Central Asian Journal of Medical Sciences
CAJMS

Original Article

Cent Asian J Med Sci. 2018 March;4(1):69-75. https://doi.org/10.24079/CAJMS.2018.03.009

The Adiponection/Leptin Ratio and Insulin Resistance among Mongolians with Metabolic Syndrome

Batnaran Dagdan[1,3], Ariunbold Chuluun-Erdene[1], Munkhzol Malchinkhuu[2], Munkhtsetseg Janlav[1]

[1]Department of Biochemistry and Laboratory Medicine, School of Pharmacy and Bio-Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia; [2]Department of Pathophysiology, School of Pharmacy and Bio-Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia; [3]Coronary Care Unit, Cardiovascular Center, The Shastin Central Hospital, Ulaanbaatar, Mongolia.

Submitted: December 13, 2017
Revised: March 6, 2018
Accepted: March 11, 2018

Corresponding Author
Munkhtsetseg Janlav, PhD, Ass.Prof
Department of Biochemistry and Laboratory Medicine, School of Pharmacy and Bio-Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar 14210, Mongolia
Tel: +976-99092287
E-mail: munkhtsetseg.j@mnums.edu.mn

Objectives: In this study, we aimed to determine the relationship between adiponectin/leptin (A/L) ratio and insulin resistance among Mongolian subjects with metabolic syndrome (MetS). **Methods:** The study was comprised of 364 adults. Fasting blood glucose, total cholesterol, triglyceride, and high density lipoprotein cholesterol were measured. Serum adiponectin and leptin were measured using enzyme-linked-immunoassay. Low density lipoprotein cholesterol and homeostatic model assessment-insulin resistance (HOMA-IR) were calculated. **Results:** Serum adiponectin was inversely correlated with diastolic blood pressure, body mass index, waist circumference, serum triglyceride, and fasting insulin level ($r=-0.118$, $r=-0.190$, $r=-0.244$, $r=-0.231$, and $r=-0.165$, respectively) ($p<0.001$). Serum leptin was significantly correlated with all risk factors of metabolic syndrome, except for lipid parameters ($p<0.001$). In the multiple regression analysis, HOMA-IR was significantly associated with adiponectin and A/L ratio among males with MetS, after adjustment for other factors. **Conclusion:** The A/L ratio was a significant predictor for insulin resistance among male adults with MetS.

Keywords: Metabolic Syndrome, Adiponectin, Insulin, Leptin, Insulin Resistance

Introduction

Metabolic syndrome (MetS), formerly known as Syndrome X, is characterized by the following metabolic abnormalities: resistance to insulin-stimulated glucose uptake, glucose intolerance, hyperinsulinemia, hypertriglyceridemia, hypo-high-density lipoprotein cholesterolemia, and hypertension [1]. Adipocytes-derived hormones, also known as adipokines, serve as mediators linking adipocytes-dysfunction to MetS. Two commonly studied adipokines, adiponectin and leptin,

have been shown to be critical in the development of MetS. Adiponectin, the most abundant adipokine found in circulation, has direct effects on insulin sensitivity, glucose metabolism, and central fat distribution [2]. The risk of MetS is higher among those with low adiponectin and severe insulin resistance [3, 4].

Leptin serves as a major 'adipostat' by repressing food intake and promoting energy expenditure. Independent of these effects, leptin improves peripheral (hepatic and skeletal muscle) insulin sensitivity and modulates pancreatic b-cell function. In a majority of obesity cases, leptin fails to induce weight loss, despite intact leptin receptors and high circulating leptin levels. This diminished response to the anorexigenic and insulin sensitizing effects of leptin is called leptin resistance [5, 6]. Leptin resistance is the main predictor of insulin resistance [7].

Although adiponectin and leptin seem to be independently associated with metabolic risk factors, the evaluation of an adiponectin/leptin (A/L) ratio has been proposed as a useful parameter to assess insulin resistance and beneficial as an atherosclerotic index among patients with type 2 diabetes. Several studies have demonstrated that the A/L ratio has shown to have a stronger association with MetS than leptin or adiponectin independently [8-10]. The purpose of our study was to find predictive factors using adipokine levels for the evaluation of insulin resistance among Mongolian subjects. In this study, we investigated the associations between A/L ratio, the homeostatic model assessment-insulin resistance (HOMA-IR), and other risk factors of MetSe among Mongolian subjects. We also analyzed if the A/L ratio has a more predictable role in the assessment of insulin resistance than HOMA-IR.

Materials and Methods

1. Study subjects

A total of 364 subjects (48.35% male, 51.64% female), aged 18-60 years old, were randomly selected from those who received a health check at The Shastin Central Hospital in Ulaanbaatar, Mongolia. The clinical criteria for MetS was defined according to the Joint Interim Statement of the International Diabetes Federation (IDF), American Heart Association (AHA), and National Heart, Lung, and Blood Institute (NHLBI) [11]. The criteria was the presence of any 3 of 5 risk factors: high blood pressure (systolic blood pressure (SBP) ≥130 mmHg and/or diastolic blood pressure (DBP) ≥85 mmHg, under treatment, or lready diagnosed with hypertension), high serum triglyceride (TG) (≥150 mg/dL or under treatment), decreased high density lipoprotein cholesterol (HDL-C) (<40 mg/dL for males and <50 mg/dL for females, or under treatment), hyperglycemia (fasting blood glucose (FBG) ≥100 mg/dL, under treatment, or previously diagnosed with diabetes mellitus), and waist circumference (WC) cutoffs for Asian populations (WC ≥90 cm for males and ≥80 cm for females). Individuals who were diagnosed diabetes mellitus or other uncontrolled endocrine disease, a cardiovascular condition (e.g. acute coronary syndrome, cerebrovascular event, symptomatic peripheral arterial disease), cancer, impaired renal and liver dysfunction, or were taking glucocorticoids or oral contraceptives were excluded.

2. Clinical and biochemical assessments

Questionnaires and anthropological measurements were used to obtain data. Height, weight, WC, hip circumference (HC) and SBP and DBP were measured in duplicate, and results were averaged. Weight and height were measured in kg and cm, respectively, to two decimal places. Body mass index (BMI) was calculated as weight (kg) divided by squared height (m^2). Blood samples were taken after overnight fasting; serum was separated and analyzed at a later time. FBG, total cholesterol (TC), TG, and HDL-C were measured. The hexokinase method was used to measure FBG, and an enzymatic colorimetric test was used to measure TC, TG, and HDL-C. Serum adiponectin level was measured using an enzyme-linked immunosorbent assay (Human Total Adiponectin ELISA Kit (Cat AM056711-RUO)), and leptin was measured using enzyme-linked immunoassay (Leptin Sandwich ELISA (EIA-2395); DRG Instruments GmbH, Germany). Low density lipoprotein cholesterol (LDL-C) and HOMA-IR [fasting insulin (mIU/mL) × FBG (mg/dL)]/405) were calculated using standard methods [12, 13].

3. Ethical review

All participants gave their informed consent. The study was approved by The Institutional Review Board of Ministry of Health of Mongolia and Ethics Committee of Mongolian National University of Medical Sciences.

4. Statistical analysis

Statistical analyses were conducted using the SPSS Version 21.0 (IBM Corp., USA). T-test was used to determine significant differences for normal distributions, resented as the mean ± SD. Mann-Whitney U Test was used for not normally distributed variables and represented as the median (interquartile range). The Pearson and Spearman correlation tests were utilized to identify correlations among all variables. The multiple linear regression model was performed to determine which model parameter (adiponectin, leptin, or A/L ratio) was the potential indicator for insulin resistance. Statistical significance was set at $p<0.05$.

Results

1. General characteristics of participants

The main characteristics are presented in Table 1, by gender and according to the presence or absence of MetS. Among both genders, the group with MetS had significantly higher SBP, DBP, BMI, WC, FBG, TG than the group without MetS ($p<0.001$ for all parameters). Among both genders, HDL-C was significantly lower among the group with MetS than the group without MetS ($p<0.001$).

2. Bivariate correlation analyses between HOMA-IR, adiponectin, leptin or A/L ratio, and various parameters.

Bivariate correlation analysis between HOMA-IR, adiponectin, leptin, A/L ratio, and other factors of MetS is shown in Table 2. Serum adiponectin showed significant positive correlations with age (r=0.125) and HDL-C (r=0.226) and inverse correlations with DBP (r=-0.118), BMI (r=-0.190), WC (r=-0.244), TG (r= 0.231), fasting insulin (r=-0.165) and HOMA-IR (r=-0.149). Serum leptin showed significant positive correlations with all

Table 1. Baseline characteristics by gender and according to the presence or absence of MetS

	Male			Female		
Clinical features	With MetS m± SD	Without MetS m± SD	p-value	With MetS m±SD	Without MetS m±SD	p-value
Age, years	40.41±11.35	36.57±11.05	0.01	46.61±9.38	36.62±9.14	<0.001
SBP, mm Hg	133.56±15.76	117.72±14.19	<0.001	129.49±14.71	108.22±12.49	<0.001
DBP, mm Hg	89.25±10.10	79.92±11.36	<0.001	90.39±9.10	73.44±9.53	<0.001
BMI, kg/m2	32.11±4.56	26.65±4.21	<0.001	30.52±4.16	25.17±4.36	<0.001
WC, cm	106.27±11.38	91.48±11.81	<0.001	97.05±10.51	82.56±11.24	<0.001
FBG, mg/dL	90.19±38.59	75.03±23.90	<0.001	92.26±64.18	69.63±18.93	<0.001
TC, mg/dL	174.25±40.83	156.40±40.61	.001	154.99±40.61	147.29±37.48	0.101
TG, mg/dL	163.00 (113.95-207.05)	80.14 (59.32-101.70)	<0.001	92.70 (64.64-138.40)	59.91 (48.90-78.12)	<0.001
HDL-C, mg/dL	33.93±12.59	43.61±12.68	<0.001	38.63±9.55	46.14±15.56	<0.001
LDL-C, mg/dL	100.35±40.95	97.89±36.02	0.628	93.95±35.09	88.52±36.78	0.228
Fasting insulin, µIU/ml	13.97 (9.12-20.49)	8.39 (3.82-13.39)	0.001	13.32 (7.35-20.27)	7.18 (3.27-12.6)	.005
HOMA-IR	3.10 (1.49-4.45)	1.49 (0.70-2.63)	0.001	2.36 (1.22-4.21)	1.33 (0.53-2.34)	.002
Adiponectin, mcg/ml	5.52 (3.86-8.35)	6.43 (3.05-10.64)	0.046	7.46 (5.38-9.93)	10.09 (5.77-13.91)	0.004
Leptin, ng/ml	7.20 (4.87-11.34)	2.36 (1.71-4.72)	<0.001	17.80 (10.57-28.43)	10.12 (5.31-15.80)	<0.001
A/L ratio	0.73 (0.39-1.37)	1.47 (0.39-8.04)	0.008	0.41 (0.22-0.69)	1.29 (0.40-3.08)	<0.001

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; WC, waist circumference; FBG, fasting blood glucose; TC, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; HOMA-IR, homeostatic assessment model of insulin resistance; A/L, adiponectin/leptin.

Table 2. Correlations between metabolic factors, HOMA-IR, and adipokines

	Age (years)	SBP (mm Hg)	DBP (mm Hg)	BMI (kg/m2)	WC (cm)	FBG (mg/dl)	TC (mg/dl)	TG (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dL)	Fasting insulin (µIU/ml)	HOMA-IR	Adiponectin (mcg/ml)	Leptin (mcg/ml)	A/L ratio
Age (years)	1														
SBP (mm Hg)	0.366*	1													
DBP (mm Hg)	0.298*	0.852*	1												
BMI (kg/m2)	0.361*	0.496*	0.462*	1											
WC (cm)	0.388*	0.559*	0.528*	0.858*	1										
FBG (mg/dl)	0.350*	0.276*	0.176*	0.308*	0.269*	1									
TC (mg/dl)	0.211*	0.219*	0.105*	0.125*	0.193*	0.161	1								
TG (mg/dl)	0.157*	0.363*	0.309*	0.437*	0.486*	0.149*	0.414	1							
HDL-C (mg/dl)	0.007	-0.094*	-0.063	-0.197	-0.191	0.024	0.140*	-0.193	1						
LDL-C (mg/dL)	0.185*	0.160*	0.048	0.092*	0.154*	0.090*	0.893*	0.230*	-0.124	1					
Fasting insulin (µIU/ml)	0.109*	0.208*	0.163*	0.436*	0.415*	0.273*	0.027	0.224*	-0.170	-0.015	1				
HOMA-IR	0.166*	0.239*	0.166*	0.452*	0.432*	0.471*	0.054	0.246*	-0.154*	-0.007	0.966*	1			
Adiponectin (mcg/ml)	0.125*	-0.094	-0.118*	-0.190*	-0.244*	0.054	0.056	-0.231*	0.226*	0.044	-0.165*	-0.149*	1		
Leptin (mcg/ml)	0.289*	0.149*	0.223*	0.521*	0.328*	0.158*	-0.061	0.094	0.087	-0.116	0.414*	0.412*	0.176*	1	
A/L ratio	-0.108	-0.183*	-0.318*	-0.477*	-0.387*	-0.020	-0.031	-0.183*	-0.087	0.047	-0.449*	-0.385*	0.559*	-0.625*	1

* p<0.001

factors of MetS, except lipid parameters: age (r=0.289), SBP (r=0.149), DBP (r=0.223), BMI (r=0.521), WC (r=0.328), FBG (r=0.158), fasting insulin (r=0.414), HOMA-IR (r=0.412), and adiponectin (r=0.176). The correlation of leptin with BMI was stronger than other risk factor (r=0.521; p<0.001). Furthermore, HOMA-IR was inversely correlated with A/L ratio (r=-0.385, p<0.001).

3. Multiple regression analyses with HOMA-IR

Multiple linear regression analyses with HOMA-IR as the dependent variable is presented in Table 3. Among males with MetS, adiponectin and A/L ratio were significant determinants for HOMA-IR (R^2=0.423, F=3.38), after adjusting for other confounding variables including BMI, WC, SBP, and leptin. Among females without MetS, age and TC were associated with HOMA-IR (R2=0.397, F=2.18).

Discussion

Our previous study revealed that leptin levels were a promising marker for MetS among Mongolian subjects [14]. This was significant because the nutritional habits of Mongolians differ from some other Asian ethnic groups, including Japanese and Koreans who intake high amounts of dietary carbohydrate [15-17]. In this study, we analysed the associations of A/L ratio and HOMA-IR among Mongolian subjects with MetS. Due to gender differences of adipokines secretion, we analysed the A/L ratio by gender among those with and without MetS [18]. Our study found that the A/L ratio was significantly lower among those with MetS in both genders, compared to those without MetS.

Studies performed in Asian populations have reported conflicting findings [9, 20]. In a study performed among Chinese

Table 3. Multiple linear regression analysis of HOMA-IR level by gender and according to the presence of absence of MetS

Independent variables	MetS						Without MetS					
	Male			Female			Male			Female		
	B coef	p-value	Partial correlation	B coef	p-value	Partial correlation	B coef	p-value	Partial correlation	B coef	p-value	Partial correlation
Age (years)	-0.189	0.085	-0.191	-0.128	0.515	-0.119	0.096	0.630	0.089	0.370	0.027	0.245
TC (mg/dl)	-0.146	0.942	-0.133	-0.126	0.475	-0.146	-0.028	0.894	-0.024	-0.426	0.025	-0.185
TG (mg/dl)	-0.004	0.978	-0.005	-0.138	0.470	-0.132	0.173	0.390	0.157	0.125	0.489	0.123
HDL-C (mg/dl)	-0.116	0.455	-0.124	-0.178	0.322	-0.181	-0.125	0.508	-0.121	0.122	0.458	0.123
LDL-C (mg/dl)	-0.141	0.393	-0.141	-0.201	0.256	-0.207	-0.135	0.254	-0.154	-0.145	0.354	-0.136
Adiponectin (mcg/ml)	0.444	0.021	0.128	0.354	0.112	-0.141	0.036	0.857	0.033	-0.063	0.703	-0.068
A/L ratio	-0.510	0.006	-0.179	-0.097	0.634	-0.087	-0.079	0.684	-0.075	-0.042	0797	-0.046
	R^2=0.423, F=3.38			R^2=0.420, F=2.27			R^2=0.479, F=3.97			R^2=0.397, F=2.18		

Dependent variable: HOMA-IR, R^2: R square, F: F test

subjects, the A/L ratio showed a higher odds ratio and a higher area under the curve among patients with MetS, compared to adiponectin or leptin alone, suggesting the possibility that the A/L ratio is a better diagnostic marker for MetS than individual adipokine levels [9]. However, in a study performed among 60 Korean adults with type 2 diabetes, subjects with MetS showed a lower A/L ratio than those without MetS, similar to our findings. Although adiponectin and leptin seem to be independently associated with metabolic risk factors, the evaluation of the A/L ratio has been proposed as a useful parameter to assess insulin resistance and beneficial as an atherosclerotic index among patients with type 2 diabetes [18, 20, 21, 23]. The A/L ratio has shown to have a stronger association with the MetS than adiponectin or leptin independently [8-10]. Similar to a previous study, our study showed that A/L ratio was negatively correlated with BMI, fasting insulin, and HOMA-IR [24].

The results of our study showed that the A/L ratio was statistically significant for insulin resistance among male adults. This suggests that the A/L ratio might be a more effective indicator of insulin resistance than leptin or adiponectin alone. In some studies, the ratio of adipokines was considered a strong predictor among males, which matches the findings of our study [2, 25, 26]. Our study has several limitations, including a non-probabilistic sampling method due to the small number of participants from one city and thus, a limited predictive power. If our study was performed among a larger number of participants, the result may have revealed more insight on role of A/L ratio in predicting insulin resistance. Despite these limitations, we conclude that although the A/L ratio was not associated with insulin resistance among women in our study, A/L ratio was a better determinant than adipokines or leptin alone for insulin resistance (HOMA-IR) among men with MetS.

Conflict of Interest

The authors declare that they have no competing interests.

Acknowledgements

This study was funded by the Health Project of the Millennium Challenge Account Mongolia (2012-2013) through a grant entitled "Metabolic Syndrome: Key to Diabetes and Cardiovascular Disease" (#75-105).

Reference

1. Shiwaku K, Nogi A, Kitajima K, Anuurad E, Enkhmaa B, Yamasaki M, et al. Prevalence of the metabolic syndrome

using the modified ATP III definitions for workers in Japan, Korea and Mongolia. J Occup Health 2005; 47: 126-35.
2. Mirza S, Qu HQ, Li Q, Martinez PJ, Rentfro AR, McCormick JB, et al. Adiponectin/leptin ratio and metabolic syndrome in a Mexican American population. Clin Invest Med 2011; 34: E290.
3. Yun JE, Sull JW, Lee HY, Park E, Kim S, Jo J, et al. Serum adiponectin as a useful marker for metabolic syndrome in type 2 diabetic patients. Diabetes Metab Res Rev 2009; 25: 259-65.
4. 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.
5. Rabe K, Lehrke M, Parhofer KG, Broedl UC. Adipokines and insulin resistance. Mol Med 2008; 14: 741-51.
6. Park HK, Ahima RS, Leptin signaling. F1000Prime Rep 2014; 6: 73.
7. Martins Mdo C, Faleiro LL, Fonseca A. Relationship between leptin and body mass and metabolic syndrome in an adult population. Rev Port Cardiol 2012; 31: 711-9.
8. López-Jaramillo P, Gómez-Arbeláez D, López-López J, López-López C, Martínez-Ortega J, Gómez-Rodríguez A, et al. The role of leptin/adiponectin ratio in metabolic syndrome and diabetes. Horm Mol Biol Clin Investig 2014; 18: 37-45.
9. 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.
10. Agostinis-Sobrinho CA, Lacerda Mendes E, Moreira C, Abreu S, Lopes L, Oliveira-Santos J, et al. Association between Leptin, Adiponectin, and Leptin/Adiponectin Ratio with Clustered Metabolic Risk Factors in Portuguese Adolescents: The LabMed Physical Activity Study. Ann Nutr Metab 2017; 70: 321-8.
11. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009; 120: 1640-5.
12. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. J Clin Chem 1972; 18: 499-502.
13. Turner RC, Holman RR, Matthews D, Hockaday TD, Peto J. Insulin deficiency and insulin resistance interaction in diabetes: estimation of their relative contribution by feedback analysis from basal plasma insulin and glucose concentrations. Metabolism 1979; 28: 1086-96.
14. Dagdan B, Chuluun-Erdene A, Sengeragchaa O, Sanjmyatav P, Janlav M. Higher Leptin Level among Mongolians with Metabolic Syndrome as a Predictor of Cardiovascular Risk. Cent Asian J Med Sci 2017; 3: 41-6.
15. Anuurad E, Shiwaku K, Enkhmaa B, Nogi A, Kitajima K, Yamasaki M, et al. Ethnic differences in the formation of small LDL particles in Asians: a comparison of Koreans, Japanese and Mongolians. Eur J Clin Invest 2004; 34: 738-46.
16. Kim S, Moon S, Popkin BM. The nutrition transition in South Korea. Am J Clin Nutr 2000; 71: 44-53.
17. Nakamura M, Tajima S, Yoshiike N. Nutrient intake in Japanese adults - from The National Nutrition Survey, 1995-99. J Nutr Sci Vitaminol (Tokyo) 2002; 48: 433-41.
18. Abdella NA, Mojiminiyi OA, Moussa MA, Zaki M, Al Mohammedi H, Al Ozairi ES, et al. Plasma Leptin concentration in patients with Type 2 diabetes. Diabet Med 2005; 22: 278-85.
19. Ko SH. The adiponectin/leptin ratio and metabolic syndrome in healthy Korean adult males. Korean Diabetes J 2010; 34: 220-1.
20. Lee JM, Kim SR, Yoo SJ, Hong OK, Son HS, Chang SA. The relationship between adipokines, metabolic parameters and insulin resistance in patients with metabolic syndrome and type 2 diabetes. J Int Med Res 2009; 37:1803-12.
21. Ryo M, Nakamura T, Kihara S, Kumada M, Shibazaki S, Takahashi M, et al. Adiponectin as a biomarker of the metabolic syndrome. Circ J 2004; 68: 975-81.
22. Oda N, Imamura S, Fujita T, Uchida Y, Inagaki K, Kakizawa H, et al. The ratio of leptin to adiponectin can be used as an index of insulin resistance. Metabolism 2008; 57: 268-

73.

23. Thorand B, Zierer A, Baumert J, Meisinger C, Herder C, Koeniq. Associations between leptin and the leptin/adiponectin ratio and incident Type 2 diabetes in middle-aged men adn women: results from the MONICA/KORA Augsburg study 1984-2002. Diabet Med 2010; 27: 1004-11.
24. Gannage-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. Euro J Endocrinol 2006; 155: 167-76.
25. Vega GL, Grundy SM. Metabolic risk susceptibility in men is partially related to adiponectin/leptin ratio. J Obes 2013: 409679.
26. Zaletel J, Barlovic DP, Prezelj J, Adiponectin-leptin ratio: a useful estimate of insulin resistance in patients with Type 2 diabetes. J Endocrinol Invest, 2010; 33: 514-8.