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# The Association of Resistin Levels with Resistance to Insulin in Iraqi Type 2 Diabetes Mellitus Patients

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## Abstract:

Resistin, is suggested as an important factor in pathogenesis of insulin resistance associated with obesity, and so might lead to development to T2DM. We want to verify the correlation between resistin and glycaemic parameters and marker of obesity in Iraq T2DM patients.

## Aims:

To test the association of resistin with BMI and insulin resistance in T2DM.

## Methods:

In this study 400 participant's was included divided in to two groups (200) T2DM patients and (200) healthy control persons. The biochemical and anthropometric parameters included are body mass index (BMI), fasting resistin level, fasting blood glucose (FBG) ,HOMA-IR and fasting insulin level.

## Results :

The positively significant correlation between resistin and BMI ($r = 0.939$, $p<0.0001$), insulin ($r = 0.917$, $p < 0.0001$), FBS($r = 0.966$, $p<0.0001$) and HOMA-IR ($r = 0.947$, $p<0.0001$) in T2DM were noted.

## Conclusion :

Resistin might be consider as potent link between obesity, insulin resistance and diabetes through disruption the signaling pathway of insulin that may lead to development of insulin resistance and diabetes.

## Keywords:

T2DM, Resistin, BMI, FBS, Insulin, HOMA-1R

## 1.Background

Diabetic is one of the extreme challenged health problems of the 21st century. Type 2 diabetes mellitus (T2DM), representing (90-95%) of the overall cases of diabetes patients, ranging from mostly resistance to insulin with relative

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deficiency of insulin to mostly defect in insulin secretion with resistance to insulin (1). It affects 317 million individuals in the worldwide, but its spread is rapidly increasing due to population and heave of obesity in many countries including republic of Iraq (2). The results of the comprehensive survey indicated that a total prevalence of T2DM was (10.9%) of the population of Iraq (1), it is therefore important to investigate the causes and risks of T2DM. It became clear that the fatty tissue is an active member in the endocrine system. In the past few years, many proteins, called adipokines, have been discovered, produced by fatty tissue (3), which may provide a link between obesity, insulin resistance, and diabetes development; one of such molecule is resistin (4,5).

One of adipose-macrophage-derived hormone is resistin, in mice it lead to development of insulin resistance induced by diet. Administration of injection contains anti-resistin antibodies in these mice result in lowering blood glucose concentrations and improved sensitivity to insulin (6). Although the role of resistin causes insulin resistance in humans is still inconsistent, Resistin is usually thought to interfere with insulin signalling by inhibiting the insulin receptor's ability to recruit and activate the insulin receptor substrate-1(7). Emanuelli mention that resistin encourages the suppressor expression of signaling-3 of cytokine which has been implicated as an mediator through it insulin negatively regulates its own signaling cascade (8). In humanized resistin mice the resistin was found to be implicated in raising the free fatty acids through elevating the activity sensitive lipase hormone and lowering the lipoprotein lipase (9). Available information leaves gaps studied and identified, as the resistin role in the T2DM pathophysiology is still vague and it's role in obesity is unclear as well as controversially. In current study we aims to examine if there is any association between serum resistin and insulin resistance, and also estimation the levels of resistin in T2DM.

## 2. Materials and methods

The research was done in the Postgraduate Laboratory Department of Biochemistry/University of Kufa/Faculty of Medicine. A case control study was ran on 400 participants, they were divided in to two groups' type 2 diabetic patients (200) and healthy control group (200). The period of the study was from July 2016 till June 2017. Participants were selected from the Diabetes Center in AL-Sader Teaching Hospital/Al-Najaf Al-Ashraf province. Diagnosis of patients was done by Specialist Physicians. The patients' ages ranged from 41-69year with a Mean±SD 56.58±7.64year The ages ranged from 45-69year with a Mean±SD of 57.51±8.96year. The biochemical parameters include FBS , fasting serum resistin and insulin level, and HOMA-IR was measured for all participants, the anthropometric parameters include age, gender and BMI was also measured.

### 2.1. Estimation of serum glucose level

Glucose-oxidase enzyme (GOD) act to oxidize glucose and the result is gluconate with hydrogen peroxide, depending on the following chemical reaction (10,11). The reagents preparation and procedure were followed according to the leaflet of the kit (no 80009).

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$$Glucose+O_2+H_2 \xrightarrow{GOD} Gluconic\ acid+H_2O$$

$$2H_2O+Phenol+4\text{-}Amino\text{-}antipyrine \xrightarrow{Peroxidase} Quinonimin+4H_2O$$

### 2.2. Determination of insulin concentration

The enzyme linked immune sorbent assay (ELISA) was used to measure the level of Insulin. The procedure was ran as described in the leaflet of the kit (no2935).

Determination of resistin concentration

An enzyme linked immune sorbent assay (ELISA) method was used for determination of resistin concentration. The procedure was followed as described in the leaflet of the kit (no 3010135)

### 2.3. Insulin resistance estimation

To calculate insulin resistance and the function of beta-cells, we used the homeostatic model assessment (HOMA) method. The following formula was used to estimate the HOMA index.

HOMA-IR =conc. of glucose (mg/dl) x conc. of Insulin (µU/ml)/405

### Statistical analysis

The analyzes of results were down by the use SPSS program version 21 depending on

| parameters | healthy | diabetes | P value |
|---|---|---|---|
| **No (M/F)** | 200 (101 /99 ) | 200 (109 /91 ) | |
| **Age** | 54.16 ± 10.71 | 52.78 ± 7.05 | 0.13 |
| **BMI (kg/m$^2$)** | 29.36± 5.23 | 32.09 ± 3.9 | < 0.0001 |
| **FBG (mg/dl)** | 90.42± 14.21 | 196.11 ± 35.9 | < 0.0001 |
| **Insulin (µU/ml)** | 15.66±5.57 | 31.37±8.8 | < 0.0001 |
| **Resistin (ng/ml)** | 8.4±4.23 | 16.13±3.14 | < 0.0001 |
| **HOMA-IR** | 3.5±1.37 | 15.14±4.9 | < 0.0001 |

Mean ± SD, t-test, significant variation (P value) and linear regression analysis(r).

## 3. Results

The anthropometric and biochemical parameters for all participants was as demonstrated in table 3.1

### 3.1. The Correlation of resistin with BMI in T2DM

A significant correlation was noted between resistin levels and BMI in T2DM ( r= 0.939 , p< 0.0001) as shown in (Fig.3-1) .

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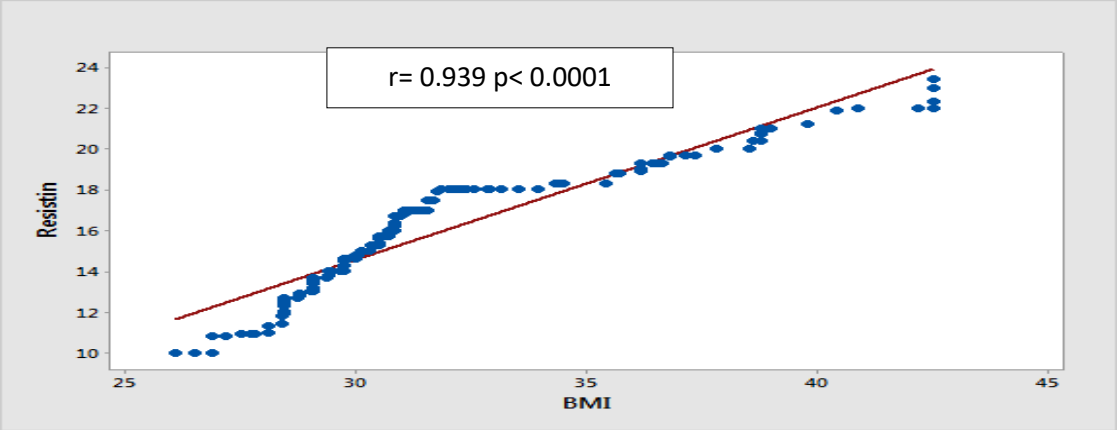


Figure (3-1): The correlation of resistin with BMI in T2DM.

### 3.2. The Correlation of resistin with FBS in T2DM

A significant correlation was noted between resistin and FBS in T2DM (r= 0.966, p< 0.0001) as shown in (Fig.3-2) .

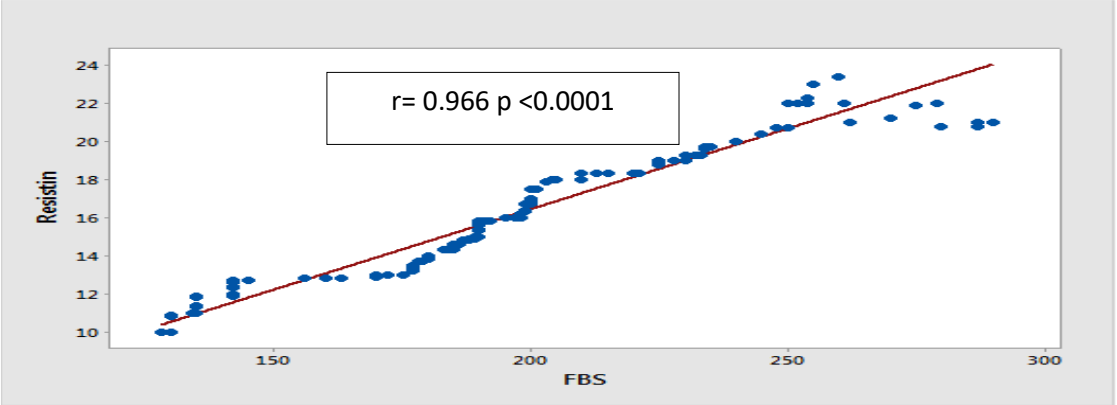


Figure (3-2): The correlation of resistin with FBS in T2DM.

### 3.3. The Correlation of resistin with insulin levels in T2DM

A significant correlation was noted between resistin and insulin levels in T2DM (r=0.917, p< 0.0001) as shown in (Fig.3-3) .

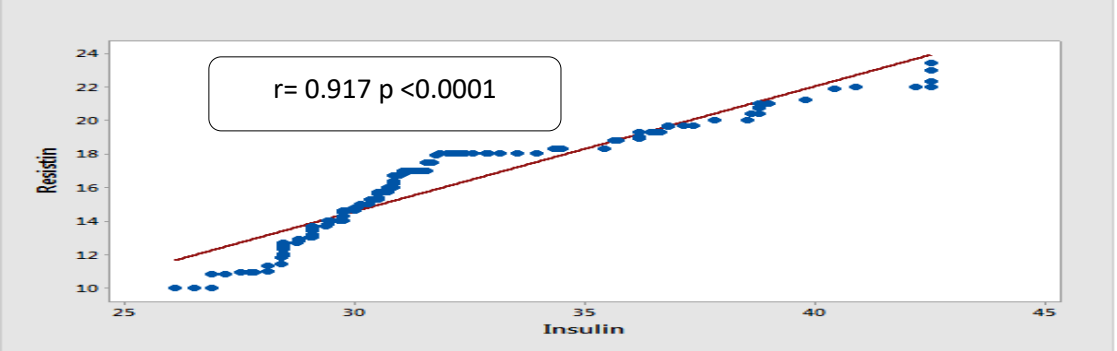


Figure (3-3): The correlation of resistin with insulin levels in T2DM.

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### 3.4. The Correlation of resistin with HOMO-IR in T2DM

A significant correlation was noted between resistin and HOMO-IR in T2DM (r=0.947, p< 0.0001) as shown in (Fig.3-4) .

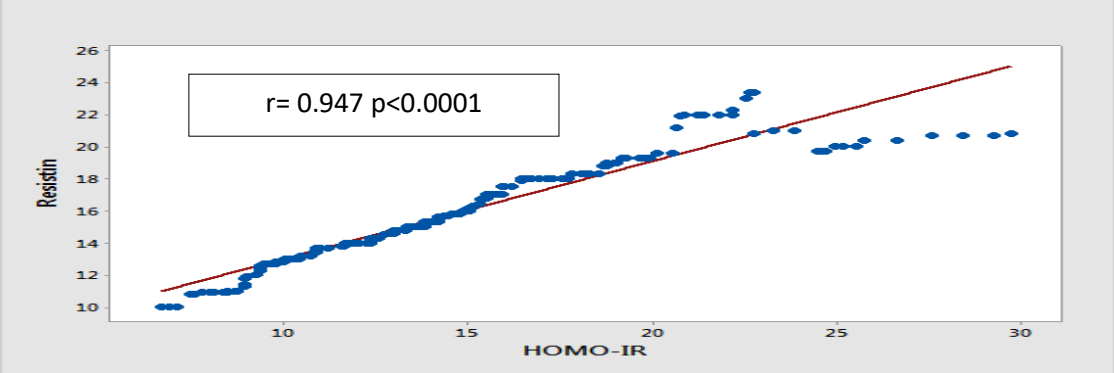


Figure (3-3): The correlation of resistin with HOMO-IR in T2DM.

## 4. Discussion

In present study we compared plasma resistin levels between T2DM and healthy individuals. It shown significant elevated plasma resistin level in diabetic individuals when compare to healthy. This findings is in harmony with Other studies linking resistin with diabetes and the degree of obesity (13,14).On the other hand other researchers do not found such correlation (15,16).

The BMI of diabetic individuals was significantly elevated when compared with healthy. There was a significant positively correlation between plasma resistin levels and BMI in diabetic patients and healthy control and it was highly significant in diabetics. In the same line with our finding researchers demonstrated a positive correlation between plasma resistin leveland BMI (13,17).

In diabetic the control of glycaemic was significantly poured when compare with healthy as shown by significant increased in FBS levels in diabetic subjects. A positively significant correlation between plasma resistin levels and FBS in diabetic individuals was noted and this is in harmonious with other studies demonstrated the same correlations (14,18). On the other hand, other studies do not found such associations (13, 15).

In current study revealed that plasma resistin levels was correlated positively with HOMA-IR and fasting insulin levels in diabetic individuals. And this is in the same line with previous research that reported an significant correlation between the resistin levels and HOMA-IR (13,19). Thus our data have been added to the growing evidence that serum resistin is closely related to resistance to insulin. It was found that an increased in obesity is associated with an increased level of plasma resistin and is directly associated with resistance to insulin (19). The important and important question here is, whether resistin is the factor that affects resistance to insulin? The obtained data in current showed increase in concentrations of fasting serum sugar, resistin, insulin and HOMO-IR (resistance to insulin) in T2DM wile in healthy group did not do so. This proposes that resistin might

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cause initiation of resistance to insulin or vice versa when a certain critical levels of insulin reached. Nevertheless, many of studies have reported that adipokines, such as leptin, resistin and adiponectin, is altered in T2DM and these may be in the development of resistance to insulin (21). Resistin might be consider as potent link between obesity, insulin resistance and diabetes through disruption the signalling pathway of insulin that may lead to develop of insulin resistance and diabetes.

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# ارتباط مستويات الريسيستين بمقاومة الأنسولين في مرضى السكري العراقين من النوع الثاني

د. ماجد كاظم حسين
د. حيدر فرحان سلمان د. حمزة جاسم محمد

## الخلاصة:-

**الخلفية** الريسيستين يقترح كعامل مهم في التسبب في مقاومة الأنسولين المرتبطة بالسمنة ، وبالتالي قد يؤدي إلى تطوير مرض السكر من النوع الثاني. نحن نريد التحقق من العلاقة بينالريسيستين المعلمات نسبة السكر في الدم ومؤشر السمنة في المرضى العراق بداء السكري من النوع الثانيز

**الهدف :**لاختبار ارتباط الريسيستين مع مؤشر كتلة الجسم ومقاومة الأنسولين في مرض السكر من النوع الثاني.

**طريقة العمل:** تم في هذه الدراسة تضمين 400 مشارك مقسمين إلى مجموعتين (200) من مرضى السكري من النوع الثاني و (200) أشخاص اصحاء ولا يعانون من اي مرض. وتشمل المعلمات البيو كيميائية والقياسات الأنثروبومترية مؤشر كتلة الجسم (BMI) ، ومستوى الريسيستين حالة الصيام ، ومستوى السكر في الدم في حالة الصيام و ( FBG، HOMA-IR ومستوى الأنسولين الصائم.

**النتائج :** تم ملاحظة الارتباط الإيجابي الهام بين الريسيستين ومؤشر كتلة الجسم $r=0.939, p < 0.0001$ والانسولين$r=0.917, p < 0.0001$ وسكر الدم $r=0.917, p < 0.0001$ ومقاومة الانسولين$r=0.947, p < 0.0001$ .

**الخلاصة**: قد يعتبر الريسيستين رابطًا قويًا بين السمنة ومقاومة الأنسولين ومرض السكري من خلال تعطيل مسار الإشارة للأنسولين الذي قد يؤدي إلى تطور مقاومة الأنسولين ومرض السكري.