tr>
<th>Category</th>
<th>Level mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;150mg/dl</td>
</tr>
<tr>
<td>Borderline</td>
<td>150-199mg/dl</td>
</tr>
<tr>
<td>High</td>
<td>200-499mg/dl</td>
</tr>
<tr>
<td>Very High</td>
<td>&gt;500 mg/dl</td>
</tr>
</tbody>
</table>
v) Blood Pressure

Classification of blood pressure levels of the British Hypertension Society for
Adults age \( \geq 20 \) years is as follow.

<table>
<thead>
<tr>
<th>Category</th>
<th>Systolic Blood Pressure (mmHg)</th>
<th>Diastolic Blood Pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal</td>
<td>&lt; 120</td>
<td>&lt; 80</td>
</tr>
<tr>
<td>Normal</td>
<td>120-129</td>
<td>80-84</td>
</tr>
<tr>
<td>High Normal</td>
<td>130-139</td>
<td>85-89</td>
</tr>
<tr>
<td>Hypertension i</td>
<td>140-159</td>
<td>90-99</td>
</tr>
<tr>
<td>Hypertension ii</td>
<td>160-179</td>
<td>100-109</td>
</tr>
<tr>
<td>Hypertension iii</td>
<td>( \geq 180 )</td>
<td>( \geq 110 )</td>
</tr>
</tbody>
</table>

Statistical Analysis

A spreadsheet was made in Microsoft Excel and data was analyzed in MINITAB V13.0 using t-test and Z-test.
Results
RESULTS

In the study the effect of altitude on various parameters of life style has been investigated. The populations at low level, moderate and comparatively higher altitudes have been sampled for the analysis.

Glycemia

The random glycemic status studied at high altitude (1801-3000meter) in the subjects was found to be 97.34±1.35mg/dl whereas it was 116.63 ± 3.99 mg/dl in lowlanders. Results showed a significant decrease in high altitude subjects (P<0.05). The Fasting Blood Glucose (FBG) level was 94.0±2.1 mg/dl at moderate altitude (1200-1800 meter) and 100.4±1.8 mg/dl at comparatively high altitude (>1800 meter) and that was statistically increase (P<0.05) (Fig. 1).

Fig. 1. Random glycemia in Lowlander (LL) & Highlander (HL) and fasting blood glucose level (mg/dl) of subject living at <1800 & >1800 meter. Significant difference *P<0.05.

Genderwise FBG level was 111.49±5.13mg/dl and 123.15±6.18 mg/dl in males and females of lowland respectively. It was 96.7 ± 3.4 mg/dl and 91.4±2.5 mg/dl in males and females respectively at moderate altitude. At comparatively high
altitude, FBG level was found to be 96.3±2.5 mg/dl and 105.7±2.3 mg/dl in male and female subjects respectively. The data shows that blood glucose level in females was significantly higher than males in the subject living >1800 meter (P<0.05) (Fig. 2).

Fig. 2: Fasting Blood Glucose (mg/dl) of the males and the females compared inhabiting Lowland (LL), Moderate altitude <11800 meter and >1800 meter. Significant difference *P<0.05.

Fig. 3: Fasting Blood Glucose (mg/dl) in the male subjects inhabiting Moderate (<1800m) and High altitude (>1800m).
Fig. 4: Fasting Blood Glucose (mg/dl) in the female subjects inhabiting Moderate (<1800m) and High altitude (>1800m). Significant difference *P<0.05.

Blood glucose level of male subjects of moderate and high altitude was observed in closer range; whereas female subjects living at high altitude exhibited significantly higher blood glucose level (P<0.05).

BMI

The mean BMI value of subjects at the altitude of <1800 meter was found to be 22.77 ± 0.14 kg/m² whereas the BMI of lowlanders was found to be 28.13±0.89 kg/m². There is a marked & significant decrease in BMI of the average of both moderate and comparatively high altitude subjects. The level of BMI at <1800 meter and >1800 meter altitude were found 22.91±0.20 kg/m² and 20.59±0.33 kg/m² respectively which shows that the subjects at high altitude have still lower BMI compare to those of the moderate altitude (P<0.05) (Fig 5).

Gender wise BMI at altitude less than 1800 meter was found to be 22.97 ± 0.27 kg/m² and 22.86 ± 0.30 kg/m² for male and female respectively and the
difference was found non significant. BMI value at > 1800 meter was 21.68±0.33 kg/m² for males and 19.18± 0.62 kg/m² for females (Fig. 6).

![BMI Chart](image)

Fig. 5. Body Mass Index (BMI) kg/m² of Lowlander (LL) & Highlander (HL) and of subjects living at <1800 & >1800 meter. Significant difference *P<0.05.

![BMI Chart](image)

Fig. 6. Comparison of Body Mass Index (kg/m²) in Moderate and Comparatively High-altitude Male Sampled Population
Fig. 7. Comparison of Body Mass Index (kg/m²) in Moderate and Comparatively High-altitude Female Sampled Population. Significant difference *p<0.05.

When compared, gender wise, the high altitude females have significantly lower BMI than those of the moderate altitude (P<0.05).

The data shows that both male and female subjects of high altitude have significantly decreased BMI than that of moderate and as well as that of low land subjects (P<0.05).

**Cholesterol**

The cholesterol level was found to be 185±4.57mg/dl and 167.07±2.32mg/dl in lowlanders and high altitude subjects respectively. At moderate altitude (1200-1800 meter), cholesterol level was 171.7±4.6mg/dl where as it was 163.7±2.0mg/dl at comparatively high altitude (>1800 meter). The circulatory cholesterol was demonstrated to gradually decreasing with the increase in the altitude. The level of the both the higher altitude was significantly lower than the lowlander (P<0.05), however, there was no significant difference among the both highlanders category (Fig 8).
Fig. 8. Serum Cholesterol mg/dl of Lowlander (LL) & Highlander (HL) and of subjects living at <1800 & >1800 meter. Significant difference *P<0.05.

In lowlanders levels were 177.08±5.15mg/dl and 193.28±7.37 mg/dl in male and female subjects respectively exhibiting significant greater level in the females. At moderate altitude, level was 174.0±6.1mg/dl and 168.9±7.1mg/dl in males and females respectively Fig. 9). Unlike the lowlanders in this category females have lower cholesterol levels, however, statistically non significant (Fig. 10).

Fig. 9. Comparison of Cholesterol Level (mg/dl) in Moderate and Comparatively High-altitude Male Sampled Population.
Fig. 10. Comparison of Cholesterol Level (mg/dl) in Moderate and Comparatively High-altitude Female Sampled Population.

At comparatively high altitude, value was found to be 162.7±3.2mg/dl and 164.6±2.9mg/dl in males and females respectively. Data shows that cholesterol level of male subjects living at high altitude was significantly lower than that of moderate altitude subjects (P<0.05) while in females values are not significant.

Triglyceride (TG)

Result shows that triglyceride levels at higher altitudes (>1200 meter) was 147.99±7.68 mg/dl compare to 252.2±11.6 mg/dl in lowlanders. A marked and significance lower level of the fraction prevails in the higher altitude population compare to the lowlanders (P<0.05). At moderate altitude (1200-1800 meter), its level was 169±16 mg/dl and at high altitude it was 135.8±7.6 mg/dl. Triglyceride level of the subjects at high altitude was significantly lower than those of moderate altitude (P<0.05) (Fig. 11).

In the gender comparisons in lowlanders, level of triglyceride was 230.6±14.8mg/dl and 274.8±17.3mg/dl in males and females respectively. At moderate altitude, it was 203±26mg/dl in males and 127.4±11mg/dl in females.
Compare to the males where the difference between low land and moderate high land subjects was non significant in females the fraction level was even less than half of the lowlander females to the moderate high land thus statistically highly significant (P<0.001)

Fig. 11. Serum Triglyceride (TG) mg/dl of Lowlander (LL) & Highlander (HL) and of subjects living at <1800 & >1800 meter. Significant difference **P<0.001 & *P<0.05).

Fig. 12: Comparison of Triglyceride Level (mg/dl) in Moderate and Comparatively High-altitude Male Sampled Population. Significant difference *P<0.05).
Fig. 13: Comparison of Triglyceride Level (mg/dl) in Moderate and Comparatively High-altitude Female Sampled Population.

In males, triglyceride level was 143.1±12mg/dl and 127.4±8.8mg/dl in females at high altitude respectively. Data shows that at moderate altitude (1200-1800 meter) females have comparatively lower triglyceride level than the males subjects and difference was significant (P<0.05) (compare Figs. 12& 13).

Data shows that male subjects of high altitude have significantly lower level of triglycerides than males of moderate altitude (P<0.05) but in female subjects the values were in a closer range (Fig.13).

Systolic Blood Pressure

Average systolic blood pressure (SBP) value in subjects of both higher altitudes studied was 118.81±0.59mmHg. Separately, subjects of moderate altitude and high altitude had the mean value of 122.2±0.93mmHg and 115.8±0.71 mmHg respectively. The SBP of lowlander had a mean value of 125.25±1.95mmHg. Highlander showed comparatively slightly lower average value of SBP than the lowlanders, however, statistically, significant (P<0.05) (Fig. 14).
Fig. 14. Systolic Blood Pressure in mmHg (BPS) collectively of higher altitude and separately of Moderate <1800 meter and High altitude >1800 meter Sampled Population.

Systolic blood pressure of lowland male subjects was 124.5 ± 2.5 mmHg and that of females was 126 ± 1.6 mm Hg. It was measured at 122.5±1.4 mmHg and 121.4±1.3 mmHg in male and female subjects of moderate altitude respectively. In the females of moderate highland SBP was slightly lower, however, significant statistically than lowlander females (Figs 15 & 16).

Fig. 15. Comparison of Systolic Blood Pressure (mmHg) in Moderate and Comparatively High altitude Male Sampled Population. Significant difference *P<0.05).
In subjects of comparatively high altitude subjects, systolic blood pressure value was 115.6±0.88 mmHg and 116.0±1.2 mmHg in males and females respectively (Figs. 15 & 16).

![Bar chart showing systolic blood pressure comparison between <1800 and >1800 altitude in meter.](image)

Fig. 16. Comparison of Systolic Blood Pressure (mmHg) in Moderate and Comparatively High altitude Female Sampled Population. Significant difference *P<0.05).

The data shows that both male and female subjects living at high altitude have lower systolic blood pressure than those of moderate altitude (P<0.05).

**Diastolic Blood Pressure**

Diastolic blood pressure value of the subject measured in the subjects of both the higher altitude was 78.72±0.38 mmHg. Separately, in subjects of moderate altitude, diastolic blood pressure was 79.4±0.54 mmHg and at high altitude value was 78.1±0.52mmHg (Fig 17). The average diastolic blood pressure of lowlanders was 75±1.3mmHg.

Gender wise diastolic blood pressure of low land male subjects was 75.5 ± 1.3 mm Hg and that of females was 76.5 ± 1.4 mm Hg.
Fig. 17. Diastolic Blood Pressure in mmHg (BPD) collectively of Higher altitude and separately of Moderate <1800 meter and High altitude >1800 meter Sampled Population.

The diastolic blood pressure was 79.2±0.83 mmHg and 79.2±0.78 mmHg in male and female subjects of moderate altitude respectively.

Fig. 18. Comparison of Diastolic Blood Pressure (mmHg) at Moderate and Comparatively High-altitude Male Sampled Population.

Diastolic blood pressure value was 77.9±0.66 mmHg in male and 78.5±0.83 mmHg in female subjects inhabiting high altitude. Data shows that diastolic blood pressure of the moderate and high altitude subjects and also in different genders did not show noticeable differences.
Hematocrit

The average hematocrit value of lowland subject of both the gender was measured at 50.7±1.05. Compare to this the average values of the subjects inhabiting both the category of higher altitude studied was 50.39±0.65%. Separately at moderate altitude, hematocrit level was 51.20±0.74% and 48.35±1.20% in subjects of comparatively high altitude. Hematocrit level of the high altitude subjects was significantly higher than those of moderate altitude (P<0.05).
Gender wise level was $52.31 \pm 0.89\%$ and $49.15 \pm 1.2\%$ in male and female subjects of moderate altitude. In comparatively high altitude values were $50.78 \pm 1.3\%$ and $45.23 \pm 1.6\%$ in male and females. Males have significantly higher value than females ($P<0.05$) (Figs 21-23).

![Graph](image)

**Fig.21.** Hematocrit (Hct) % of the Male and Females subjects separately living at Moderate and High altitude. Significant difference $*P<0.05$).

![Graph](image)

**Fig. 22.** Comparison of hematocrit (Hct) % between Moderate and High altitude Male Sampled Population.
The values of the hematocrit of male subjects inhabiting moderate and high altitude were in closer range, however, in the female subjects of high altitude there was comparatively decreased hematocrit level but it did not reach statistical significance.

![Hematocrit Bar Chart]

**Fig. 23.** Comparison of hematocrit (Hct) % between Moderate and Comparatively High-altitude Female Sampled Population

**Pulse Rate**

The averaged pulse rate recorded in subjects of moderate altitude subjects was 76.5±1.4/min and 70.5±0.72/min in subjects of high altitude. There had been noticeable decrease in the pulse rate of the subjects living at high altitudes studied and the difference is statistically significant (P<0.05) (Fig.24).

Gender wise pulse rate at moderate altitude was 73.2±1.7/min in males and 82.6±2.2/min in females. At high altitude, pulse rate in males was 68.5±1.0/min and in females, it was 72.5±1.1/min. The pulse rate values have been found to be higher in the females of both the altitude studied compare to their respective male groups. The rate is highest in the females of the moderate altitude and lowest in the males of the high altitude (Fig. 25).
Fig. 24. Comparison of pulse rate (beats/minute) between Moderate and Comparatively High-altitude Sampled Population.

Fig. 25. Comparison of pulse rate (beats/minute) in both the genders separately living at Moderate and Comparatively High-altitude Sampled Population.
Tables
### Overview of the Data at Each of the altitude Studied and Compared in the Genders

**Table 1.** Comparison of different parameters at altitude between 1200 to 1800 meter in both the genders.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Gender</th>
<th>Mean Value</th>
<th>Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FBG</strong></td>
<td>Male</td>
<td>96.70±3.40 mg/dl</td>
<td>Non significant</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>91.40±2.50 mg/dl</td>
<td></td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>Male</td>
<td>22.97±0.27 kg/m²</td>
<td>Non significant</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>22.86±0.30 kg/m²</td>
<td></td>
</tr>
<tr>
<td><strong>Cholesterol</strong></td>
<td>Male</td>
<td>174.0±6.1 mg/dl</td>
<td>Non significant</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>168.9±7.1 mg/dl</td>
<td></td>
</tr>
<tr>
<td><strong>Triglyceride</strong></td>
<td>Male</td>
<td>203±26.0 mg/dl</td>
<td>Significant P = 0.019</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>127.4±11.0 mg/dl</td>
<td></td>
</tr>
<tr>
<td><strong>Systolic Blood Pressure</strong></td>
<td>Male</td>
<td>122.50±1.40 mmHg</td>
<td>Non significant</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>121.40±1.31 mmHg</td>
<td></td>
</tr>
<tr>
<td><strong>Diastolic Blood Pressure</strong></td>
<td>Male</td>
<td>79.22±0.83 mmHg</td>
<td>Non significant</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>79.24±0.78 mmHg</td>
<td></td>
</tr>
<tr>
<td><strong>Pulse</strong></td>
<td>Male</td>
<td>73.2±1.7 beats/min</td>
<td>Significant P = 0.001</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>82.6±2.2 beats/min</td>
<td></td>
</tr>
<tr>
<td><strong>Hematocrit</strong></td>
<td>Male</td>
<td>52.31±0.89%</td>
<td>Significant P = 0.04</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>49.15±1.24%</td>
<td></td>
</tr>
</tbody>
</table>
Table 2. Comparison of different parameters at altitude >1800 meter in both the genders.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Gender</th>
<th>Mean Value</th>
<th>Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBG</td>
<td>Male</td>
<td>96.3±2.5 mg/dl</td>
<td>Significant</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>105.7±2.3 mg/dl</td>
<td>P = 0.008</td>
</tr>
<tr>
<td>BMI</td>
<td>Male</td>
<td>21.68±0.33 kg/m²</td>
<td>Significant</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>19.18±0.62 kg/m²</td>
<td>P = 0.000</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>Male</td>
<td>162.7±3.2 mg/dl</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>164.6±2.9 mg/dl</td>
<td>Non significant</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>Male</td>
<td>143.1±12 mg/dl</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>127.4±8.8 mg/dl</td>
<td>Non significant</td>
</tr>
<tr>
<td>Systolic Blood Pressure</td>
<td>Male</td>
<td>115.6±0.88 mmHg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>116.0±1.2 mmHg</td>
<td>Non significant</td>
</tr>
<tr>
<td>Diastolic Blood Pressure</td>
<td>Male</td>
<td>77.9±0.66 mmHg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>78.5±0.83 mmHg</td>
<td>Non significant</td>
</tr>
<tr>
<td>Pulse</td>
<td>Male</td>
<td>68.5±1.0 beats/min.</td>
<td>Significant</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>72.5±1.1 beats/min.</td>
<td>P = 0.007</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>Male</td>
<td>50.78±1.3%</td>
<td>Significant</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>45.23±1.6%</td>
<td>P = 0.016</td>
</tr>
</tbody>
</table>
Table 3. Comparison of different parameters studied in subjects inhabiting 1200-1800 and >1800 meter altitude.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Altitude Meter</th>
<th>Mean Value</th>
<th>Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBG</td>
<td>1200-1800</td>
<td>94.03±2.1 mg/dl</td>
<td>Significant</td>
</tr>
<tr>
<td></td>
<td>&gt; 1800</td>
<td>100.4±1.8 mg/dl</td>
<td>P=0.018</td>
</tr>
<tr>
<td>BMI</td>
<td>1200-1800</td>
<td>22.91±0.20 kg/m²</td>
<td>Significant</td>
</tr>
<tr>
<td></td>
<td>&gt; 1800</td>
<td>20.59±0.33 kg/m²</td>
<td>P=0.000</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>1200-1800</td>
<td>171.7±4.6 mg/dl</td>
<td>Non significant</td>
</tr>
<tr>
<td></td>
<td>&gt; 1800</td>
<td>163.7±2.2 mg/dl</td>
<td></td>
</tr>
<tr>
<td>Triglyceride</td>
<td>1200-1800</td>
<td>169.00±16 mg/dl</td>
<td>Significant</td>
</tr>
<tr>
<td></td>
<td>&gt; 1800</td>
<td>135.8±7.6 mg/dl</td>
<td>P = 0.037</td>
</tr>
<tr>
<td>Systolic Blood</td>
<td>1200-1800</td>
<td>122.2±0.93 mmHg</td>
<td>Significant</td>
</tr>
<tr>
<td>Pressure</td>
<td>&gt; 1800</td>
<td>115.8±0.71 mmHg</td>
<td>P=0.000</td>
</tr>
<tr>
<td>Diastolic Blood</td>
<td>1200-1800</td>
<td>79.4±0.54 mmHg</td>
<td>Non significant</td>
</tr>
<tr>
<td>Pressure</td>
<td>&gt; 1800</td>
<td>78.1±0.52 mmHg</td>
<td></td>
</tr>
<tr>
<td>Pulse</td>
<td>1200-1800</td>
<td>76.5±1.4 beats/min.</td>
<td>Significant</td>
</tr>
<tr>
<td></td>
<td>&gt; 1800</td>
<td>70.5±0.72 beats/min.</td>
<td>P = 0.000</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>1200-1800</td>
<td>51.20±0.74%</td>
<td>Significant</td>
</tr>
<tr>
<td></td>
<td>&gt; 1800</td>
<td>48.35±1.20%</td>
<td>P = 0.046</td>
</tr>
</tbody>
</table>
Table 4. The proportion of subjects with anomalous values of the parameters in the studied population reflecting the risk of Coronary Heart Disease (CHD) at both Moderate and Comparatively High altitude (1200 to >1800 meter).

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
</tr>
<tr>
<td>Obesity&gt;30kg/m²</td>
<td>20</td>
</tr>
<tr>
<td>Cholesterol&gt;200mg/dl</td>
<td>10</td>
</tr>
<tr>
<td>Triglyceride&gt;250mg/dl</td>
<td>11</td>
</tr>
<tr>
<td>BPS&gt;180 mmHg</td>
<td>50</td>
</tr>
<tr>
<td>BPD&gt;110 mmHg</td>
<td>77</td>
</tr>
</tbody>
</table>
General Characteristics
Proportion of anomalous value of the parameters in the studied population at higher altitude

The values of the total measured samples in each parameter were scanned to find the anomalous value beyond a conventional clinical healthy range. The summary of this study is presented in Table 4.

BMI

A total of 927 subjects volunteered for the collection of the data of BMI. A total of 56 subjects had BMI value greater than 30 kg/m². The females outnumbered the males in this category with 20 males and 36 females.

The average BMI in the total population studied was 22.77 ± 0.14 kg/m² compare to an average of the lowlanders population studied where the average value was 28.13±0.89 kg/m².

A healthier profile in term of BMI is exhibited in the highlander. Nevertheless a total of 6.04% of the studied population exhibited abnormal BMI even at the higher altitude. The greater proportion of females with anomalous BMI compare to males is noteworthy.

Serum Cholesterol

In the lowlander population studied the cholesterol level was found to be 185±4.57mg/dl. Compare to that average value in the populations of both the altitude studied was estimated to be 167.07±2.32mg/dl. In both the groups of lowlanders and highlanders the serum cholesterol level is in the healthier range.
A total of 156 subject samples were assayed for serum cholesterol. Among these 19 subjects demonstrated serum cholesterol greater than 200mg/dl. Among these 10 were the males and the remaining 9 were the females.

In general, in the females compare to that of the males the cholesterol level had been non significantly lower. Despite greater incidence of higher values of BMI in the females of higher altitude populations the incidence of greater cholesterol values had been lower,

A noticeable percentage of 12.34 demonstrated serum cholesterol leve greater than 200mg/dl.

**Triglycerides**

The fraction level in the lowlanders was at an average of $252.2\pm11.6$ mg/dl. This exhibits higher tendency of the fraction in the lowland population. Compare to it a far lower level of the fraction has been estimated at an average value of $147.99\pm7.68$ mg/dl. This demonstrates that triglyceride levels are in quite a healthy range in the inhabitants of the highlander.

A total of 153 subject sera samples were estimated for triglyceride. Among these only 16 showed the values greater than 250mg/dl concentration of the fraction. The males shared the greater proportion with 11 in number compare to the females with 5 only.

It appears that in general triglyceride level in the highlander generally remains in the healthier range.
Systolic Blood Pressure

A confident data of 973 subjects for the measurement of systolic blood pressure had been obtained. A noticeable number of the subject 135 had the value of the systolic blood pressure greater than 180mmHg indicating the severe hypertension. Thus a percentage of 12.94 is calculated in the highlander is calculated to suffer from excessive systolic blood pressure.

Among these 50 were the males and the remaining 76 were the females. The greater proportion of the females even at the higher altitude suffers from severe hypertension compare to the males. This characteristic of greater female proportion is similar to that of BMI parameter. These two parameters may have positive correlation in the highlander studied population.

Recalling the pattern of systolic blood pressure in the populations of lowland and of the highland, there had not been the marked differences in the values of SBP. Highlander showed slightly lower, however, significant value than the lowland average.

The comparisons of the gender demonstrated no significant difference in the parameter.

Diastolic Blood Pressure

A confident data of 973 subjects for the measurement of diastolic blood pressure had also been obtained. A noticeable number of the subject 180 had the value of the diastolic blood pressure greater than 180mmHg indicating the severe hypertension. Thus a percentage of 12.94 is calculated in the highlander is calculated to suffer from excessive systolic blood pressure.
Among these 77 were the males and the remaining 103 were the females. Again in diastolic values it is demonstrated that the greater proportion of the females even at the higher altitude suffers from severe hypertension compare to the males. Again it is assessed that this characteristic of greater female proportion is similar to that of BMI parameter. It may be pointed out that three parameters of BMI, SBP & DBP may have positive correlation in the highlander studied population.

Recalling the pattern of diastolic blood pressure in the populations of lowland and of the highland, there had not been the marked differences in the values of DBP. It is obvious that DBP in the highlander is slightly greater than of the lowlander however statistically non significant.

The comparisons of the gender demonstrated no significant difference in the parameter.
Discussion
DISCUSSION

The subjects of high altitude are living a simple life with obligatory physical activity. Their life is, no doubt, tough and difficult as compare to lowlanders. In this study area ranged 1200 to 3000 meter high, with inconsiderable transport facilities majority of the people are poor but are physically hard working. The results obtained from this study show low value of the parameters of blood glucose level, BMI, blood pressure, total cholesterol triglyceride and pulse rate, however, hematocrit was increased. These parameters are now conventionally assessed to measure the potential of degenerative diseases in the life style of the populations. The results from such point of view reflect largely the healthy profile of the populations inhabiting higher altitudes.

The study revolves around the glycemic status and related risk factors at high altitude. As it is already indicated, people of that area take simple food. Normally they do not take refined carbohydrates and refined sugar. So the intake of glucose in high altitude subjects is comparatively low than lowlanders. Results have shown random blood sugar levels in lowlanders have a mean value of 116.63 mg/dl, and at high altitude, the mean value was 97.34mg/dl showing a considerable difference between the glucose level of lowlanders and high altitude residents, and showing clearly that with the increase of altitude, glucose level decreases. This decrease reflects the low risk of diabetes in the inhabitants of higher altitude.

There are reports of the biochemical adaptation at high altitude as Vats et al., (1999) results showed that exposure to high altitude caused alteration in metabolic process in carbohydrates. McClelland (1998) in rats have observed decreased utilization of carbohydrate. Similarly, in women, unlike in men, exposure to high altitude caused decreased utilization of carbohydrates (Braun et al., 2000).
The cause of low utilization of carbohydrates is also supported by the studies where high altitude residence is well known to modify body chemistry and hormone status (Savourey et al., 1998). High altitude dwellers are less sensitive to insulin compared with sea level (Braun et al., 2001). Balasubramanyam (1991) after an experiment, suggested that the activity of PDE-3 increased by regular exercise that perhaps reflex a greater sensitivity to insulin.

Thus it is understandable that in addition to the kind of carbohydrates consumed by the population of high altitude the biochemical adaptation of low carbohydrate utilization also contribute in the healthy glycemic pattern in such populations.

The high altitude living not only from life style but also due to the specific environment contributes in comparatively healthy profiles. Lee et al., (2003) studied the improving effect of hiking at high altitudes. He concluded that glucose tolerance appears to be influenced by the geographic environment. He suggested that high altitude living conditions and activities may possibly be developed as potential natural medicines for the prevention and treatment of type-2 diabetes in the future.

Over the past four decades, there has been an increase in the prevalence of overweight and obesity in adults across all genders, ages, and racial/ethnic groups (Ichinohe et al., 2004). The negative effects of obesity on both the individual and society are serious and multi-dimensional that it has become a risk factor for many health problems, including coronary heart disease, certain forms of cancer, type 2 diabetes, hypertension, dislipidemia, stroke, gall bladder diseases, osteoarthritis, sleep apnea, and gout and is associated with increases in all-cause mortality (Cataldo, 1999).
In the present study the influence of higher altitude living is evident as BMI is marked lower than those of lowlanders. Compare to moderate altitude at high altitude females have still the lower BMI. That is unlike the lowlanders where in the females the incidence of higher BMI is greater than the males.

In a study, a positive association reported between BMI and glycemic index and also the relationship between the type of carbohydrate and body weight (Yunsheng et al., 2005). It is likely that the food contributes in low BMI of the high altitude population. The diet of people living at high altitude is very simple. They take maize rice and pulses, cereals and green vegetables. Fresh fruits are also the major part of their diet. Consumption of red meat, fried and fatty food, fast food and soft drinks is inconsiderable. From the dietary side, they are taking very good and healthy food. Factors that disturb the metabolic status drastically are not the part of their diet, so we can say that they are in safe hands from the dietary point of view.

The altitude population is not totally devoid of unhealthy studied profile as there are about 6% of the studied subjects with BMI greater than 30 kg/m². It is observed that subjects with very high BMI were mostly of moderate altitude inhabitants and exposed to recent life style similar to that of lowlanders.

Obesity cannot be ignored when we talk about the risk factors. If only diabetes is taken, the patient of type 2-diabetes shows a typical type of obesity, known as truncal obesity. BMI has direct relation with obesity. When BMI is >25 kg/m², person is grouped under overweight and when it is >30kg/m², that person is considered as obese. Higher the BMI, more the body weight, which comprise mostly on fats, so high BMI is another risk factor for cardiovascular problems.

In this study results show that at high altitude, glucose, cholesterol, triglycerides BMI, and obesity (in relation to BMI) all are low. The lower values these
parameters compare to lowlanders exhibit of healthier factors that subsequently lowers the risk of life threatening danger of diabetes and CVD problems.

At high altitude, physical activity is greater than the lowlanders due to many factors. One of those is the low literacy rate and less job availability, men are mostly laborers, doing much more physical work as compared to lowland subjects. Women also work hard in fetching the water and the fire wood. Roads and transport facilities are meager, so they have to walk a lot. In females the strenuous work is comparatively low, however, their hormonal female indisposition estrogen play very important role in decreasing cholesterol and triglyceride levels and decrease the incidence of heart attack and stroke in females.

Another important parameter, studied was cholesterol level. As already discussed about dietary profile, normally taken food is low in fats, and due to increased physical activity, there is increase in lipolysis. Serum cholesterol level is markedly lower in highlander compare to lowlanders and the lowering of the fraction increases with increase in the altitude living. An average value of 185 mg/dl and 167.07mg/dl is calculated in lowland and high altitude subjects, showing a marked lowering of 18 mg/dl and it is statistically. Naturally such low level of cholesterol in high altitude subjects reduces the risk of CVD.

The result is in conformity as it is reported that total cholesterol decreased with increasing altitude whereas high-density lipoprotein cholesterol (HDL-C) increased (Sharma, 1990),

Result of present study have shown the triglyceride levels at higher altitudes (>1200 meter) was 147.99±7.68 mg/dl compare to 252.2±11.6 mg/dl in lowlanders. A marked and significance lower level of the fraction prevails in the higher altitude population compare to the lowlanders. At moderate altitude (1200-1800 meter), its
level was 169±16 mg/dl and at high altitude it was 135.8±7.6 mg/dl. Triglyceride level of the subjects at high altitude was significantly lower than those of moderate altitude.

The levels of triglycerides are substantially low in highlander than the lowlanders. Regular exercise has consistently been shown to be effective in reducing levels of triglyceride-rich VLDL. The life pattern of the highlander as discussed earlier contributes in low level of circulatory triglycerides.

There are also biochemical factors contributing in low triglyceride levels. In a study it has been reported that high altitude acclimation alone greatly stimulate lipolysis (Grant et al., 2001). Glisezinski et al., (1999) in a study to examine the effect of prolonged hypoxia on adipose tissue lipolysis, in relation to the weight loss, usually observed at high altitude, concluded that prolonged exposure to hypobaric hypoxia led to a potent reduction in lipid mobilization through a decrease in the efficiency of β-adrenergic, GH and PTH. The main finding of the studies indicated that decreased BMI in both men and women significantly decreased cholesterol and triglyceride in women and a significant correlation between glucose and BMI were observed.

BMI direct relationship to the level of cholesterol and triglycerides may also cause hypertriglyceridemia. In a study conducted at high altitude by Mohanna et al., (2006) it was found that high BMI have a high prevalence of hypercholesterolemia (34.3%) and hypertriglyceridemia (53.9%) in both genders at high altitude which are the risk factors for cardiovascular diseases and coronary heart disease.

The normal values of blood pressure are 120/80mmHg. Lowlanders have comparatively high blood pressure than high altitude subjects. Average systolic blood pressure (SBP) value in subjects of both higher altitudes studied was 118.81±0.59 mmHg and those of lowlander had a mean value of 125.25±1.95mmHg. Diastolic
blood pressure values present almost the similar pattern. DBP in the subjects of both
the higher altitude was 78.72±0.38 mmHg and the average diastolic blood pressure of
lowlanders was 75±1.3mmHg. The values of SBP & DBP compare to the lowlanders
demonstrate healthier cardiovascular status of the highlanders in relation to vascular
pressures.

The results are in confirmation to other reports. A Peruvian study reported
that the prevalence of hypertension at high altitude was lower than in a low altitude
population (Wolff et al., 1994). A study in Central Asia also in agreement as it
demonstrated that hypertension was more prevalent at lower altitude than at high
altitude (Fiori et al., 2000). A Russian study on high altitude also reported that
hypertension was significantly higher among residence in low altitude region
compared with residents in high altitude region (Mirakhimov et al., 1985).

Fatty food, static life style, stress and tension, increased levels of cholesterol,
triglycerides and genetic predisposition are the factors that increase blood pressure.
When we compare the blood pressure of male and female subjects at same altitude,
females show high levels as compared to males. Physical activity decreases the blood
pressure so it may be the only cause of low blood pressure in males than females at
same altitude.

In an experiment conducted by Smith (1999) on Sherpa men in Nepal, data
showed that obese men (>30 kg/m²) were 8.6-9.1 times more likely to have elevated
B.P. Higher altitude dwellers usually have lower B.P (Liu, 1990).

The higher values of hematocrit are observed in the highlanders compare to
that of lowlanders. Other studies have similar results as increase in hematocrit is
particularly pronounced in Andean high-altitude dwellers (Beall et al., 2002),
Increased hematocrit is the adaptation of body against hypoxic conditions at high altitude. More oxygen is required for more physical activity and more RBCs to carry oxygen and supply to whole body. Hypoxia stimulates the erythropoietin release, which increase the production of RBCs in the body. More the RBCs, thicker will be the blood. This thick blood circulates slowly and has a higher chance to form clots/thrombus. These microthrombi move with circulation and blocks small blood vessels and endings of large vessels resulting in acute attack of myocardial infarction or stroke. So this increased homatocrit level, known as polycythemia, is the only factor which increase the risk of cardiovascular problems and stroke. Wu et al. (2005) has shown that hemoglobin increase with increasing altitude leads to an increased atherosclerotic process.

The anomalous values in the subjects of higher altitude populations demonstrate a strong relationship between obesity, systolic and diastolic blood pressures. There is greater incidence of anomalous values of these three parameters in the female compare to the male subjects. The direct correlation is also observed in these parameters even at higher altitude like that of lowlanders. In other studies also elevated blood pressure has been proposed to be associated with elevated BMI (Smith, 1999).

In short it is observed that physiological parameters in the highlanders of the area studied demonstrate the healthier picture clearly from those of the lowland dwellers.
Conclusion
CONCLUSION

The glycemic status and the associated parameters of the lipid profile and the cardiovascular activity indices in the high altitude inhabitants (1200-3000 meter) as compared to the lowlanders demonstrate evidently of healthier nature. The glycemia, body mass index, serum cholesterol, serum triglycerides, systolic blood pressure and diastolic blood pressure values were lower than the comparable parameter of the lowlanders. In most of the parameters it was also observed that in the comparison of the moderate altitude (1200-1800 meter) and high altitude (1801-3000 meter) the values were further lower in the high altitude than those of the moderate altitude. The most contrasting result in these parameters is of triglycerides. In comparison the concentration of triglycerides in highlanders is even lower than half of the lowlander's values. The area studied is low in development and the highlanders live a strenuous life furthermore, they consume carbohydrates with low glycemic index, therefore these factors may be accounted for the low values of the studied parameter. The studies carried at other highland areas of the world have reported the results similar to the present study findings which have mainly attributed to the biochemical adaptation at the higher altitudes. Therefore in this area studied the biochemical adaptations of high altitude are also taken into considerations.

In an assessment of the values of the parameters that have deviated considerably from the average of the population BMI deviated about 6%, cholesterol about 12%, triglycerides approximately 10.5%, systolic blood pressure about 13%and
diastolic blood pressure about 18.5%. Female gender showed greater incidence in the anomalous values in BMI, SBP and DBP. It also clearly exhibited that these three parameter have positive correlation even at the higher altitude living.

In short it is observed that physiological parameters in the highlanders of the area studied demonstrate the healthier picture clearly from those of the lowland dwellers.
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