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Lipid and Hematological Parameters in Hyperleptinemic Healthy Arab Male Youth in Jordan

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Abstract: To analyze the influence of hyperleptinemia on fasting lipid and hematological parameters in healthy Arab male youth in Jordan, this cross-sectional study was carried out in April 2009 on a sample of 120 students aged 18-24 years. Subjects were stratified by fasting leptin into two groups (control, <12.7 ng mL^{-1} vs. hyperleptenimic, e_<12.7 ng mL^{-1}) and BMI (normal weight, <25 kg m^{-2} vs. overweight/obese, BMI e_<25 kg m^{-2}). Fasting serum leptin, blood glucose, lipid profile and hematological parameters values were determined by standard kit methods. Mean serum leptin concentrations were more than five times as high in hyperleptenemic subjects than in control subjects ($p<0.001$). Compared with control group, significant elevations ($p<0.01$) were observed in the means total cholesterol, LDL cholesterol and triglyceride levels of hyperleptenemic group whereas no significant differences was detected in HDL-cholesterol. Except the changes of WBC count, MCH and slightly MCHC, there were no differences between both groups in any other term of hematological parameters. In conclusion, changes in lipid variables and some hematological parameters may increase plasma viscosity as a step during atherosclerosis pathogenesis in male youth at risk for dyslipidemia and cardiovascular diseases. Thus, hyperleptinemia could be a useful index in identifying healthy youth male subjects but this hypothesis needs further investigation.

Key words: Hyperleptinemia, lipid profile, hematological parameter, dyslipidemia

INTRODUCTION

Leptin, the peptide encoded by the obesity gene, is secreted by adipose cells and plays an important role in regulating food intake and energy expenditure (Anubhuti, 2008; Hinuy *et al*., 2010). Plasma leptin concentration is proportional to body adiposity and is markedly increased in obese individuals (Beltowski, 2006). Obesity is a strong risk factor for the development of type 2 diabetes mellitus and cardiovascular disease CVD but the pathophysiological mechanisms that link obesity with CVD are poorly defined.

An enhanced lipid profiles rise occurs in some conditions that are associated with an increased risk of vascular disease such as hypertension, (Beltowski, 2006; Ren, 2004) diabetes mellitus DM (Boersma *et al*., 2011) and obesity (Hinuy *et al*., 2010).

Although recent reviews have identified the importance of preventive medicine (McKee *et al*., 2011; Toledo-Corral *et al*., 2011; Hankinson *et al*., 2010), significant percentage of those studies have been conducted on a patient population and show an association between hyperleptinemia and increased TC, LDL and TG in CAD and diabetes patients (Packard, 2006; Olszanecka *et al*., 2010; Shankar and Xiao, 2010; West *et al*., 2009).

Such as those highlighted the same association among healthy and young population are less consistent and controversial. Wu *et al*. (2001) showed that children with higher plasma leptin levels have significantly higher TG, LDL and Apo B levels than those with relatively lower leptin levels. Furthermore, Okada *et al*. (2010) also reported that leptin/leptin receptor gene polymorphisms may partly contribute to serum lipid profile in Japanese

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obese children. These results were not confirmed by Reinehr *et al.* (2009) who found that baseline leptin concentrations were not associated with blood lipids in multiple regression analyses. Haluzik *et al.* (2000) also noted that a relationship between leptin concentrations and lipid or lipoprotein levels was not statistically significant.

On the other hand, almost no data are available assessing a possible link between lipid and hematological parameters with hyperleptenemia in youth. Most limited available data , however, from studies involving patients and healthy samples were less consistent and controversial. Wang *et al.* (2004) showed that increased white blood cells and red blood cells counts were associated with a variety of metabolic syndrome features in a Taiwan Chinese population. Similarly, in hemodialysis patients, Nasri (2007) found a positive association between serum leptin and lymphocytes. Recently but in children with steady-state sickle cell disease, Seixas *et al.* (2010) found a positive association of HDL cholesterol with hemoglobin and hematocrit with total cholesterol. In healthy subjects, positive correlations were observed between hyperleptinemia and Mean Corpuscular Hemoglobin Concentration (MCHC) and Mean Corpuscular Volume (MCV) in Thai overweight subjects. Tungtrongchitr *et al.* (2000) also, with platelets count in obese adolescents according to Foschini *et al.* (2008) results and finally with WBC count in obese Jordanian male youth (Abu-Samak *et al.*, 2008). In contrast, no relationships were observed between serum leptin with leukocyte or platelets counts in healthy term infants (Koc *et al.*, 2001). Also in a study by Tungtrongchitr *et al.* (2000), there was a negative correlation between serum leptin with hemoglobin and hematocrit in overweight and obese subjects That is, obesity gene product leptin, is gaining more importance, since clarify the mechanisms leading to T2DM and CAD during early stages of youth life are more comprehensible as indicated in the previous studies .Thus, the aim of the study was to examine whether lipids and hematological parameters vary by serum leptin levels in Arab youth males in Jordan.

MATERIALS AND METHODS

This was a cross sectional study carried out in the Applied Science University, Amman, Jordan during the period from January to April 2009. This study was performed using a protocol for the protection of human subjects approved by the Applied Science University Ethical Committee, Amman, Jordan. Written informed consent and demographic characteristics and current medications were obtained from each subject. To avoid confounding factors known to affect leptin levels, subjects with chronic disease such as diagnosed cardiovascular diseases, cerebrovascular disease, dyslipidemia, stable hypertension treated by drugs, chronic hepatic, renal, or taking any kind of medications during the previous 2 months were excluded.

One hundred and twenty Jordanian male nursing students aged 18-24 years were stratified by fasting leptin into two groups. Control group, subjects, (n = 70) with normal serum leptin levels <9.4 ng mL^{-1} and hyperleptinemic subjects (n = 50) considered to have hyperleptinemia if they had values of >9.4 ng mL^{-1}. BMI, used as an index of general obesity (nonobese, <25 kg m^{-2} vs. overweight / obese, BMI.

Fasting venous blood samples were obtained, centrifuged and stored at -20°C until assayed. The following parameters were measured: blood glucose levels (using one touch test; Lifescan; Johnson and Johnson, Palmitas, CA, USA), serum leptin levels (by enzyme immunoassay; ELISA kit, DRG Diagnostics, Marburg, Germany), triglycerides, total cholesterol and high density lipoprotein cholesterol (HDL) (by enzymatic colorimetric kits, Linear Chemicals, Barcelona, Spain). Low density lipoprotein cholesterol (LDL) was calculated from the (Friedewald *et al.*, 1972) equation.

Clinical hematology parameters were measured for all volunteers, platelets count, total leukocyte count, differential leukocyte counts, hematocrit, hemoglobin and RBC indices (Mean Cell Hemoglobin [MCH], Mean Cell Volume [MCV], Mean Cell Hemoglobin Concentration [MCHC]), mean platelets count. Complete blood count was performed on the (COBAS MICROS OT 18, Roche, France).

Statistical analysis: Statistical analyses were performed using the STATISTICA 6.0 for Windows software (StatSoft, Tulsa, Oklahoma). Data were expressed as Means±SD. Differences were considered significant at $p<0.05$.

RESULTS

Table 1 summarizes the anthropometric measurements, fasting biochemical variables and clinical characteristics of the 120 healthy subjects in the present study. Mean age, height and fasting blood glucose were similar in both groups. The mean of ages for all subjects (n = 120) was 21.98±1.78 years and ranged from 18-24 years. Mean BMI and weight were significantly higher in subjects with hyperleptinemia compared with those without hyperleptinemia ($p<0.0001$).

Table 1: Subjects characteristics of the two study groups subdivided by the serum levels of leptin (Mean±SD)

Leptin	Normal leptin level	Hyperleptinemic	p-value
Weight	71.4±9.2	89.8±13.4	<0.0001
Height	175.0±6.0	175.8±5.8	0.519
BMI	23.3±2.4	29.1±4.4	<0.0001
TG	116.0±41.1	157.2±50.8	<0.0001
Chol	169.6±29.3	186.7±30.3	0.002
HDL	51.7±8.2	48.5±7.1	0.032
LDL	97.0±28.6	117.2±24.7	<0.0001
WBC	5.4±1.4	6.7±1.7	<0.0001
RBC	5.4±0.7	5.2±0.6	0.131
Hgb	15.8±1.1	16.1±1.3	0.153
PCV	46.7±4.5	46.2±4.7	0.631
MCV	86.7±4.7	88.0±3.7	0.094
MCH	29.4±3.0	31.1±2.1	0.001
MCHC	34.1±2.4	35.0±1.7	0.020
FBG	87.2±8.1	86.2±8.7	0.540
Lymph	35.9±8.2	36.2±6.4	0.817
Mono	6.3±1.7	6.1±1.8	0.651
Granulated	58.375±8.7126	57.9±7.4	0.753
Platelet	255.32±68.548	260.1±43.1	0.674
Age	21.94±1.665	22.2±1.6	0.436

The values of clinical and laboratory features of the leptin and blood lipids for hyperleptinemic subjects (n = 50) as well as for controls (n = 70) are given in Table 2.

Mean serum leptin concentrations were more than seven times as high in hyperleptenemic subjects than in control subjects (28 vs 4) ($p<0.0001$). Significant differences were noted in serum levels of LDL-C ($p<0.0001$), TG ($p<0.0001$) and TC ($p = 0.002$) between the two study groups, whereas, the difference in the serum high HDL-C was less significant ($p = 0.032$). Of all hematological parameters, only significant differences were observed between means of WBC ($p<0.0001$), MCH ($p<0.001$) and MCHC ($p = 0.002$) in study groups.

Correlation of hyperleptinemia with anthropometric, lipid and hematological parameters: The data indicates that irrespective of the levels of leptin in both groups are completely mediated by subject's body weight and the relationship seems to be more stronger in subjects with hyperleptinemia (pearson correlation coefficient: 0.546 vs. 0.360) (Table 2). The data also reveals that many other subjects' variable in addition to body weight may have an effect on the serum level of leptin. To establish a relationship between leptin serum levels and subjects' characteristics, linear regression analysis was carried out considering the following independent variables: body weight, MCHC, TG, cholesterol, HDL, FBG, RBC-count and WBC-count (Table 3). Five different models had significance value of the F statistic (ANOVA) less than 0.0001 which means that the variation explained by any of the model is not due to chance. The only variables that remained in the models were body weight, MCHC, TG, RBC-count and WBC-count. The models were 1: (body weight), 2: (body weight, MCHC), 3: (body weight, MCHC, TG), 4: (body weight, MCHC, RBC), 5: (body weight, MCHC, RBC, WBC). The multiple correlation coefficients of the five models had large values (0.816, 0.876, 0.884, 0.888 and 0.849) which indicated strong relationships (Fig.1). The squared value of the multiple correlation coefficients showed that about two thirds of the variation in leptin serum levels time is explained by the models (0.67, 0.76, 0.78, 0.78 and 0.79). As a further measure of the strength of the model fit, the standard errors of the estimate in the models were compared to the standard deviation of leptin serum level (9.3). All the linear regression models, the errors of the estimates were lower (8.0, 6.7, 6.6, 6.5 and 6.3).

One of the major flaws in the models was that dependent predictors were inter-related as can be seen in Table 2. Running the collinearity diagnostics confirmed that there were serious problems with multi-co-linearity. A Variance Inflation Factor (VIF) greater than 2 is usually

Table 2: The pearson correlation between subjects' characteristics and leptin serum level in subjects with normal serum levels of leptin; subjects with hyperleptinemia and in all subjects irrespective of normality of serum level of leptin

	Control subjects		Hyperleptinemic subjects		All subjects	
Variable	r	p-value	r	p-value	r	p-value
Fasting serum leptin						
Weight	0.360**	0.002	0.546**	<0.0001	0.721**	<0.0001
Height	0.119	0.327	-0.033	0.825	0.052	0.578
BMI	0.378**	0.001	0.575**	<0.0001	0.756**	<0.0001
TG	0.116	0.339	0.086	0.556	0.737**	<0.0001
Chol	0.130	0.285	0.091	0.536	0.370**	<0.0001
HDL	0.179	0.140	0.138	0.344	0.267**	0.003
LDL	0.025	0.840	0.062	0.675	-0.082	0.375
WBC	0.166	0.170	0.224	0.122	0.297**	0.001
RBC	0.102	0.401	0.039	0.788	0.396**	<0.000
Hgb	-0.019	0.873	0.044	0.763	-0.081	0.381
PCV	-0.013	0.912	-0.010	0.945	0.120	0.195
MCV	0.047	0.700	-0.084	0.567	-0.041	0.660
MCH	0.072	0.554	-0.036	0.807	0.102	0.272
MCHC	0.040	0.740	0.121	0.406	0.241**	0.008
FBG	0.085	0.485	0.159	0.275	0.210*	0.022
Lymph	0.024	0.857	-0.066	0.653	0.030	0.749
Mono	-0.051	0.698	-0.014	0.922	-0.002	0.984
Granulated	0.007	0.958	0.045	0.757	-0.046	0.632
Platelet	-0.045	0.727	0.065	0.655	-0.006	0.949
Age	-0.061	0.619	0.088	0.546	0.044	0.647

** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2-tailed)

Table 3: Pearson correlation between some subjects' characteristics and body weight in all subects of study groups (n = 120)

Parameter	Pearson correlation coefficient	p-value
TG	0.322	<0.0001
Chol	0.208	0.023
HDL	0.010	0.913
WBC	0.366	<0.0001
RBC	-0.121	0.190
MCHC	0.277	0.002
FBG	-0.045	0.624

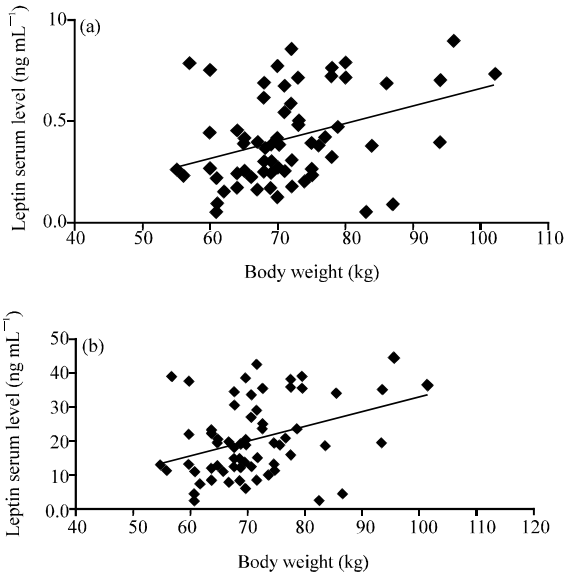

Fig. 1: Scatter plot of the relationship between subjects' body weight and leptin serum level in (a) control subject group and (b) hyperleptinemic subject group

considered problematic and the smallest VIF in the regression analysis for the included parameters was 12. Several eigenvalues were close to 0, indicating that the predictors are highly inter-correlated and that small changes in the data values may lead to large changes in the estimates of the coefficients. The square roots of the ratios of the largest eigenvalue to each successive eigenvalue were calculated (condition indices). Values greater than 30, indicates serious co-linearity problem.

Seven of these indices were larger than 30, suggesting a very serious problem with co-linearity. The co-linearity problem was fixed by re-running the regression using z scores of the variables (body weight, TG, MCHC, WBC and RBC) and the stepwise method of model selection. This is in order to include only the most useful variables in the model. The process ended with a single model with a single variable; the body weight.

DISCUSSION

In this study, we report here that LDL cholesterol, triglycerides and total cholesterol are strongly associated with fasting hyperleptinemia in healthy Arab male youth in Jordan. While the same association did not hold true for HDL-Cholesterol.

Present results confirm the results a number of previous studies among different ethnicities. Thai children and adolescents (Popruk *et al*., 2008), Colombian male school children (Poveda *et al*., 2007), Canadian youth aged from 12-15 years (Mahmud *et al*., 2009) and finally in Japanese male high schools aged 16 to 17 years (Nakatani *et al*., 2008). The strong association which we found is that hyperleptinemia is not mediated only by body weight but also by lipid parameters except HDL-cholesterol.

This observation may explain the fact that leptin is an independent risk factor for coronary heart disease as was shown in the WOSCOPS study (Wallace *et al*., 2001) and conversely to Baratta *et al*. (2004) who noted that the same association was entirely mediated by BMI.

It is difficult to answer, whether leptin is a major mediator or a reflection of other more critical endocrine and growth-related processes (Alexe *et al*., 2006), therefore, we studied leptin influence at an earlier ages of youth life which may clarify a part of leptin gene activity during this period.

The age of an individual, when the disease is diagnosed, is an important factor in determining the influence of particular risk factor of the disease (Yoon *et al*., 2003) which reflects and emphasizes the importance of early life environment in programming the susceptibility to chronic diseases in later life (Hales and Barker, 2001) but inability to undertake longitudinal studies from early to late life makes it difficult to directly evaluate the existence of such associations (Alexe *et al*., 2006).The strength of this study its homogenous sample in terms of age, gender and ethnicity which may explain why the results of some previous studies for hematological (Wang *et al*., 2004; Seixas *et al*., 2010) and lipid (Baratta *et al*., 2004; Gannage-Yared *et al*., 2006) parameters differ from our results. Notably, recent studies have demonstrated that leptin modulates lipid transport in rodents and human. Some reports have been conducted that leptin amplifies the pro-atheromatic properties of human monocytes (Ngai *et al*., 2010; Konstantinidis *et al*., 2009). Similarly, Hongo *et al*. (2009) suggested that leptin accelerates cholesteryl ester accumulation in human monocyte-derived macrophages by increasing ACAT-1 expression, thereby suppressing cholesterol efflux. Subsequently, Kosztaczky *et al*. (2007) have noted that leptin enhances cholesterol synthesis through a statin-sensitive pathway in circulating monocytes. In contrast to previous studies, Gannage-Yared *et al*. (2006) found , in healthy elderly male population, a weak relationship of leptin to lipid but strongly with insulin resistance, this is not confirmed by Galili *et al*. (2007) who found that early obesity is characterized by endothelial dysfunction in association with increased levels of leptin occurs before the development of insulin resistance.

In recent molecular studies, it has been found leptin/leptin receptor gene polymorphisms may partly contribute to serum lipid profile in Japanese obese children (Okada *et al*., 2010) and partly to testosterone effect on leptin gene expression in adipocytes according to Horenburg *et al*. (2008). Therefore, the major limitations of current study were: First, the study was cross-sectional and thus it is not possible to discern cause and effect using this design. Future studies of the impact of lipid and hematological parameters on longitudinal changes in leptin levels will be of value. Second, we did not have access to direct, detailed measures of some outcome variables such as waist circumflex, physical inactivity, testosterone levels and blood viscosity . Third, subjects were volunteers and hence, this might lead to biased associations compared with a random sample of the population.

Finally, almost no data are available assessing a possible link between lipid and hematological parameters with leptin levels in healthy Arab. However, our findings were in consistent with the limited available previous studies that have shown a positive associations between leptin levels with selected hematological parameters, particularly MCHC (Tungtrongchitr *et al*., 2000) platelet count (Foschini *et al*., 2008) and WBC count (Abu-Samak *et al*., 2008). Interestingly, our data for hematological parameters, partly, are in agreement with previous by Moriarty and Gibson (2005) who reported that the ability of HDL - cholesterol to reverse atherosclerosis and reduce cardiovascular disease via improving all of the rheological mediators.

CONCLUSION

Present data support the hypothesis that leptin may affect serum lipids independently. These results suggest that change in lipid variables and some hematological parameters may increase plasma viscosity as a step of atherosclerosis pathogenesis mechanism in healthy male youth but this hypothesis needs further investigation.

REFERENCES

Abu-Samak, M., K. Rula, M. Abu-Hasheesh, J. Malak and F. Mohammad, 2008. Relationship of vitamin B12 deficiency with overweight in male jordanian youth. J. Applied Sci., 8: 3060-3063.

Alexe, D., G. Syridou and E. Petridou, 2006. Determinants of early life leptin levels and later life degenerative outcomes. Clin. Med. Res., 4: 326-335.

Anubhuti, S.A., 2008. Leptin and its metabolic interactions. Diabetes Obes. Metab., 10: 973-993.

Baratta, R., S. Amato, C. Degano, M.G. Farina, G. Patane, R. Vigneri and L. Frittitta, 2004. Adiponectin relationship with lipid metabolism is independent of body fat mass: Evidence from both cross-sectional and intervention studies. J. Clin. Endocrinol. Metabol., 89: 2665-2671.

Beltowski, J., 2006. Leptin and atherosclerosis. Atherosclerosis, 189: 47-60.

Boersma, G.J., L. Benthem, G. van Dijk and A.J.W. Scheurink, 2011. Individual variation in the (patho)physiology of energy balance. Pathophysiol. Behav., (In Press). 10.1016/j.physbeh.2010.12.026.

Foschini, D., R.V. Santos, W.L. Prado, A. de piano and M.C. Lofrano *et al*., 2008. Platelet and leptin in obese adolescents. J. Pediatr. (Rio J.), 84: 516-521.

Friedewald, W.T., R.I. Levy and D.S. Fredrickson, 1972. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin. Chem., 18: 499-502.

Galili, O., D. Versari, K.J. Sattler, M.L. Olson and D. Mannheim *et al*., 2007. Early experimental obesity is associated with coronary endothelial dysfunction and oxidative stress. Am. J. Physiol. Heart Circ. Physiol., 292: 904-9011.

Gannage-Yared, M.H., S. Khalife, M. Semaan, F. Fares, S. Jambart and G. Halaby, 2006. Serum adiponectin and leptin levels in relation to the metabolic syndrome androgenic profile and somatotropic axis in healthy non-diabetic elderly men. Eur. J. Endocrinol., 155: 167-176.

Hales, C.N. and D.J. Barker, 2001. The thrifty phenotype hypothesis. Br. Med. Bull., 60: 5-20.

Haluzik, M., J. Fiedler, J. Nedvidkova and R. Ceska, 2000. Serum leptin levels in patients with hyperlipidemias. Nutrition, 16: 429-433.

Hankinson, A.L., M.L. Daviglus, C. Bouchard, M. Carnethon and C.E. Lewis *et al*., 2010. Maintaining a high physical activity level over 20 years and weight gain. J. Am. Med. Assco., 15: 2603-2610.

Hinuy, H.M., M.H. Hirata, M.F. Sampaio, D.Armagamjan, S.S. Arazi, L.A. Salazar and R.D. Hirata, 2010. Relationship between variants of the leptin gene and obesity and metabolic biomarkers in Brazilian individuals. Arq. Bras. Endocriol. Metabol., 54: 282-288.

Hongo, S., T. Watanabe, S. Arita, T. Kanome, H. Kageyama, S. Shioda and A. Miyazaki, 2009. Leptin modulates ACAT1 expression and cholesterol efflux from human macrophages. Am. J. Physiol. Endcrinol. Metab., 297: 474-482.

Horenburg, S., P. Fischer-Posovszky, K.M. Debatin and M. Wabitsch, 2008. Influence of sex hormones on adiponectin expression in human adipocytes. Horm. Metab. Res., 40: 779-786.

Koc, E., A. Bideci, P. Cinaz, E. Ergenekon and Y. Atalay, 2001. Relationships between levels of leptin and hematological parameters in healthy term infants. J. Pediatr. Endocrinol. Metab., 14: 1129-1132.

Konstantinidis, D., K. Paletas, G. Koliakos and M. Kaloyianni, 2009. Signaling components involved in leptin-induced amplification of the atherosclerosis-related properties of human monocytes. J. Vasc. Res., 46: 199-208.

Kosztaczky, B., G. Foris, G. Paragh, I. Seres, E. Zsiros, P. Koncsos, Z. Balogh and G. Paragh, 2007. Leptin stimulates endogenous cholesterol synthesis in human monocytes: New role of an old player in atherosclerotic plaque formation. Leptin-induced increase in cholesterol synthesis. Int. J. Biochem. Cell Biol., 39: 1637-1645.

Mahmud, F.H., D.J. Hill, M.S. Cuerden and C.L. Clarson, 2009. Impaired vascular function in obese adolescents with insulin resistance. J. Pediatr., 155: 678-682.

McKee, M.D., S.E. Rubin, G. Campos and L.F. O'Sullivan, 2011. Challenges of providing confidential care to adolescents in urban primary care: Clinician perspectives. Ann. Fam. Med., 9: 37-43.

Moriarty, P.M. and C.A. Gibson, 2005. Association between hematological parameters and high-density lipoprotein cholesterol. Curr. Opin. Cardiol., 20: 318-323.

Nakatani, H., H. Hirose, Y. Yamamoto, I. Saito and H. Itoh, 2008. Significance of leptin and high-molecular weight adiponectin in the general population of Japanese male adolescents. Metabolism, 57: 157-162.

Nasri, H., 2007. The association between serum leptin and blood lymphocytes in hemodialysis patients. Bratisl. Lek. Listy., 108: 122-127.

Ngai, Y.F., W.L. Quong, M.B. Glier, M.M. Glaves, S.L. Babich, S.M. Innis, T.J. Kieffer, W.T. Gibson, 2010. Ldlr-/-mice display decreased susceptibility to Western-type diet-induced obesity due to increased thermogenesis. Endocrinology, 151: 5226-5236.

Okada, T., T. Ohzeki, Y. Nakagawa, S. Sugihara and O. Arisaka, 2010. Impact of leptin and leptin-receptor gene polymorphisms on serum lipids in Japanese obese children. Order Acta Pediatr., 99: 1213-1217.

Olszanecka, A., A. Posnik-Urbanska, K. Kawecka-Jaszcz, D. Czarnecka and D. Fedak, 2010. Adipocytokines and blood pressure, lipids and glucose metabolism in hypertensive perimenopausal women. Kardiol. Pol., 68: 753-760.

Packard, C.J., 2006. Small dense low-density lipoprotein and its role as an independent predictor of cardiovascular disease. Curr. Opin. Lipidol., 17: 412-417.

Popruk, S., R. Tungtrongchitr, S. Petmitr, P. Pongpaew and T. Harnroongroj *et al*., 2008. Leptin, soluble leptin receptor, lipid profiles and LEPR gene polymorphisms in Thai children and adolescents. Int. J. Vitam. Nutr. Res., 78: 9-15.

Poveda, E., N.E. Callas, C.M. Baracaldo, C. Castillo and P. Hernandez, 2007. Leptin levels in school age children associated with anthropometric measurements and lipid profiles. Biomedica, 27: 505-514.

Reinehr, T., M. Kleber, G. de Sousa and W. Andler, 2009. Leptin concentrations are a predictor of overweight reduction in a lifestyle intervention. Int. J. Pediatr. Obes., 4: 215-223.

Ren, J., 2004. Leptin and hyperleptinemia-from friend to foe for cardiovascular function. J. Endocrine, 181: 1-10.

Seixas, M.O., L.C. Rocha, M.B. Carvalho, J.F. Menezes and I.M. Lyra *et al*., 2010. Levels of high-density lipoprotein cholesterol (HDL-C) among children with steady-state sickle cell disease. Lipid Health Dis., 27: 79-91.

Shankar, A. and J. Xiao, 2010. Positive relationship between plasma leptin level and hypertension. Hypertension, 56: 623-628.

Toledo-Corral, C.M., J.N. Davis, T.L. Alderete, M.J. Weigensberg and C.T. Ayala *et al*., 2011. Subclinical atherosclerosis in Latino youth: Progression of carotid intima-media thickness and its relationship to cardiometabolic risk factors. J. Pediatr.,

Tungtrongchitr, R., P. Pongpaew, B. Phonrat, S. Tribunyatkul and D. Viroonudomphol *et al*., 2000. Leptin concentration in relation to Body Mass Index (BMI) and hematological measurements in Thai obese and overweight subjects. Southeast Asian J. Trop. Med. Public Health, 31: 787-794.

Wallace, A.M., A.D. McMahon, C.J. Packard, A. Kelly, J. Shepherd, A. Gaw and N. Sattar, 2001. Plasma leptin and the risk of cardiovascular disease in the West of Scotland Coronary Prevention Study (WOSCOPS). Circulation, 104: 3052-3056.

Wang, Y.Y., S.Y. Lin, P.H. Liu, B.M. Cheung and W.A. Lai, 2004. Association between hematological parameters and metabolic syndrome components in a Chinese population. J. Diabetes Complications, 18: 322-327.

West, N.A., R.F. Hamman, E.J. Mayer-Davis, R.B. D'Agostino and S.M. Marcovina *et al*., 2009. Cardiovascular risk factors among youth with and without type 2 diabetes: Differences and possible mechanisms. Diabetes Care, 32: 175-180.

Wu, D.M., M.H. Shen and N.F. Chu, 2001. Relationship between plasma leptin levels and lipid profiles among school children in Taiwan-the Taipei Children Heart Study. Eur. J. Epidemiol., 17: 911-916.

Yoon, P.W., M.T. Scheuner and M.J. Khoury, 2003. Research priorities for evaluating family history in the prevention of common chronic diseases. Am. J. Prev. Med., 24: 128-135.