Correlation of the Leptin-to-Adiponectin Ratio (LAR) with Insulin Resistance in Lean and Obese Saudi Females with Type 2 Diabetes

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Abstract: Objectives: The role of various adipokines as a link between obesity and diabetes mellitus has recently been better elucidated. The aim of this study was to investigate the correlation of the leptin/adiponectin ratio (LAR) with insulin resistance in obese and diabetic Saudi females. **Methods:** This study included 373 Saudi females divided into two groups: type 2 diabetic (n=196) and normal control (n=177).The groups were further divided according to BMI into normal obese (n=85), normal non-obese (n=92), diabetic obese (n=118) and diabetic non-obese (n=78) subgroups. For all studied groups, levels of leptin, adiponectin, insulin and C-reactive protein were measured using (ELISAs).The glucose, triglyceride, cholesterol, LDL and HDL levels were determined using colorimetric assays, and the homeostasis model assessment ratio (HOMA-IR) was determined using a formula derived from fasting insulin and glucose levels. **Results:** The leptin levels were significantly higher and the adiponectin levels were significantly lower in the diabetic group compared to the normal control group *(P* value < 0.05). The LAR showed a significant positive correlation with the HOMA-IR (r=0.129, *P*=0.01) and a highly significant positive correlation with BMI, glucose, cholesterol, LDL and insulin (r=0.220, *P*=0.00; r=0.135, *P*=0.009; r=0.201, *P*=0.000; r=0.215, *P*=0.000; and r= 0.212, *P*=0.000, respectively). There was a statistically significant difference among all subgroups for the LAR (F=20.60, *P*=0.00) and for the HOMA-IR (F=17.73, *P*= 0.001). Conclusion: The LAR has the potential to become a new laboratory marker for insulin resistance in patients with obesity and type 2 diabetes mellitus.
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Key words: the Leptin-to-Adiponectin Ratio (LAR), Insulin Resistance, Obesity, Diabetes, Lean, Homeostatic Model Assessment of insulin resistance (HOMA-IR)

Abbreviations: The Leptin-to-Adiponectin Ratio(LAR), type 2 diabetes mellitus (T2DM), the homeostasis model assessment ratio (HOMA-IR), triglycerides (TG), C-reactive protein (CRP),High density lipoproteins (HDL) ,Low Density Lipoproteins (LDL)

1. Introduction

White adipose tissue is storage and release site for fatty acids and a major secretory organ for many proteins known as 'adipokines'. The types of adipokines include proinflammatory cytokines, chemokines, acute-phase proteins, adiponectin and leptin [1].Obesity is closely related to insulin resistance, glucose intolerance and type 2 diabetes. The mechanisms linking insulin resistance and obesity are not yet fully understood, but adipose tissue may play a role in this association because it is an active metabolic organ that releases different adipocytokines. Leptin and adiponectin, two of the most abundant adipocyte products, are thought to link obesity, insulin resistance, and related disorders [2]. Unlike other adipocytokines such as leptin, interleukin 6, and resistin, adiponectin levels decrease with increased adipose tissue [3]. Circulating adiponectin levels lower than the control level have been observed in human subjects with any of obesity, type 2 diabetes mellitus, and cardiovascular disease [4]. Leptin, identified from the ob/ob mouse (the animal model that is genetically susceptible to obesity), regulates body weight, modulating appetite and energy expenditure by acting on the hypothalamus and inhibiting the release of neuropeptide Y in mice and humans [5]. The effects of adiponectin and leptin on energy metabolism differ; leptin improves insulin sensitivity through activation of adenosine monophosphate–activated protein kinase (AMPK), which controls the cellular concentrations of malonyl-CoA, thereby inhibiting acetyl-CoA carboxylase [6]. As a result, both intracellular malonyl-CoA and the lipogenesis associated with increased fatty acid beta-oxidation decrease. Adiponectin enhances insulin sensitivity through activation of AMPK [7] and also affects hepatic glucose production by decreasing the mRNA expression of two essential gluconeogenesis

enzymes: phosphoenolpyruvate carboxykinase and glucose-6-phosphatase [8].

Insulin resistance is particularly prevalent in obese humans, and an independent association between insulin resistance and elevated plasma leptin levels has been reported [9].Another study showed a negative correlation of serum adiponectin levels and body mass index BMI and a positive correlation between serum leptin levels and BMI [10]. Evaluation of the leptin/adiponectin ratio (LAR) has been suggested as a useful parameter for assessing insulin resistance in patients with and without diabetes [11-13]. Inoue *et al.* [11, 12] reported that the LAR was a more effective measure of insulin resistance than either adiponectin or leptin alone, and it was a more sensitive and reliable marker of insulin resistance than the homeostasis model assessment of insulin resistance (HOMA-IR) in subjects without hyperglycemia, as well as in type 2 diabetics. Our aims were to evaluate the utility and potential benefits of determining the correlation between the LAR and the HOMA-IR as a measure of insulin resistance in obese and lean diabetic females and to assess the correlation between the LAR and other measures, such as glucose, triglycerides (TG), cholesterol, LDL, HDL, insulin and C-reactive protein (CRP).

2. Subjects and Methods:

2.1. Study population

This study was cleared by the Faculty of Medicine Ethics Review Board for Human Studies at Umm Al-Qura University and has complied with the principles laid down in the Declaration of Helsinki, adopted by the 18th World Medical Assembly, Helsinki, Finland, June 1964, and recently amended at the 59th World Medical Assembly, Seoul, Korea, October 2008. All subjects provided signed informed consent for participation in the study as required.

The subjects (n=373) were adult Saudi females aged 30-60 years. They were divided into two groups. The type 2 diabetic group (n=196) attended diabetic clinics at Al-Noor Specialized Hospital, Al-Zaher Hospital or Al-Khansah Hospital in the Makkha region, KSA from September 2009 to September 2011. This group was further divided into two subgroups according to BMI: diabetic obese (Dob) (n=118) and diabetic non-obese (Dn) (n=78).The subjects were considered non-obese if their BMI was 18-25 and obese if their BMI was above 30. The control group (n=177) was composed of females who were clinically free; they were subdivided into two groups according to BMI: normal obese (Nob) (n= 85) and normal non-obese (Nn) (n=92). The exclusion criteria for all groups were pregnancy, hypertension, endocrinal disorders, hormonal therapy and lipid-lowering medications.

2.2. Measurement of anthropometric and metabolic characteristics

For all subjects, comprehensive questionnaires were used to collect medical information. Complete history was obtained, physical and clinical examinations were performed. Measurements of height and weight were performed to the nearest 0.1 kg and 0.5 cm, respectively. BMI was calculated as weight (kg) divided by height (m) squared. Blood samples were collected from subjects after overnight (12 hours) fasting using BD vacutainer serum tubes. The samples were transported in portable insulated bags containing ice packs (at 0-4°C) and processed by centrifugation within (2 hours) of collection. The serum was stored at (-70° C) until its use in subsequent assays.

The concentration of leptin (ng/mL) was determined using ELISA kits provided by Millipore (Missouri, USA).The concentrations of adiponectin (µg/ml) and insulin (µU/mL) were determined using sandwich ELISAs with kits provided from ALPCO Diagnostics (North Carolina, USA). The concentration of CRP was also measured using ELISA kits from Chemi-Con (Temecula, USA). All procedures in the manufacturer's instructions were followed, and quality control measurements were within the ranges recommended by the manufacturer. The minimum detectable concentration for the leptin kit was 0.25 ng/mL, and its intra-assay and inter-assay coefficients of variation (CVs) ranged from 3.0% to 6.2%. The minimum detectable concentration for the adiponectin kit was 0.15 ng/mL, and its intra-assay and inter-assay coefficient of variation (CVs) ranged from 2.9% to 6.6%.The adiponectin values in this study represented the total measurements of trimer, hexamer and high molecular weight (HMW) forms of adiponectin in blood plasma. Fasting blood glucose was determined using a glucose oxidase assay and the serum concentrations of LDL cholesterol, HDL cholesterol and triglycerides (TG) were determined using colorimetric enzyme kits from Spinreact (Bas Gerona, Spain). The insulin resistance indices were calculated using the formula described by Matthews *et al.* [14]: insulin resistance (HOMA-IR) = fasting glucose (mg/dl) x fasting insulin (µU/mL) / 405.

2.3. Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 17.0 for Windows (SPSS Inc., Chicago, IL, USA). A value of $P<0.05$ was considered statistically significant for all analyses. The data are

presented as the mean and standard deviation. Spearman correlation coefficients (r) were used to describe the association between the variables. Student's t-test for independent samples and one-way analysis of variance (ANOVA) were used to compare the results of different subgroups.

3. Results

3.1. Characteristics of all groups

The studied subjects were all Saudi females. The mean age ± SD of each group was as follows: healthy non-obese (Nn) women, 40.86 ± 10.88 years; healthy obese women (Nob), 47.08 ± 13.99 years; diabetic non-obese (Dn) women45.64 ±12.79 years; and diabetic obese (Dob) women, 44.55 ± 10.07.

3.2. Correlation analysis of different parameters

Pearson baivariate correlation analyses for adiponectin, leptin and other parameters revealed that leptin had a highly significant positive correlation with BMI, cholesterol, TG, LDL,CRP and the LAR (r=0.560,*P*=0.00; r =0.420, *P*=0.00; r=0.240, *P*=0.00; r= 0.240, *P*=0.000; r=0.372, *P*=0.00; and r=0.402, *P*= 0.000,respectively) and a highly significant negative correlation with adiponectin (r=-0.268; *P*=0.000). Adiponectin had a highly significant negative correlation with BMI, glucose, cholesterol, TG, LDL, insulin, CRP, the LAR and the HOMA-IR (r=-0.328,*P* =0.000; r= -0.261, *P*=0.001; r= -0.208,*P* =0.003; r= -0.203, *P* =0.000; r=-0.343,*P*=0.000; r=-0.176, *P*=0.001; r=-0.343, *P* =0.003; r = -0.301, *P* =0.000; r = -0.166; *P* =0.001; and r = -0.268, *P*=0.000, respectively) (Table-1). The LAR had a significant positive correlation with the HOMA-IR, BMI, glucose, cholesterol, LDL and insulin (r= 0.129, *P*=0.01; r = 0.220,*P*=0.00; r= 0.135, *P*= 0.009; r= 0.201, *P*=0.000; r= 0.215, *P*= 0.000; and r=0.212, *P*=0.000, respectively), but the LAR also had a significant negative correlation with HDL (r= -0.144,*P* =0.005). The HOMA-IR had a highly significant positive correlation with BMI, glucose, LDL, insulin, and CRP (r= 0.158, *P*=0.002; r= 0.372, *P*=0.00; r=0.256, *P*=0.00; r= 0.931, *P*=0.000; and r= 0.186, *P*=0.00, respectively). The HOMA-IR also had a significant negative correlation with HDL and adiponectin (r=-0.152, *P* =0.003; and r= -0.166, *P*=0.001, respectively) (Table-2).

3.3. Significant differences for the LAR, the HOMA-IR and all other parameters in studied groups and subgroups

The independent samples t-test revealed a significant statistical difference (*P* value < 0.05) between the control group and the diabetic group for adiponectin, leptin, glucose, HDL, triglycerides, insulin, the LAR and the HOMA-IR, but cholesterol, LDL and C-reactive protein showed non-significance differences (Table 3).

The independent samples t-test was used to compare the normal obese (Nob) and normal non-obese (Nn) control subgroups. There was a significant difference for leptin, adiponectin, cholesterol, TG, insulin, CRP, the LAR and the HOMA-IR, but there was no significant difference for HDL, LDL and glucose (Table-4).Comparing the diabetic obese (Dob) and diabetic non-obese (Dn) subgroups revealed a significant difference for leptin, LDL, triglycerides, cholesterol and the LAR but no significance difference for adiponectin, HDL, glucose and the HOMA-IR (Table 5).

One–way ANOVA was used for comparison of the LAR and HOMA-IR between the normal obese and non-obese subgroups and between the diabetic obese and non-obese subgroups (Table 6).The analysis revealed that there was a statistically significant difference between the four groups, as determined by the one-way ANOVA for the LAR (F=20.60, *P*=0.000) and the HOMA-IR (F=17.73, *P*=0.001). Turkey's post-hoc test revealed that there was a statistically significant difference for the LAR among the normal control non-obese (2.74±1.22), the normal obese (6.37± 3.50,*P*=0.01),the diabetic non-obese (10.94±3.55, *P*= 0.041) and the diabetic obese subgroups (14.52±7.7, *P*=0.00).There was also a significant difference among the normal obese, the diabetic non-obese (*P*=0.041) and the diabetic obese subgroups (*P*=0.00).Additionally, there was a significant difference between the diabetic non-obese and the diabetic obese (*P* =0.00) subgroups. For the HOMA-IR, post-hoc tests revealed that there was a statistically significant difference between the normal control (1.9374± 0.93), the normal obese (4.29± 1.04, *P*=0.024), the diabetic non-obese (9.22 ± 2.76, *P*=0.00) and the diabetic obese (10.5 ± 5.76, *P* =0.00) subgroups. There was also a significant difference among the normal obese, the diabetic non-obese (*P*=0.006) and the diabetic obese subgroups (*P*=0.00), but there was no statistically significant difference between the diabetic non-obese and the diabetic obese subgroups (*P*=0.146).

Table 1: Pearson Correlation of leptin, adiponectin, with various parameters

	Leptin		Adiponectin	
Parameters	r	P value	r	P value
BMI	.560	**.000****	-.328	**.000****
Glucose	.113	**.030***	-.261	**.000****
Cholesterol	.420	**.000****	-.208	**.000****
TG	.240	**.000****	-.203	**.000****
LDL	.240	**.000****	-.343	**.000****
HDL	-.056	.279	.120	**.021***
Insulin	.094	.070	-.176	**.001****
CRP	.372	**.000****	-.343	**.000****
LAR	.402	**.000****	-.301	**.000****
HMOA-IR	.060	.249	-.166	**.001****
Leptin	-	-	-.268	**.000****
Adiponectin	-.268-	**.000****	-	-

* *P* value significant at ≤ 0.05.

Table 2: Pearson Correlation of LAR, HMOA-IR, with various parameters

Parameters	**LAR**		**HMOA-IR**	
	r	P value	r	P value
BMI	.220	**.000****	.158	**.002****
Glucose	.135	**.009****	.372	**.000****
Cholesterol	.201	**.000****	.061	.242
TG	.058	.267	.069	.181
LDL	.215	**.000****	.256	**.000****
HDL	-.144	**.005****	-.152	**.003****
Insulin	.212	**.000****	.931	**.000****
CRP	.069	.185	.186	**.000****
LAR	-	-	.129	**.012***
HMOA-IR	.129	**.012***	-	-
Leptin	.402	**.000****	.060	.249
Adiponectin	-.301-	**.000****	-.166	**.001****

* *P* value significant at ≤ 0.05

Table 3: Correlation of leptin, adiponectin, lipid profile, Insulin , C reactive protein, LAR and HOMA-IR in normal control and diabetic groups.

Parameters	Normal Control N (n=177)	Diabetic D (n=196)	*P*. value
BMI	27.81±11.32	34.9 ±7.37	0.000*
Adiponectin (µg/ml)	7.71± 2.90	4.75 ±1.15	0.000*
Leptin (ng/ml)	22.66± 10.40	33.96 ±14.32	0. 032*
Glucose (Mg/dl)	94.62 ±19.36	149.41±21.50	0.000*
Cholesterol (Mg/dl)	132.45 ±46.73	160.41 ±56.33	**0.335**
Triglyceride(Mg/dl)	130 ±33.27	174 ±45.75	0.000*
LDL(Mg/dl)	99.45 ±19	143± 22.41	**0.161**
HDL(Mg/dl)	46.46 ± 8.23	40.21± 5.48	0.039*
Insulin (µU/mL)	12.86 ±2.33	30.31± 8.25	0.000*
CRP (µg/ml)	7.073± 3.90	11.35± 2.41	0.048 *
LAR	3 .43 ± 1.70	9 .96 ± 4.32	0.000*
HOMA-IR	3.06 ± 1.04	11.2 ± 4.33	0.000*

* *P* value significant at ≤ 0.05

Table 4: Correlation of leptin, adiponectin, lipid profile, Insulin, C reactive protein, LAR and HOMA-IR in normal obese and non obese control subgroups

Parameters	Control non-obese Nn (n=92)	Control obese Nob (n=85)	*P*. value
BMI	20.40 ± 2.71	35.37 ± 5.8	**0.000***
Leptin (µ/l)	18.80± 9.17	25.25 ± 10.77	**0.000***
Adiponectin (µl/l)	7.27 ± 4.29	4.85 ± 2.71	**0.000***
LDL (µl/l)	95.74 ± 14.2	103.15 ± 22.5	0.064
HDL (µl/l)	46.90 ± 6.43	46.02 ± 9.76	0.535
Triglyceride(mg/dl)	117 ± 38.9	143.15 ± 19.33	**0.001***
Cholesterol (mg/dl)	101.92 ± 16.77	162.99 ± 47.20	**0.000***
Glucose (mg/dl)	88.35 ± 15.8	100.9 ± 20.7	0.108
Insulin (µU/mL)	8.88 ±3.53	17.18 ±6. 23	**0.000***
CRP (µg/ml)	4.88 ± 2.94	7.44 ± 3.57	**0.048***
LAR	2.74± 1.22	6.37± 3.50	**0.000***
HOMA-IR	1.93 ± 0.93	4.29± 1.04	**0.000***

**P* value significant at ≤ 0.05

Table 5: Correlation of leptin, adiponectin, lipid profile, Insulin, C reactive protein, LAR and HOMA-IR in Diabetic obese and non obese subgroups

Parameters	Diabetic non-obese Dn (n=78)	Diabetic obese Dob (n=118)	*P*. value
BMI	25.66 ± 2.70	35.85 ± 4.74	**0.000***
Leptin (µ/l)	22.20 ± 12.22	34.03± 14.4	**0.001***
Adiponectin (µl/l)	2.98 ± 1.55	2.56 ± 1.57	0.692
LDL (µl/l)	133.38 ± 22.9	150 ± 19.4	**0.000***
HDL (µl/l)	40.60 ± 5.81	39.93 ± 5.27	0.634
Triglyceride(mg/dl)	131.72 ± 36.95	183 ± 49.59	**0.007***
Cholesterol (mg/dl)	152.42 ± 21.70	180.67 ± 64.63	**0.000***
Glucose (mg/dl)	153.28 ± 51.32	146.6 ± 51.9	0.396
Insulin (µU/mL)	24.48 ± 9.38	34.16 ± 14.23	**0.001***
CRP (µg/ml)	5.73 ± 3.10	11.76 ±3.40	**0.030***
LAR	10 .94 ± 3.55	14 .52 ± 7.7	**0.000***
HOMA-IR	9.22 ± 2.76	10.5 ± 5.76	0.071

* *P* value significant at ≤ 0.05

Table 6: One-way ANOVA for comparison of LAR, HMOA-IR in all subgroups.

Variables	**Subgroups**	**Subgroups**	***P* Value**
LAR	**NN**	**Nob**	**0.001***
		Dnob	**0.041***
		Dob	**0.000***
	Nob	**Dnob**	**0.035***
		Dob	**0.000***
	Dnob	**Dob**	**0.000***
HMOA-IR	**NN**	**Nob**	**0.024***
		Dnob	**0.000***
		Dob	**0.000***
	Nob	**Dnob**	**0.006***
		Dob	**0.000***
	Dnob	**Dob**	0.146

Light shaded rows indicate comparisons of variables in Normal obese in relation to other subgroups; dark shaded rows indicate comparisons of variables in Diabetic non obese in relation to other subgroups. Non shaded areas indicate comparison of normal non-obese in relation to other subgroups

* *P* value significant at ≤ 0.05

4. Discussion

Obesity is a major risk factor for insulin resistance and type 2 diabetes. The recent focus on adipose tissue as an endocrine organ that secretes signaling proteins, collectively termed adipokines, has prompted current interest in the association of adipokines with insulin resistance and type-2 diabetes. Our results revealed that leptin was significantly high and adiponectin was significantly low in the diabetic group compared to the normal group and in the normal obese subgroup compared to the normal non-obese subgroup. However, leptin and adiponectin did not reach a statistically significant level in the diabetic obese subgroup when compared to the diabetic non-obese subgroup .These finding were in agreement with those of other researchers, who found high leptin and low adiponectin levels in obese and type 2 diabetic patients [15,4]. Adiponectin decreases as body mass index BMI increases, and it is negatively correlated with insulin resistance [16, 17, 4]. Similarly, Considine *et al.* reported that, in obese people, the expression of leptin in adipose cells and the concentration of leptin in blood were significantly high; therefore, leptin can be used as a sensitive chemical marker for the diagnosis of obesity and obesity-related diseases [18]. In contrast to leptin, adiponectin was under-expressed in obese patients with insulin resistance, type2 diabetes and coronary heart disease [19].

Our results showed a highly significant negative correlation for leptin and adiponectin in all studied groups. Meanwhile, leptin was positively correlated with BMI, and adiponectin was negatively correlated with BMI. Leptin was positively correlated with glucose, TG, cholesterol and LDL, but adiponectin was negatively correlated with glucose, TG, cholesterol and LDL and was positively correlated with HDL. Previous studies in Japanese individuals have shown that the adiponectin concentration was negatively correlated with body mass index BMI; accordingly, it was lower in obese subjects than in lean subjects [20, 16]. Inoue *et al.* [17] reported that adiponectin and leptin levels tend to correlated with BMI, TG and HDL in an opposite manner.

Leptin and adiponectin are each known to be involved in the pathogenesis of obesity [21]. In obesity-related conditions such as metabolic syndrome and type 2 diabetes mellitus, leptin levels are higher and adiponectin levels are lower; thus, the LAR could be relatively high [22]. Insulin resistance plays an important role in the pathogenesis of obesity, metabolic syndrome and type 2 diabetes mellitus. Therefore, quantitative measurements of insulin resistance are clinically meaningful and may help researchers to better understand the etiology of these conditions. The most established quantitative measurements of insulin resistance are the hyperinsulinemic-euglycemic clamp, the minimal model assessment and the homeostatic model assessment (HOMA) methods [23]. Thus we evaluated the correlation of the LAR with measures of insulin resistance to determine calculated value of HOMA-IR using the formula derived from fasting insulin and glucose levels described by Matthews *et al.*[14]. Our results for the LAR in all groups showed a highly significant positive correlation with the HOMA-IR and with BMI. These finding were in agreement with other studies that have shown that the LAR is as strongly associated with the hyperinsulinemic-euglycemic clamp, the gold-standard measure of insulin resistance, as it is with other currently used parameters, such as fasting insulin or the HOMA-IR levels in the Ely and European Group for the Study of Insulin Resistance (EGIR) [24]. Moreover, some studies have reported that the LAR was a more effective indicator of insulin resistance than adiponectin, leptin, or the HOMA-IR in non-diabetic healthy Korean males [25] and type 2 diabetes patients [26,11,13]. The LAR was reported to be a more sensitive and reliable marker of insulin resistance than the HOMA-IR in patients with elevated FPG levels and type 2 diabetes mellitus [12]. Recently, Kotani and Sakane [27] reported that the LAR could serve as a clinically useful marker for detecting metabolic syndrome in the general Japanese population. Our results showed that the LAR had a highly significant positive correlation with glucose, cholesterol, LDL and insulin and a highly significant negative correlation with HDL. These findings were in agreement with those of Yoon *et al.* [28], who reported that the LAR had more predictive power than the HOMA-IR for the lipid components of metabolic syndrome such as TG and HDL cholesterol because the LAR is based on the presence of leptin and adiponectin. Both of these adipokines are closely linked to fat metabolism and indicate an enhancement of the oxidation of fatty acids in peripheral tissues by AMPK [6, 7], resulting in an improvement of insulin resistance and obesity. Therefore, lipid metabolism linked to the LAR could provide a different explanation than insulin resistance for the pathophysiology of metabolic syndrome [28].

ANOVA tests of the LAR showed a highly significant difference among all subgroups, while the HOMA-IR exhibited no significant difference between the obese and non-obese type 2 diabetics. This result may indicate that the LAR was better than the HOMA-IR at discriminating diabetic from non-diabetic females. Interestingly, Oda *et al.* [26] reported that the LAR may be an excellent clinical predictor for insulin resistance in diabetic patients, and they stated that, if diabetic patients are evaluated

for insulin resistance using the HOMA-IR, it is essential that their fasting plasma glucose is greater than 140 mg/dL to avoid erroneous results [29]. Our study demonstrated that the LAR was more closely correlated with insulin resistance than with leptin, adiponectin alone or the HOMA-IR. Indeed, several investigators reported that the HOMA-IR and insulin levels do not correlate significantly, particularly in individuals with impaired glucose tolerance [30] and in elderly patients with poorly controlled type 2 diabetes mellitus [31]. Ono *et al.* [32] reported that the HOMA-IR is a useful index for determining insulin resistance in obese patients with type 2 diabetes mellitus at FPG range of 80-170 mg/dL.

Our results showed that the LAR was associated with the calculated value of insulin resistance, the HOMA-IR. The LAR was more closely correlated with insulin resistance than with leptin, adiponectin alone or the HOMA-IR in all studied groups; therefore, we concluded that the LAR has the potential to become a new laboratory marker for insulin resistance in patients with obesity and Type 2 diabetes mellitus.

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