Indian Journal of Clinical Biochemistry, 2010 / 25 (1) 51-56

ORIGINAL ARTICLE

MODERATELY HIGH ALTITUDE HABITATION MODULATES LIPID PROFILE AND ALKALINE PHOSPHATASE ACTIVITY IN AGED *KHASIS* OF MEGHALAYA

H S Ranhotra and R Sharma*

*Department of Biochemistry, St. Edmund's College, Shillong, *North-Eastern Hill University, Shillong, Meghalaya, India*

ABSTRACT

The indigenous Khasis inhabit different geographical and climatic locations of Meghalaya. In this study, we intended to find out whether habitation in moderately high altitude place has any effect on the lipid and liver profile amongst the aged Khasis. The level of various serum parameters under lipid and liver profile were analyzed and compared from aged (65-70 years) male Khasi residents of moderately high (Shillong city) and low (Byrnihat) altitude places. Results obtained from the lipid profile data show decreased total serum cholesterol (29%), triglyceride (27%) and LDL-cholesterol (42%) level in the old Khasis of Shillong compared to Byrnihat. Furthermore, the alkaline phosphatase activity was significantly raised (47%) in the old Khasis from Shillong as against Byrnihat. The decreased level of total cholesterol, triglyceride and LDL-cholesterol in old Khasis from Shillong may be due to living and acclimatization in high altitude with low annual temperature. Moderately high elevation could have acted as a stressor, thereby reducing the level of serum cholesterol, triglyceride and LDL-cholesterol, which may put them at a lower risk of cardiovascular diseases. In comparison, old residents of Byrnihat with high cholesterol, triglyceride and LDL-cholesterol levels may elevate their risk of coronary complications. The raised alkaline phosphatase activity amongst the old Khasis of Shillong could be due to increased bone and/or intestinal turnover as a result of living in high altitude, which, however, may elevate the risk of osteoporosis. Taken together, we conclude that low cholesterol, triglyceride and LDL-cholesterol levels, accompanied with high alkaline phosphatase activity amongst the old Khasis of Shillong, could be due to the influence of high altitude and mild climatic conditions that prevails.

KEY WORDS

Altitude, Lipid profile, Liver profile, Aged, Khasis, Alkaline phosphatase.

INTRODUCTION

It is now widely believed that aging operates at the cellular and molecular levels (1). The ability to adapt to internal as well as external variations declines during this phase and may lead to fall in homeostatic balance (2). Although numerous research have and is being carried out to find out the causes of aging, however, till date, little is known at the molecular level as to what triggers aging (3). Aging is a complex and gradual process and its ongoing operation is present to some degree in all individuals. It is a journey to the maturity as well as to the degeneration of the body.

Address for Correspondence :

Dr. Harmit S. Ranhotra,
Department of Biochemistry,
St. Edmund's College, Shillong 793 003, India
Tel: +91-364-2534619
E-mail: harmitran@gmail.com

Aging has become an important area of study due to the rapid increase in number of old age people that has enormous social implications. By 2020, there will be 1 billion aged people with over 700 million living in the developing world (4). Improvements in sanitation, housing, nutrition, medical innovations etc have contributed to the steep increase in the number of people reaching older age. Human aging and the biochemical, molecular and physiological variations associated with it has received increased focus particularly in the western countries, including Japan. In Japan, for instance, detailed clinical studies have been undertaken amongst the aged inhabitants of the island of Okinawa, which has the world's highest longevity (5-7). However, fewer scientific investigations have been directed especially towards the indigenous tribes of the world, who are considered to harbor a rich gene pool. Hence, biochemical and molecular data from the aged populations of such indigenous people are extremely insufficient.

Modern clinical research on the elderly population in India is still in its infancy. Hence, insufficient data is being generated, which is hampering the understanding of clinical changes in the older population, thereby putting them in a disadvantage. This is applicable to the growing number of older people in India. The Indian subcontinent in particular, boasts of a diverse community of ethnic tribes, inhabiting different geographical locations with contrasting climate. It's an irony that negligible clinical studies have been undertaken amongst these indigenous populations.

One of such tribes of India, the *Khasis* represents an indigenous inhabitant of the North-Eastern part of India (8). They possess unique lifestyle, social customs, dietary habit and perhaps gene pool (9). In the state of Meghalaya, the *Khasis* inhabit different geographical regions including the Shillong plateau and Ri Bhoi (Byrnihat) plains bordering the state of Assam (10). Shillong has low annual temperature and mild climate as it is located at a moderately high altitude. On the other hand, Byrnihat has a low elevation with high annual temperature compared to the Shillong plateau. Negligible biological or clinical studies have been undertaken on this ethnic group within the same or different inhabiting locations. Also, no age-related clinical and/or molecular variations study has been reported from this tribe. Furthermore, no data are presently available which compares the levels of different blood biochemical constituents especially within the tribe's older population. In the present study, we assumed that there could be variations in the levels of some of the serum biochemical constituents amongst the old *Khasis* residing in the two contrasting geographical and climatic locations. Hence, this study is perhaps the first that has attempted to evaluate the levels of few clinically important blood constituents from the old *Khasis* residents of two opposing climatic conditions. We chose to include the analyses of serum lipid and liver profile parameters as they are one of the most widely and routinely prescribed clinical tests by physicians for diagnosing and ascertaining normal human health. It has been observed that humans who normally acclimatize to moderate and high altitude places have altered body biochemistry as against those who live in low altitude (11). Few reports show that people who inhabit moderate and high altitude places from around the world have significantly altered levels of many serum biochemical parameters as compared to their low altitude counterparts (12, 13). Therefore, the aim of the present study was to find whether physical and environmental factors such as altitude and temperature can be contributory factors that may modulate the lipid and liver profile in aged *Khasis* from the two distinct regions.

MATERIALS AND METHODS

Blood sampling from donors: This study was approved by the Institutional Ethics Committee (IEC) of North-Eastern Hill University, Shillong, to which the college is affiliated. Blood collection from subjects was carried out according to the applicable guidelines of the IEC and Indian Council of Medical Research (ICMR). Subjects were selected adopting a population-based study design. Initially, brief, validated questionnaires were prepared during survey from a total of 377 *Khasi* males that included the profession, residency, martial status, diet, physical activity and medical history (including personal details, place of birth etc). Subjects were non-related individuals, who have been resident of respective locations for at least 15 years. Finally, blood was obtained from sixty five (n = 65) old (65-70 years) *Khasi* males of Shillong city and Byrnihat town (Ri Bhoi). Blood sample was also collected from sixty five (n = 65) young *Khasi* male subjects (15-20 years) of respective locations in order to have age-related correlations. Only informed consent individuals became the subjects and were volunteers. Participant inclusion criteria included subjects in stable clinical conditions, similar dietary habit and other lifestyles in order to minimize experimental variations. Participant exclusion criteria were subjects who were diabetic, with known cardiovascular and liver/kidney diseases, hypertension, hormonal disorders etc, which could modify lipid and liver profile. Also, subjects who were on any kind of medication, including vitamins, minerals and lipid-modifying drugs were excluded. 5ml of blood was collected from overnight-fasted subjects using sterile, single-use disposable syringe by a trained nurse. All biochemical tests were carried out in duplicate with a single blood sample drawn from each subject.

Serum biochemical tests: Sera from the blood drawn from subjects was isolated by centrifuging glass tubes containing 5 ml blood in a laboratory centrifuge at a moderate speed for 5 min. Serum isolated was then be analyzed for liver profile that included total serum protein, albumin, globulin, total bilirubin, serum alkaline phosphatase (ALP), aspartate aminotransferase (AST) and alanine aminotransferase activities (ALT). Lipid profile (total cholesterol, triglyceride, LDL- and HDL-cholesterol levels) of each subject's serum were also determined. All the above biochemical analysis was performed using Erba-Chem7 (Model no. Chem 7) biochemistry analyzer (Transasia Bio-Medicals Ltd, Mumbai, India) by trained technicians in the Pathology Department of Woodland Hospital, Shillong. The analyzer was calibrated every alternate day for the various serum tests according to manufacturer's instruction to ensure strict quality control. All serum tests were performed strictly according to manufacturer's guide that included: Total Cholesterol: Using cholesterol-DES kit (Source: Erba Manhiem, India); Triglyceride: By enzymatic colorimetric method using Autopak kit (Source: Bayer Diagnostics, India); HDL-Cholesterol: By two-point kinetic method (Source: Synergy Bio, India); LDL-Cholesterol = (Total cholesterol) - (HDL- Cholesterol) - (Triglyceride)/5; Total protein: Biuret method using Autopak kit (Source: Bayer Diagnostics, India); Albumin: BCG method using Autopak kit (Source: Bayer Diagnostics, India); Globulin = Total protein – Albumin; SGOT (AST) and SGPT (ALT): By UV kinetic (IFCC) method using Autopak kit (Source: Bayer Diagnostics, India); Alkaline Phosphatase: *p*NPP-AMP (IFCC) kinetic assay using Autospan kit (Source: Cogent, India); Total Bilirubin: Jendrassik and GROF method using Autopak kit (Source: Bayer Diagnostics, India); IFCC (International Federation of Clinical Chemistry) denotes IFCC recommended tests.

Chemicals and controls: All kits used for the various lipid and liver profile tests were obtained from manufacturers as indicated above in parentheses. All the other chemicals employed were obtained from ErbaManhiem, India and Wako, Japan. Internal (level 1 and level 2) and external controls (Clinical Chem Monthly Program) was purchased from Bio-Rad Laboratory (Irvine, USA).

Statistical analysis: Results obtained were analyzed statistically. The level of each of the serum constituents were compared and analyzed statistically using Student's 't'-test. All results with a value of $P<0.05$ were deemed significant. Quantitative values for the various serum parameters measured are expressed as mean ± *SD*.

RESULTS

The present study attempted to evaluate and compare the levels of some of the clinically significant blood constituents between the old male *Khasi* subjects of two contrasting climatic region of Meghalaya, the Shillong plateau and Byrnihat. The geographical and climatic feature of the two regions show significant differences and are being shown in Table 1. There is a huge difference in the altitude (above sea level) between the two regions, with Shillong exhibiting six times higher elevation compared to Byrnihat. Hence, Shillong has a cooler climate through out the year compared to Byrnihat as shown in the comparison of maximum and minimum annual temperature in Table 1. Hence, the *Khasi* inhabitants of the Shillong plateau are exposed to a mild, cooler climate as opposed to Byrnihat, where the climate is warm and tropical.

Table 1: Altitude and temperature profile of Shillong and Byrnihat

Features	Shillong	Byrnihat
Altitude* (m)	1495	250
Average Temperature (°C)		
Maximum	20	30
Minimum	14	22

**above sea level*

The old *Khasi* males chosen for the present study from the two different places were between the age group of 65-70 years. In order to have age-related correlations, various serum biochemical parameters were also investigated in young *Khasi* males (15-20 years) of the respective locations. The mean and median age of young and old *Khasis* of Shillong and Byrnihat are shown in Table 2.

Table 2: Mean and median age of young and old *Khasis* from Shillong and Byrnihat

Age (yrs)	Shillong		Byrnihat	
	Young	Old	Young	Old
Mean ± SD	17.8 ± 3.23	68.1 ± 4.62	18 ± 4.0	68.25 ± 3.89
Median	18	69	18	69

The various lipid and liver profile tests performed on the blood samples collected from young and old *Khasis* of the two regions are summarized in Table 3. We found that the lipid profile data obtained from the old *Khasis* of Shillong and Byrnihat shows significant difference in the levels of total cholesterol, triglyceride and LDL-cholesterol. There is a remarkably higher level ($P<0.05$) of serum cholesterol (29%), triglyceride (27%) and LDL-cholesterol (42%) amongst the old *Khasis* of Byrnihat (O_B) as compared to the old *Khasis* of Shillong (O_S). In other words, the O_B subjects appear to be hyperlipidemic if compared to O_S. Under the liver profile test, a decreased (47%) ($P<0.05$) serum alkaline phosphatase (ALP) activity was detected from old *Khasis* of Byrnihat (O_B) compared to Shillong (O_S). However, no statistically significant differences were observed in other lipid and liver profile parameters between O_B and O_S.

Table 3: Levels (mean ± *SD*) of various serum biochemical parameters under lipid and liver profiles obtained from young and old *Khasis* of Shillong and Byrnihat (*n* = 65)

Serum Biochemical Tests	Shillong		Byrnihat		Normal reference values
	Young (Y_S)	Old (O_S)	Young (Y_B)	Old (O_B)	
Lipid Profile					
Total Cholesterol (mg/dl)	150 ± 50	142 ± 32	168 ± 56	200 ± 46[a]	120 - 220 mg/dl
Triglyceride (mg/dl)	97 ± 32[e]	134 ± 30[g]	158 ± 52	184 ± 42[b]	< 200 mg/dl
LDL-Cholesterol (mg/dl)	90.6 ± 24	71.2 ± 20[h]	90.9 ± 22[i]	123.2 ± 32[c]	<130 mg/dl
HDL-Cholesterol (mg/dl)	40 ± 13	44 ± 10	45.5 ± 15	40 ± 9.2	30 - 70 mg/dl
Liver Profile					
Total Protein (g/dl)	6.3 ± 2.1	6.7 ± 1.54	6.2 ± 2.0	6.1 ± 1.4	6.7 - 8.7 g/dl
Albumin (g/dl)	3.8 ± 1.2	3.9 ± 0.9	3.9 ± 1.32	4.0 ± 0.96	3.5 - 5.5 g/dl
Globulin (g/dl)	2.5 ± 0.8	2.8 ± 0.6	2.3 ± 0.76	2.1 ± 0.48	2.3 - 3.6 g/dl
AST (IU/l)	29.5 ± 9.8	31.6 ± 7.2	30.0 ± 10	29.1 ± 6.7	0 - 42 IU/l
ALT (IU/l)	30 ± 10	25.5 ± 5.8	26.5 ± 8.8	25.6 ± 5.9	0 - 42 IU/l
Alkaline Phosphatase (IU/l)	91 ± 30[f]	114 ± 26.1	70 ± 23	60.0 ± 14[d]	15 - 120 IU/l
Total Bilirubin (mg/dl)	0.70 ± 0.23	0.61 ± 0.13	0.52 ± 0.17	0.43 ± 0.10	0 - 1.0 mg/dl

Y_S-Young subject of Shillong; O_S-Old subject of Shillong; Y_B-Young subject of Byrnihat; O_B-Old subject of Byrnihat; a: 29 % more total cholesterol in O_B compared to O_S (P < 0.05), b: 27 % more serum triglyceride in O_B compared to O_S (P < 0.05), c: 42% higher LDL-cholesterol in O_B compared to O_S (P < 0.05), d: 47% less alkaline phosphatase activity in O_B compared to O_S (P < 0.05), e: 39 % less triglyceride level in Y_S compared to Y_B (P < 0.05), f: 23 % higher alkaline phosphatase activity in Y_S compared to Y_B (P < 0.05), g: 28 % greater triglyceride level in O_S compared to Y_S (P < 0.05), h: 21% less LDL-cholesterol in O_S compared to Y_S (P < 0.05), i: 26 % less LDL-cholesterol in Y_B compared to O_B; AST-Aspartate aminotransferase; ALT-Alanine aminotransferase; IU-International Unit.

Comparison of the serum lipid and liver profile data between the young age group of Shillong (Y_S) and Byrnihat (Y_B) show a 39% decreased triglyceride level in Y_S compared to Y_B (Table 3). Also, a 23% increased ALP activity was detected in Y_S compared to Y_B. Age-correlation data between the young and old *Khasis* of respective region shows definite correlation. A 28% higher (P<0.05) triglyceride level was detected from O_S compared to Y_S. Additionally, a 21% less LDL-cholesterol level is seen in O_S compared to Y_S. However, interestingly, an elevated (26%) LDL-cholesterol level was detected in O_B compared to Y_B, which is in contrast to what is observed between O_S and Y_S. However, the level of various other lipid and liver profile parameters measured between Y_B and O_B show no differences.

DISCUSSION

The evaluation and comparison of the levels of various lipid and liver profile parameters amongst the young and old male *Khasi* subjects of the two different climatic region of Meghalaya was challenging, as no such clinical study was previously undertaken or reported from this tribe. Data obtained from the various serum tests performed amongst the old *Khasi* participants from the two locations show a number of significant differences. However, there is no data available on the genetic profiles of the *Khasis*. The dietary intake, lifestyles etc of the *Khasis* were taken into account while selecting subjects in this study. *Khasis* from both the regions have a very similar dietary habit with the food consists mainly of carbohydrate (rice, vegetables, fruits etc), proteins (meat/fish) and fats (mainly from pork) (8, 9). Vegetarian *Khasis* are almost non-existent and have not encountered anybody who was purely a vegetarian. In fact, almost all *Khasis* in Meghalaya are non-vegetarians. However, vegetarian foods (rice, vegetables, pulses etc) are also amply consumed. However, milk is hardly consumed by the old *Khasis* and they continue to remain non-vegetarian in their later life. Overall old *Khasi* males maintain good health status, with reasonable daily physical and social activities.

It is now widely believed that interplay between environmental exposures and human biology limits longevity and quality of life and that healthful aging in human may depend on polygenic regulation as well as environmental influences. The higher level of total serum cholesterol, triglyceride and LDL-cholesterol reported from O_B as compared to O_S population might suggest a modulatory role of environmental factors prevailing in the respective region. The *Khasis* from these two location shares the same gene pool, however, they are under the influence of different climatic conditions. Amongst the environmental influences, it is now acknowledged that high or low temperature does modulate the metabolic rate of an individual (14). Increased level of serum total cholesterol, triglyceride and LDL-cholesterol observed in case of O_B may perhaps be due to higher environmental temperature that is prevalent in Byrnihat which increases the general metabolic processes and ultimately the metabolic rate. A possible explanation for this increase in metabolic rate may be as a result of increased mobilization of these lipids through the blood plasma to various tissues. Hence, a higher cholesterol, triglyceride and LDL-cholesterol level which is detected in O_B as compared to O_S, may reflect a relevant biochemical adaptive response.

Additionally, lipid metabolism in humans has been shown to be altered with exposure to high altitude (15, 16). Acclimatization to high altitude led to increased circulating triglyceride levels and reduced or unchanged plasma cholesterol concentration as reported by Young *et al* (17), which partly corroborate with our finding, whereby the O_S population has reduced cholesterol level but not triglyceride. The effects of exposure to high altitude on lipid metabolism appear to be complex, interrelated processes involving multiple responses by the human body. The report of elevation of serum total cholesterol and LDL-cholesterol in people from high altitude areas by few investigators (18-20) is however not supported by our finding, wherein we report a decreased total cholesterol and LDL-cholesterol levels in O_S subjects. Our finding is also in contrast to another report where there is a significantly higher serum triglyceride level in subjects who are inhabitants of moderately high altitude (21).

Lipid profiles, among other factors, are associated with risk of cardiovascular disease (CVD). Ironically, a higher cholesterol, triglyceride and LDL-cholesterol levels in the blood of O_B populations may elevate their risk of CVDs such as coronary heart disease and stroke as compared to the O_S population. A lower level of total serum cholesterol, triglyceride and LDL-cholesterol in case of O_S may perhaps be due to high elevation accompanied with mild climate that is prevalent in Shillong. In other words, the O_S populations may be a little better protected against CVDs. Residence in hilly area seems to have a “protective effect” from coronary mortality and this association could help to explain the lower cardiovascular mortality rate that is generally observed at high altitude (22). Increased physical activity from walking on rugged terrains under conditions of mild hypoxia among the hill residents of Shillong could explain these findings, which is supported by the observation of Baibas *et al* (23). Another report (24) from study on inhabitants of high altitude populations of Peru showed no differences in total cholesterol level, whereas, the triglyceride level was markedly elevated in comparison to low altitude, which is also corroborated by other findings (25). Furthermore, the higher activity of serum ALP in O_S with respect to O_B may perhaps be due to high bone and/or intestinal turnover in high altitude O_S population leading to increased ALP release into the plasma. The report of higher ALP activity in subjects from moderately high altitude was reported earlier (21, 26), which corroborate with our findings. A higher ALP activity, however, may also correlate with an increased risk of osteoporosis in the O_S compared to O_B population.

The age-correlation data between young and old *Khasis* of respective region show a definite pattern. The higher triglyceride level along with decreased LDL-cholesterol level which is observed in O_S as opposed to Y_S, could be due to multitude of influences. It is now well-known that changes in energy regulation occur during human aging. There are also changes in patterns of dietary intake and a reduction in the variety of foods consumed in old age. These alterations in the level of triglyceride and LDL-cholesterol in O_S and Y_S could be due to differences in the mean age of young an old population. The O_S having more triglyceride compared to Y_S could be correlated with a greater risk of diseases associated with high triglyceride in elderly population compared to the young. In contrast, the lower LDL-cholesterol level in O_S shows the influence of age in this high altitude region and could be correlated with a lesser risk of atherosclerosis in old as compared to Y_S and which may indicate their healthful living. Interestingly, on the other hand, a higher LDL-cholesterol in O_B as compared to Y_B also shows the influence of age and possibly the beneficial effect of high altitude habitation compared to low.

Analysis of biochemical parameters between the young age groups of the respective locations shows some interesting variations. The decreased triglyceride level along with higher ALP activity observed in Y_S compared to Y_B may have a definite environmental influence. This modulation in the level of triglyceride and ALP activity amongst the young *Khasis* could be due to the effect of residence in high altitude and the low annual temperature which is prevalent in Shillong as opposed to Byrnihat. Additionally, modifiable factors such as quality and quantity of nutrition intake by the young population of the respective region could also be attributed for these differences.

The work reported in this paper is preliminary, nevertheless; it is a first report on any clinical study undertaken amongst the old *Khasis*. Taken together, results from this study show that there are indeed significant differences in the lipid profile and ALP activity between the old resident *Khasis* of Shillong and Byrnihat. Overall, the O_S population may perhaps be enjoying a better health condition as compared to the O_B population and these differences may ultimately reflect biochemical adaptability for survival in the respective region.

ACKNOWLEDGEMENT

The authors acknowledge the project grant support (No. F-5-01/2006-07/MRP/NERO) from the University Grants Commission, Government of India.

REFERENCES

1. Luckinbill LS, Foley P. Experimental and empirical approaches in the study of aging. Biogerontology 2000; 1: 3-13.
2. Roth GS. Mechanisms of altered hormone and neurotransmitter action during aging: the role of impaired calcium mobilization. Ann N Y Acad Sci 1988; 521: 170-76.
3. Kanungo MS. Genes and Aging. Cambridge: Cambridge University Press; 1994.
4. Ageing and Health. Geneva: World Health Organization; 1999.
5. Sharma R. Dietary restriction and its multifaceted effects. Curr Sci 2004; 87: 1203-10.
6. Akisaka M, Asato L, Chan YC, Suzuki M, Uezato T, Yamamoto S. Energy and nutrient intakes of Okinawan centenarians. J Nutr Sci Vitaminol 1996; 42: 241-48.
7. Willcox BJ, Willcox DC, Todoriki H, Fujiyoshi A, Yano K, He Q, et al. Caloric restriction, the traditional Okinawan diet, and healthy aging: the diet of the world's longest-lived people and its potential impact on morbidity and life span. Ann N Y Acad Sci 2007; 1114: 434-55.
8. Roy S, Rizvi SHM. Khasi Tribe of Meghalaya. Calcutta: B.R. Publishing Corp; 2006.
9. Meghalaya: Land and People. Shillong: Directorate of Information and Public Relations; 2002.
10. The Dwellers of the High Hills: The Khasis of Meghalaya. Shillong: Directorate of Information and Public Relations; 2003.
11. Schwartz D, Collins F. Medicine. Environmental biology and human disease. Science 2007; 316: 695-96.
12. Manolio TA. Study designs to enhance identification of genetic factors in healthy aging. Nutr Rev 2007; 65: S228-33.
13. Libert S, Pletcher SD. Modulation of longevity by environmental sensing. Cell 2007; 13: 1231-4.
14. Ganong WF. Review of medical physiology. 19th ed. Stamford: Appleton and Lange; 1999.
15. Ferezou J, Richalet JP, Coste T, Rathat C. Changes in plasma lipids and lipoprotein cholesterol during a high altitude mountaineering expedition. Eur J Appl Physiol 1988; 57: 740-45.
16. De Mendoza S, Nucete H, Ineichen E, Salazar E, Zerpa A, Glueck CJ. Lipids and lipoproteins in subjects at 1000 and 3500 meter altitudes. Arch Environ Health 1979; 5: 308-11.
17. Young PM, Rose MS, Sutton JR, Green HJ, Cymerman A, Houston CS. Operation Everest II: plasma lipid and hormonal responses during a simulated ascent of Mt. Everest. J Appl Physiol 1989; 66: 1430-5.
18. Temte JL. Elevation of serum cholesterol at high altitude and its relationship to hematocrit. Wilderness Environ Med 1996; 7: 216-24.
19. Savourey G, Garcia N, Caravel JP, Gharib C, Pouzeratte N, Martin S, et al. Pre-adaptation, adaptation and de-adaptation to high altitude in humans: hormonal and biochemical changes at sea level. Eur J Appl Physiol Occup Physiol 1998; 77: 37-43.
20. Chakraborti S, Batabyal SK, Chatterjee GC. Comparative studies of moderate and high altitude stress on humans: studies on plasma lipid profiles. Int J Environ Studies 1984; 23: 69-73.
21. Ramirez G, Bittle PA, Colice GL, Foulis PR, Agosti SJ. Biochemical adaptations to moderately high altitude living. J Wilderness Med 1991; 2: 287-97.
22. de Leon AC, Gonzalez DA, Mendez LP, Aguirre-Jaime A, Perez MCR, Coello SD, et al. Leptin and altitude in the cardiovascular diseases. Obesity Res 2004; 12: 1492-98.
23. Baibas N, Trichopoulou A, Voridis E, Trichopoulos A. Residence in mountainous compared with lowland areas in relation to total and coronary mortality. A study in rural Greece. J Epidemiol Commu Health 2005; 59: 274-78.
24. Mohanna S, Baracco R, Seclen S. Lipid profile, waist circumference and body mass index in a high altitude population. High Alt Med Biol 2006; 7: 245-55.
25. Brito J, Siques P, Leon-Velarde F, De La Cruz JJ, Lopez V, Herruzo R. Chronic intermittent hypoxia at high altitude exposure for over 12 years: assessment of hematological, cardiovascular, and renal effects. High Alt Med Biol 2007; 8: 236-44.
26. Rawal SB, Singh MV, Tyagi AK, Roy J, Dimri GP, Selvamurthy W. Effect of time exposure to high altitude on zinc and copper concentrations in human plasma. Aviat Space Environ Med 1999; 70: 1161-5.