Diabetes & Metabolic Syndrome: Clinical Research & Reviews 13 (2019) 1845–1849

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

Leptin: Adiponectin ratio discriminated the risk of metabolic syndrome better than adiponectin and leptin in Southwest Nigeria

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ARTICLE INFO

Article history:
Received 16 March 2019
Accepted 11 April 2019

Keywords:
Leptin:Adiponectin ratio
Leptin
Adiponectin
Metabolic syndrome
Nigeria

ABSTRACT

Aim: To assess the ability of leptin, adiponectin and leptin: adiponectin ratio (LAR) to discriminate apparently healthy subjects with metabolic syndrome in Southwest Nigeria.
Methods: One hundred and twenty three subjects with metabolic syndrome (cases) were age matched with 123 subjects without metabolic syndrome. The serum adiponectin and leptin levels were measured using standard procedures. The ability of serum adiponectin, leptin and LAR to discriminate metabolic syndrome and its components were determined using the receiver operating curve and linear regression.
Results: The median age of the cases (49 IQR 42, 56 years) was not significantly different from the controls (48 IQR 39, 56 years) $p = 0.252$. The adiponectin levels was reduced with increasing number of the components of metabolic syndrome from 11.6 (IQR 9.6, 13.5) among subjects without any component of metabolic syndrome to 6.5 (IQR 5.7, 7.7) in subjects with more than three components of metabolic syndrome. For leptin and LAR, the values increased with increasing components ($p < 0.001$). LAR (AUC 0.960) discriminated metabolic syndrome better than adiponectin (AUC 0.865) and leptin (AUC = 0.918) in males and females (LAR AUC = 0.966, adiponectin AUC = 0.888, leptin AUC = 0.929).
Conclusion: LAR had better ability to discriminate the risk of metabolic syndrome than adiponectin and leptin alone in males and females among apparently healthy subjects from Southwest Nigeria.

1. Introduction

Over the past decade adipose tissue has been redefined as a dynamic metabolic, endocrine organ secreting various cytokines, called adipokines in a paracrine, autocrine, and endocrine fashion [1,2]. Its dysfunction is an important contributor in defining the mechanism related to the pathogenesis of metabolic diseases such as type 2 diabetes, obesity, hypertension and metabolic syndrome [3,4].

Adiponectin and leptin are two major adipokines in the regulation of energy homeostasis. Adiponectin, the most abundant adipokine in circulation plays a major role in insulin sensitivity, glucose metabolism, central fat distribution, tissue inflammation and endothelial function [5,6]. Leptin is an adipokine which reduces appetite, increases energy expenditure, facilitates glucose utilization, increases sympathetic activity and improves insulin sensitivity [7]. Reduced adiponectin and elevated leptin levels are associated with metabolic syndrome, obesity and insulin resistance [8–10].

Although leptin and adiponectin are separately associated with the risk of metabolic syndrome, type 2 diabetes and CVD, their opposite effects on subclinical inflammation, glucose and fat metabolism birth the hypothesis of the ratio of LAR as a better marker of metabolic syndrome than leptin and adiponectin alone [11,12].

Few studies from Nigeria have demonstrated association between adiponectin and leptin with obesity, type 2 diabetes and

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https://doi.org/10.1016/j.dsx.2019.04.008
1871-4021/

metabolic syndrome [13–16]. To the best of the authors' knowledge no study has examined the association of LAR with metabolic syndrome in Nigeria. This present study which is a follow up to the study that assessed the prevalence of metabolic syndrome in a rural and urban community in Southwest Nigeria using three different definitions [17], is aimed at assessing the ability of leptin, adiponectin and LAR to discriminate apparently healthy subjects with metabolic syndrome in Southwest Nigeria.

2. Methods

A case control study was designed to assess whether LAR discriminated metabolic syndrome and its components better than adiponectin and leptin among apparently healthy subjects in Southwest Nigeria. Cases were subjects identified as having metabolic syndrome who were age matched with subjects without the metabolic syndrome (controls).

Details of study background and sampling were earlier published [17]. Briefly, subjects were apparently healthy volunteers aged 18 years and above without any medical history of hypertension or diabetes; who had resided at least 2 years in selected sites prior to recruitment into the study. Multi-stage sampling technique was used to select the two communities while volunteer subjects were consecutively recruited. On recruitment, sociodemographic details of the subjects were collected using a proforma after which anthropometric and blood pressure measurements were done. Venous blood was collected after an overnight fast for lipid profile, blood glucose, leptin and adiponectin estimation using standard procedures. Identification of metabolic syndrome was done using the Joint interim Statement of the International Diabetes Federation (IDF) Task force criteria (JIS) [17].

3. Measurements and classification of outcome variable

3.1. Measurement of anthropometric variable

Measurement of waist circumference was done using a flexible tape. The top of the illiac crest was located and measurement was taken horizontally around the abdomen above the level of the illac crest. Measurement was done to the nearest 0.1 cm.

3.2. Measurement of blood pressure

Blood pressure (BP) measurement was done in the morning in sitting position after about 5 min rest using a calibrated OMRON automated BP monitor (Omron Healthcare, Kyoto, Japan) that uses an upper arm cuff. The average of two measurements taken on the right arm of the subjects was recorded.

3.3. Biochemical analysis

Venous blood was collected from the subjects after an overnight fast (10–14 h). Blood samples were collected in appropriate tubes (fluoride oxalate for fasting blood glucose, potassium ethylene diamine tetra acetic acid (K_3EDTA) for lipid profile and plain bottles for adiponectin and leptin analysis). All serum and plasma samples were prepared in the laboratory using standard methods and stored at −20 °C until analyses were performed. Fasting plasma glucose (FPG), triglyceride and high density lipoprotein cholesterol (HDL-C) were estimated by enzymatic methods using commercial kits (Randox laboratories limited, United Kingdom). Leptin and adiponectin were measured using enzyme linked immunosorbent assay (DRG Instrument GmbH, Germany).

Commercial quality control samples were included within each batch of test assay to monitor the accuracy and precision of biochemical tests.

3.4. Definition of metabolic syndrome

Metabolic syndrome was defined using the criteria proposed by the joint interim statement of the IDF Task Force (JIS). It was recommended that metabolic syndrome should be diagnosed when three or more of the following conditions are fulfilled [18]: (1) Elevated triglycerides: 150 mg/dl (1.7 mmol/l) or history of specific treatment for this lipid abnormality; (2) Reduced HDL-C: < 40 mg/dl (1.03 mmol/l) in men and <50 mg/dl (1.29 mmol/l) in women or history of specific treatment for HDL-C; (3) Raised BP: systolic BP 130 mmHg or diastolic BP 85 mmHg or on treatment for previously diagnosed hypertension; (4) FPG ≥100 mg/dl or previously diagnosed type 2 diabetes mellitus; (5) Waist circumference ≥94 cm in men or ≥80 cm in women (as recommended for Europeans).

3.5. Ethical considerations

Approval for the study was obtained from the Health Research and Ethical Committee of the Lagos State University Teaching Hospital (LASUTH) Ikeja. Subjects were assured of strict confidentiality and relevant subjects information were anonymized.

3.6. Data analysis

Data was entered and analyzed using the Statistical Package for Social Sciences (SPSS) IBM. Armonk NY, USA version 22. Percentages, median and interquartile range of numeric variables were determined. The distribution of outcome variables were assessed using Kolmogorov-Smirnov statistics and histogram plots. Mann Whitney *U* test was used to compare median of two independent groups. Spearman rho correlation was used to assess the relationship between two numerical variables. Linear regression of the components of metabolic syndrome on adiponectin, leptin and LAR was determined. The ability of adiponectin, leptin and LAR to discriminate metabolic syndrome was assessed using receiver operating characteristic curve (ROC). For all statistical tests the confidence interval was set at 95% and statistical test were considered significant if $p < 0.05$.

4. Results

One hundred and twenty three subjects with metabolic syndrome (cases) were age matched with 123 subjects without metabolic syndrome (controls). The median age of the cases (49 IQR 42, 56 years) was not significantly different from the controls (48 IQR 39, 56 years) $p = 0.252$. The median serum level of leptin and LAR was higher among the cases than controls (27.3, IQR 21.7, 34.5 vs 12.3 IQR 8.8, 16.7) and (3.7 IQR 2.7, 5.1 vs 1.1 IQR 0.8, 1.5) respectively $p < 0.001$. However, adiponectin, leptin and LAR were higher in females compared with males ($p < 0.001$) as shown in Table 1.

The adiponectin levels was reduced with increasing number of metabolic syndrome components from 11.6 (IQR 9.6, 13.5) among subjects without any component of metabolic syndrome to 6.5 (IQR 5.7, 7.7) in subjects with more than three components of metabolic syndrome. For leptin and LAR, the values increased with increasing components ($p < 0.001$) (Table 2).

The correlation of adiponectin, leptin and LAR with the components of metabolic syndrome in males and females is shown in Table 3. In both males and females, leptin and LAR had positive correlation with all the components of metabolic syndrome except HDL-C. However, the contrary is the case for adiponectin. Among the males, the correlation of leptin with waist circumference

Table 1
Adiponectin, Leptin levels and Leptin:Adiponectin ratio by gender and presence of metabolic syndrome.

Variables	Median (IQR)	Median (IQR)	U	p
Group	**Controls (n = 123)**	**Cases (n = 123)**		
Adiponectin (μg/ml)	10.7 (IQR 8.9, 12.7)	7.4 (IQR 6.2, 9.3)	9.060	<0.001
Leptin (ng/ml)	12.3 (IQR 8.8, 16.7)	27.3 (IQR 21.7, 34.5)	10.934	<0.001
Leptin:Adiponectin ratio	1.1 (IQR 0.8, 1.5)	3.7(IQR 2.7, 5.1)	12.511	<0.001
Age	48.0 (IQR 39, 56)	49 (IQR 42, 56)	1.145	0.252
Gender	**Males (n = 74)**	**Females (n = 172)**		
Adiponectin (μg/ml)	8.4(IQR 6.2, 9.8)	9.6 (IQR 7.4, 11.9)	4.172	<0.001
Leptin (ng/ml)	10.5 (IQR 7.5, 18.1)	23.9 (IQR 16.3, 32.0)	8.654	<0.001
Leptin: Adiponectin ratio	1.3 (IQR 0.7, 2.6)	2.5 (IQR 1.3, 4.5)	5.020	<0.001

Table 2
Association of Adiponectin, Leptin and Leptin:Adiponectin ratio with increasing components of metabolic syndrome.

Number of components	n	Adiponectin (μg/ml) Median (IQR)	Leptin (ng/ml) Median (IQR)	LAR Median (IQR)
0	23	11.6(IQR 9.6, 13.5)	8.5 (IQR 3.3, 13.3)	0.7 (IQR 0.4, 0.8)
1	52	11.4 (IQR 9.6, 12.8)	12.9 (IQR 8.5, 17.3)	1.1(IQR 0.8, 1.4)
2	48	9.8 (IQR9.2, 11.8)	12.7(IQR 10.5, 21.2)	1.4 (IQR 0.9, 2.4)
3	74	8.1 (IQR 6.7, 9.6)	25.7 (IQR 21.2, 31.6)	3.1(IQR 2.4, 4.3)
>3	49	6.5(IQR 5.7, 7.7)	31.3 (IQR 22.8, 43.7)	4.9 (IQR 3.4, 6.1)

Table 3
Correlation of Adiponectin, Leptin and Leptin:Adiponectin ratio with increasing components of metabolic syndrome.

Variables	Pearson Correlation coefficient	p
Males		
Adiponectin (μg/ml)	−0.427**	0.004
Leptin (ng/ml)	0.636**	<0.001
LAR	0.683**	<0.001
Females		
Adiponectin (μg/ml)	−0.292*	0.010
Leptin (ng/ml)	0.376**	0.004
LAR	0.462**	<0.001
ALL		
Adiponectin (μg/ml)	−0.590*	<0.001
Leptin (ng/ml)	0.682**	<0.001
LAR	0.758**	<0.001

NB: ** Correlation significant at 0.01 level (2 tail).
Correlation significant at 0.05 (2 tail).
LAR = Leptin: Adiponectin ratio.

(r = 0.567) and diastolic BP (r = 0.542) was stronger than the correlation of adiponectin and LAR with waist circumference (r = −0.341 vs r = 0.498) and diastolic BP (r = −0.375 vs r = 0.515) respectively. The correlation of adiponectin with systolic BP (r = −0.545) and triglyceride (r = -0.250) was as higher than the correlation of leptin and LAR with systolic BP and triglyceride. Among the female subjects, the correlation of LAR with waist circumference (r = 0.484), Systolic BP (r = 0.285) and diastolic BP (r = 0.3150) was higher than the correlation of adiponectin and leptin with waist circumference, systolic and diastolic BP. There was no significant correlation of adiponectin, leptin and LAR with HDL-C among males (p > 0.05) however among females the contrary was the case.

The regression of the components of metabolic syndrome on adiponectin, leptin and LAR is shown in Table 4. Serum levels of adiponectin was associated with reduced waist circumference and systolic BP in males while among the females it was associated with reduced waist circumference, diastolic BP and FPG and increased with HDL-C. Serum level of leptin was associated with increased waist circumference and fasting plasma glucose in the males and triglyceride in females and reduced HDL-C in males and females. LAR was associated with increased WC, FPG in males and triglyceride in females.

Table 5 shows that LAR (AUC 0.960) discriminated metabolic syndrome better than adiponectin (AUC 0.865) and leptin (AUC = 0.918) in males and females (LAR AUC = 0.966, adiponectin AUC = 0.888, leptin AUC = 0.929).

5. Discussion

Metabolic syndrome is a constellation of interrelated risk factors of metabolic origin which has become a growing public health concern [19]. The roles of leptin and adinopectin in the development of metabolic syndrome have been reported in different ethnic populations [20,21]. Studies have further proposed LAR to be a better marker for predicting the risk of metabolic syndrome than with than leptin and adinopectin alone [22,23]. This present study demonstrates that LAR had a higher predictive power than serum adiponectin and leptin for risk of metabolic syndrome in both men and women. This finding is similar to what was reported in a prospective study from China where the AUC for LAR was larger than adiponectin and leptin [24]. Cross sectional studies from China and sub Saharan Africa also suggested LAR to be better predictor of metabolic syndrome than adiponectin and leptin [11,12]. High adiponectin and low leptin levels could offer some protection against the development of metabolic syndrome [25]. Studies have shown high leptin to be associated with vascular injury, elevation of blood pressure and vascular endothelial cell proliferation [26,27] while high adiponectin levels is said have anti-inflammatory effects and protective against atherosclerosis [28,29].

The gender differences in levels of leptin and adiponectin has been documented. This study shows that serum levels of adiponectin and leptin were higher in women than men similar to what was reported in other studies [12]. Leptin levels are higher in women than men because of the higher proportion of adipose tissue and elevated production of leptin per unit adipose tissue in women [30]. However, it has been suggested that adiponectin inhibition by androgen is responsible for the higher levels of adiponectin in women [31].

Our study shows that waist circumference is positively correlated with leptin and LAR; and negatively correlated with adiponectin in both men and women which is in harmony with some studies which showed that leptin and adiponectin are positivity and negatively linked respectively with visceral fat [32,33]. There is association between leptin and adiponectin and body fat. Excess

Table 4
Regression of adiponectin, leptin, Leptin: Adiponectin ratio with components of metabolic syndrome (n = 246).

Metabolic syndrome components	Adiponectin (μg/ml)	Leptin (ng/ml)	LAR
Males			
Waist circumference (cm)	−0.292, 0.017	0.535, <0.001	0.456, <0.001
Systolic blood pressure (mmHg)	−0.632, <0.001	0.058, 0.663	0.154, 0.276
Diastolic blood pressure (mmHg)	0.313, 0.068	0.236, 0.088	0.121, 0.407
HDL-C (mg/dl)	−0.115, 0.277	−0.199, 0.022	−0.122, 0.182
Triglyceride (mg/dl)	0.045, 0.734	−0.181, 0.085	−0.218, 0.060
FPG (mg/dl)	−0.271, 0.055	0.442, <0.001	0.521, <0.001
Females			
Waist circumference (cm)	−0.339, <0.001	0.261, <0.001	0.279, <0.001
Systolic blood pressure (mmHg)	0.025, 0.805	0.090, 0.373	0.046, 0.628
Diastolic blood pressure (mmHg)	−0.199, 0.040	0.097, 0.319	0.161, 0.081
HDL-C (mg/dl)	0.261, <0.001	−0.158, 0.014	−0.211, 0.001
Triglyceride (mg/dl)	0.021, 0.762	0.199, 0.004	0.153, 0.021
FPG (mg/dl)	−0.268, <0.001	0.263, <0.001	0.311, <0.001

Results presented represent b values (p values) assessed by linear regression adjusted for age; (b) coefficient for the relationship between the dependent variables (adiponectin, leptin and LAR) and the independent variables (components of metabolic syndrome).
HDL-C = High density lipoprotein cholesterol.
FPG = Fasting plasma glucose.

Table 5
Area under the ROC curve of Adiponectin, Leptin and Leptin:Adiponectin ratio that best predicts metabolic syndrome.

Variables	Area Under ther curve (AUC)	95%CI	p
Males			
Adiponectin (μg/ml)	0.868	0.777–0.960	0.000**
Leptin (ng/ml)	0.918	0.857–0.979	0.000*
Leptin:Adiponectin ratio	0.960	0.923–0.998	0.000*
Females			
Adiponectin (μg/ml)	0.888	0.841–0.936	0.000*
Leptin (ng/ml)	0.929	0.888–0.970	0.000*
Leptin:Adiponectin ratio	0.966	0.944–0.988	0.000*

adiposity is linked with down regulation of adiponectin and up regulation of leptin production which could results in insulin resistance and type 2 diabetes and metabolic syndrome [34,35].

In this study adiponectin, leptin and LAR exhibited opposite and variable correlations with the components of metabolic syndrome. Leptin and LAR were associated with increased blood pressure, triglyceride and fasting plasma glucose, which is in accordance with what was reported in a study from sub Saharan Africa and Yemen [11,36]. There was gender difference in the association of LAR with glucose and lipid components of metabolic syndrome in this study similar to what was reported in another study [37]. The gender differences in glucose and lipid metabolism could be responsible for our finding [38,39]. The correlation of increasing components of metabolic syndrome with LAR was better than with adiponectin and leptin in this study. The reason is not known, however the greater ability of LAR to predict metabolic syndrome than adiponectin and leptin in this study may be responsible.

6. Conclusion

LAR had better ability to discriminate the risk of metabolic syndrome than adiponectin and leptin alone among apparently healthy subjects in this study. This may be an indication that LAR could be an important biomarker to predict the risk of metabolic syndrome. However, further studies will be needed to ascertain this.

References

[1] Bluher M. Adipose tissue dysfunction in obesity. Exp Clin Endocrinol Diabetes 2009;117:241–50.
[2] Goossens GH. The role of adipose tissue dysfunction in the pathogenesis of obesity-related insulin resistance. Physiol Behav 2008;94:206–18.
[3] Wang P, Mariman E, Renes J, Keijer J. The secretory function of adipocytes in the physiology of white adipose tissue. J Cell Physiol 2008;216:3–13.
[4] Bartness TJ, Song CK. Thematic review series: adipocyte biology. Sympathetic and sensory innervation of white adipose tissue. J Lipid Res 2007;48:1655–72.
[5] Kawanami D, Maemura K, Takeda N, Harada T, Nojiri T, Imai Y, et al. Direct reciprocal effects of resistin and adiponectin on vascular endothelial cells: a new insight into adipocytokine-endothelial cell interactions. Biochem Biophys Res Commun 2004;314:415–9.
[6] Shetty GK, Economides PA, Horton ES, Mantzoros CS, Veves A. Circulating adiponectin and resistin levels in relation to metabolic factors, inflammatory markers, and vascular reactivity in diabetic patients and subjects at risk for diabetes. Diabetes Care 2004;27:2450–7.
[7] Dong M, Ren J. What fans the fire: insights into mechanisms of leptin in metabolic syndrome-associated heart diseases. Curr Pharmaceut Des 2014;20:652–8.
[8] Robinson K, Prins J, Venkatesh B. Clinical review: adiponectin biology and its role in inflammation and critical illness. Crit Care 2011;15:221.
[9] Lopez-Jaramillo P. SSA 04-3 leptin/adiponectin in cardiometabolic disease. J Hypertens 2016;34(Suppl 1-ISH 2016 Abstract Book):e7.
[10] Ghantous CM, Azrak Z, Hanache S, Abou-Kheir W, Zeidan A. Differential role of leptin and adiponectin in cardiovascular system. Int J Endocrinol 2015. https://doi.org/10.1155/2015/534320.
[11] Ayina CNA, Endomba FTA, Mandengue SH, Noubiap JJN, Ngoa LSE, Boudou P, et al. Association of the leptin-to-adiponectin ratio with metabolic syndrome in a sub-Saharan African population. Diabetol Metab Syndr 2017;9:66. https://doi.org/10.1186/s13098-017-0265-6.
[12] Kang DR, Yadav D, Koh SB, Kim JY, Ahn SV. Impact of serum leptin to adiponectin ratio on regression of metabolic syndrome in high-risk individuals: the ARIRANG study. Yonsei Med J 2017;58:339–46. https://doi.org/10.3349/ymj.2017.58.2.339.
[13] Fabian UA, Charles-Davies MA, Adebusuyi JR, Ebesunun MO, Ajobo BM, Hassan OO, et al. Leptin concentrations in African blacks with metabolic syndrome and type 2 diabetes mellitus. J US China Med Sci 2011;8:493–500.
[14] Ciroma FL, Ayo JO, Mohammed A, Akor-Dewu MB, Kana MA, Kase SN. Association between adiponectin, serum lipids and obesity in a University setting in Nigeria. Niger J Physiol Sci 2017;32:69–74.
[15] Ebesunun MO, Okeke DC. Serum leptin correlated with anthropometric indices in obese subjects. J Metab Syndrome 2014;3:157. https://doi.org/10.4172/2167-0943.1000157.
[16] Yusuf NW, Mabrouk MA, Girei AB, Mohammed A. Relationship between leptin and indices of obesity among apparently healthy adults in Kano, Northwestern Nigeria. Int J Med Sci Public Health 2015;9:1218–22.

[17] Adejumo EN, Ogundahunsi OA, Adejumo AO, Sotunsa J, Jagun O. Prevalence of metabolic syndrome in a rural and urban community in South-West Nigeria using three different definitions. Int J Trop Dis Health 2017;24. 1e9, https://doi.org/10.9734/IJTDH/2017/33993.
[18] National Cholesterol Education Program (NCEP). Expert panel on detection and treatment of high blood cholesterol in adults. Third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III) final report. Circulation 2002;106. 3143e421.
[19] Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2005;365:1415–28.
[20] Patel SB, Reams GP, Spear RM, Freeman RH, Villarreal D. Leptin: linking obesity, the metabolic syndrome, and cardiovascular disease. Curr Hypertens Rep 2008;10:131–7.
[21] Gannagé-Yared MH, Khalife S, Semaan M, Fares F, Jambart S, Halaby G. 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 2006;155:167–76.
[22] Falahi E, Khalkhali Rad AH, Roosta S. What is the best biomarker for metabolic syndrome diagnosis? Diabetes Metab Syndrome 2015;9:366–72.
[23] Lilja M, Rolandsson O, Norberg M, Soderberg S. The impact of leptin and adiponectin on incident type 2 diabetes is modified by sex and insulin resistance. Metab Syndrome Relat Disord 2012;10:143–51.
[24] Zhuo Q, Wang Z, Fu P, Piao J, Tian Y, Xu J, et al. Comparison of adiponectin, leptin and leptin to adiponectin ratio as diagnostic marker for metabolic syndrome in older adults of Chinese major cities. Diabetes Res Clin Pract 2009;84:27–33.
[25] Kim JY, Ahn SV, Yoon JH, Koh SB, Yoon J, Yoo BS, et al. Prospective study of serum adiponectin and incident metabolic syndrome: the ARIRANG study. Diabetes Care 2013;36:1547–53.
[26] Schäfer K, Halle M, Goeschen C, Dellas C, Pynn M, Loskutoff DJ, et al. Leptin promotes vascular remodeling and neointimal growth in mice. Arterioscler Thromb Vasc Biol 2004;24:112–7.
[27] Carlyle M, Jones OB, Kuo JJ, Hall JE. Chronic cardiovascular and renal actions of leptin: role of adrenergic activity. Hypertension 2002;39:496–501.
[28] Fantuzzi G. Adipose tissue, adipokines, and inflammation. J Allergy Clin Immunol 2005;115:911–9.
[29] Matsuda M, Shimomura I, Sata M, Arita Y, Nishida M, Maeda N, et al. Role of adiponectin in preventing vascular stenosis: the missing link of adipo-vascular axis. J Biol Chem 2002;277:37487–91.
[30] Hellström L, Wahrenberg H, Hruska K, Reynisdottir S, Arner P. Mechanisms behind gender differences in circulating leptin levels. J Intern Med 2000;247:457–62.
[31] Nishizawa H, Shimomura I, Kishida K, Maeda N, Kuriyama H, Nagaretani H, et al. Androgens decrease plasma adiponectin, an insulin-sensitizing adipocyte-derived protein. Diabetes 2002;51:2734–41.
[32] Staiger H, Tschritter O, Machann J, Thamer C, Fritsche A, Maerker E, et al. Relationship of serum adiponectin and leptin concentrations with body fat distribution in humans. Obes Res 2003;11:368–72.
[33] Gauthier A, Dubois S, Bertrais S, Gallois Y, Aube C, Gagnadoux F, et al. The leptin to adiponectin ratio is a marker of the number of metabolic syndrome criteria in French adults. J Metab Syndrome 2012;1:101. https://doi.org/10.4172/2167-0943.1000101.
[34] Patel SB, Reams GP, Spear RM, Freeman RH, Villarreal D. Leptin: linking obesity, the metabolic syndrome, and cardiovascular disease. Curr Hypertens Rep 2008;10:131–7.
[35] Wannamethee SG, Lowe GD, Rumley A, Cherry L, Whincup PH, Sattar N. Adipokines and risk of type 2 diabetes in older men. Diabetes Care 2007;30:1200–5.
[36] Al-Hamodi Z, AL-Habori M, Al-Meeri A. Saif-Ali R. Association of adipokines, leptin/adiponectin ratio and C-reactive protein with obesity and type 2 diabetes mellitus. Diabetol Metab Syndrome 2014;6:99. http://www.dmsjournal.com/content/6/1/99.
[37] Kotani K, Sakane N. Leptin:Adiponectin ratio and metabolic syndrome in the general Japanese population. Korean J Lab Med 2011;31:162–6. https://doi.org/10.3343/kjlm.2011.31.3.162.
[38] Tarnopolsky MA, Ruby BC. Sex differences in carbohydrate metabolism. Curr Opin Clin Nutr Metab Care 2001;4:521–6.
[39] Williams CM. Lipid metabolism in women. Proc Nutr Soc 2004;63:153–60.