Original Article

Homestasis Model Assessment–Adiponectin ratio and Adiponectin –Resistin index as markers of insulin resistance in type 2diabetes mellitus

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Summary:

Background: Insulin resistance (IR) is an important clinical and biochemical determinant of diabetes and many other clinical states. The gold standard method for IR estimation is the hyperinsulinemic euglycaemic glucose clamp. Adiponectin and resistin are adipocytes derived hormones that play important role in the regulation of glucose, fat metabolism and insulin resistance.

Objective: this study aimed to assess the validity of Homestasis Model Assessment–Adiponectin ratio and Adiponectin –Resistin index as markers of insulin resistance in type 2 diabetic mellitus (T2DM) patients.

Design: Ninety (T2DM) overweight male subjects were enrolled in this cross sectional study, detailed history, physical examination and anthropometric measures including BMI, waist, and hip circumference were done to all the participants. Fasting serum samples were obtained and used for the measurement of serum glucose, serum triglyceride, high density lipoprotein(HDL),very low density lipoprotein(VLDL),HbA1c ,also serum insulin, adiponectin ,resistin were measured and HOMA-IR, HOMA-AD and AR-index were calculated. SPSS-17 was used to analyze the data.

Results: AR-index correlates significantly with FSG, Fasting Insulin and HOMA-IR (r =0.534.p=0.005), (r=0.545, p=0.005), (r=0.506, p=0.008) respectively HOMA-AD correlates with FSG (R=0.551, P=0.001), insulin (P=0.956,p=0.000),HOMA-IR(r =0.952, p=0.000). AUC for AR-index (0.800) and for HOMA-AD (0.905).

Conclusions: HOMA-AD and AR-index are reliable and valid measures for the assessment of insulin resistance in type 2 diabetic patients.

Keywords: HOMA- Adiponectin, Adiponectin –Resistin index , insulin resistance ,type 2diabetes mellitus.

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Introduction:

Insulin resistance (IR) is a hall mark of obesity, type 2 diabetes mellitus, hypertension , cardiovascular diseases and certain types of cancer. It is the underlying mechanism and contributing factor for the development of metabolic syndrome. IR is presented as hyperinsulinemia, impaired glucose tolerance, dyslipidemia and hypertension(1).

Adiponectin and resistin are adipocytes derived hormones that play an important role in the regulation of glucose and fat metabolism(2) .Adiponectin is a multifunctional protein that shows pleiotropic insulin-sensitizing, anti-inflammatory, antiatherogenic properities, it decreases hepatic glucose production and increases glucose uptake and fatty acid oxidation in skeletal muscle, deranged levels of adiponectin have been found to be related to insulin resistance (3).

Resistin belongs to a family of cysteine-rich secreted polypeptides produced by monocytes/macrophages. It is regarded as a novel adipokine that has been suggested to play a role in the development of insulin resistance and obesity. Resistin has been suggested to play an important role in the pathogenesis of vascular disorders such as atherosclerosis, hypertension, coronary artery disease and heart failure. IR is associated with hyperresistenimia and resistin seems to link obesity with IR (4) .

Estimating insulin resistance had been the area of interest for long time, and the gold standard method is the hyperinsulinemic euglycaemic glucose clamp, which requires infusions of insulin and glucose over approximately 2 hours with estimation of blood glucose every few minutes;this method is invasive, complicated, time-consuming and impractical (5),consequently, over the years, a number of surrogate indices for insulin resistance have been developed. Homeostatic model assessment-insulin resistance (HOMA-IR) is a surrogate method for assessing B-cell function and insulin resistance .It is useful for evaluation of insulin resistance in glucose intolerant, mild to moderate diabetes, and other insulin-resistant conditions. However, in subjects with

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severely impaired or absent B-cell function, poor glycemic control, and in elderly; HOMA-IR may not give appropriate results (6) .Homestasis Model Assessment–Adiponectin ratio (HOMA-AD) and Adiponectin –Resistin index (AR –index) are relatively new surrogate marker for estimating insulin resistance (7, 8) .This study was designed to study the validity of HOMA-AD and AR –index in assessing insulin resistance in overweight male with type 2 diabetes mellitus.

Subjects and Methods:

Ninety (T2DM) patients were enrolled in this cross sectional study. They were selected from those attending the National Diabetic Center, Al-Mustansiria University, and Baghdad. The mean age (±SD) of the participants was 46 ± 6 years (30-50years)

Inclusion criteria : Being male, type 2 diabetic,nonsmokers,not hypertensive, not on insulin treatment, or any medication that affect glucose or lipid metabolism; no history of recent acute illness or clinical evidence suggestive of kidney, liver, or other endocrine diseases; no severe chronic diabetic complications.

Anthropometric parameters Weight, height, waist, hip circumference were measured for all participants , BMI was calculated as weight in kilograms divided by height in meters squared. Waist circumferences were measured in a horizontal plane midway between the inferior margin of the ribs and the superior border of the iliac crest, The hip circumference was measured at the widest part of the gluteal region. The waist-to-hip ratio (WHR) was then calculated.

Biochemical markers

Fasting venous blood samples were collected from all the subjects. The serum was used for analyzing Fasting Blood Glucose (FBG), Total cholesterol (TC), HDL-cholesterol (HDL-C), Triglycerides (TG).HbA1c was estimated by high performance liquid chromatography(supplied by Variant company, USA). Glucose level was determined spectrophotometrically using kits supplied by Randox, UK. Total cholesterol, triglycerides, high density lipoprotein were determined using kits (Biomaghrab,Sa,France), LDL-cholesterol was calculated by Friedwald and Frederickson formula. Enzyme linked immune assay were used to measure insulin (DRG kit, Germany), adiponectin (DRG kit, USA) and resistin (DRG kit, Germany)

. Insulin resistance was measured according to the following formula:(9)

HOMA-IR: fasting Glucose(mg/dl) x fasting Insulin(µU/mL) /405.

HOMA-AD index was calculated by the following formula: (10)

Fasting insulin level (mIU /L) × fasting glucose level (mg/dL)/ AD (mg/mL)

AR index=1+ log 10 (R 0) – log 10 (A 0). (8)

Note: R0 = fasting serum resistin levels (ng/mL)
A0 = fasting serum adiponectin levels (µg/mL.)

Statistical Analysis: Analysis of data was performed using statistically package for social science (SPSS) version 17.0. Results are expressed as mean ± SD, Pearson's correlation test was performed to examine correlations between various parameters. $P<0.05$ was considered statistically significant. Receiver operator curve (ROC) used to assess the area under the curve (AUC) for AR-Index and HOMA-AD.

Results:

The study included 90 diabetic (mean age: 46 ± 6).All participants were selected to be male and overweight (BMI 24.9-29.9) to avoid the confounding effect of gender and BMI.

Baseline characteristics of the studied population was shown in Table 1(results are expressed as mean± SD)

Table2 showed AR-index correlates significantly with FSG, Fasting Insulin and HOMA-IR (r =0.534.P=0.005), (r=0.545, P=0.005), (r=0.506, P=0.008) respectively HOMA-AD correlates with FSG (r=0.551, P=0.001), insulin (r = 0.956,P=0.000),HOMA-IR(r =0.952, P=0.000).

AUC for AR-index (0.800) and for HOMA-AD (0.905) as illustrated in Table 3

Table1: Baseline characteristics of the studied population, results are expressed as mean± SD

Baseline characteristics	Mean ± SD
Age (years)	46± 6
BMI (kg/m2)	26.3 ± 4.9
Waist (cm)	100± 9
Waist to hip ratio	1.1 ± 0.1
FBS (mg /dL)	184 ± 8
HbA 1c (%)	9.4 ±1.4
TC (mg/dL)	208 ± 30
TG (mg/dL)	131 ± 8
`LDL (mg /dL)	130 ± 21
HDL (mg/dl)	45.5± 2.4
VLDL (mg/dL)	25± 1.7
Insulin (µU/ml)	15.2 ± 2
Adiponectin(µg/ml)	5.7 ± 0.3
Resistin (ng/ml)	14.11 ± 1.3
HOMA – IR	7.6 ± 1.5
HOMA- AD	625.8 ± 131
AR-index	1.4

Table 2: Correlation between the studied parameters

	AR - index	HOMA-AD
FBS (mg/dL)	r =0.534** P = 0.005	r =0.551** P= 0.001
HbA1c (%)	r= 0.404* P = 0.04	r= 0.343* P=0.021
TG (mg/dL)	r= 0.311 P=0.122	r= 0.443** P=0.044
HOMA-IR	r=0.506 ** P=0.008	r=0.962** P=0.000
Insulin(µU/ml)	r=0.545** P=0.005	r =956 ** P=0.000

* Significant
**highly significant

Table 3: the Area under the curve for HOMA-AD and AR-Index using (ROC analysis)

	Area under the curve	P-value
Homa-AD	0.905	0.006
AR-index	0.800	0.043

Discussion:

IR is an important clinical and biochemical determinant, not only of diabetes but also of many other clinical states. There is a need to evaluate insulin resistance, since it is an underlying mechanism and predictor of cardio-vascular diseases, diabetes, hypertension, obesity and other consequences of metabolic syndrome (1).

The present study revealed significant correlation of HOMA-AD with FBG, HbA1c, TG, fasting serum insulin, HOMA-IR and HDL in addition HOMA-AD had a large area under the curve for predicting insulin resistance. HOMA-AD is a modified version of HOMA-IR index .Makni et al found that HOMA-AD was the most sensitive predictor of insulin resistance (11) , in addition other researcher found that the adiponecten derived index correlated best with the euglycemic hyperinsulinemic clamp derived sensitivity index as compared to other surrogate measures of insulin resistance including HOMA-IR, quantitative insulin sensitivity check index (QUICKI), fasting glucose/insulin ratio (12). Similar to the finding of other studies (13-15) T2DM patients had low serum adiponectin level and high serum resistin level .The condition of hypoadiponectinemia and hyperresistinemia tend to concurrent in patients with T2DM, Given the opposite effects of adiponectin and resistin on the insulin sensitivity, it seems that relative proportion of adiponectin-to-resistin potentially influence T2DM, so integration of adiponectin and resistin in a novel unified index would better reflect metabolic homeostasis and metabolic disorders. In this study it was found that the AR index correlated significantly with HOMA-IR,serum insulin, glucose , whole blood HbA1C and have a high area under the curve by ROC analysis. Thus, the AR index may play a greater role in reflecting circulating metabolite levels and insulin sensitivity, and these finding are similar to the finding of others (8,11) . The present study showed good correlation of both AR-index and HOMA AD with HOMA –IR ,this is of clinical importance and suggest that both AR-index and HOMA-AD are a valid tool for measurement of insulin resistance these results agreed with other studies which showed that AR –index is a reliable, precise and reproducible diagnostic biomarker (10),in addition, Matsuhisa has demonstrated that HOMA-AD performs better than HOMA-IR in Japanese subjects with higher levels of glucose and elevated BMI, which suggests that these new tools for IR estimation are promising (10). The small number of patients included in this study may be seen as limitation; therefore patients should be further studied and validated using a larger patient pool.

Conclusion:

The current study validates the use of HOMA-AD and AR-Index as tools for determining insulin resistance in overweight male type 2 diabetes mellitus.

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