Correlation of plasma resistin with obesity and insulin resistance in type 2 diabetic patients

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Abstract

Aim. – The aim of this case-control study was to assess the relationship between resistin levels and obesity and insulin resistance in type 2 diabetic patients.

Methods. – The study involved a sample of the Jordanian population that included 140 type 2 diabetic patients and 125 control subjects.

Results. – Serum resistin levels were higher in type 2 diabetic patients compared with the controls (P < 0.01). Markers of adiposity [body mass index (BMI) and waist circumference (WC)] and insulin resistance, as well as fasting blood glucose, glycated haemoglobin, urea and blood pressure were considerably higher among the studied diabetics than in the controls. When diabetic patients were subdivided into age-group categories of 10-year intervals, resistin levels significantly increased with increased age, with a significant proportion in the group aged > 60 years (P < 0.01). Similarly, there was a significant association between plasma resistin and blood urea with growing older in diabetic patients. Pearson’s analysis revealed positive correlations between plasma resistin and age, urea, creatinine, insulin, BMI, WC, body-fat content and homeostasis model assessment (HOMA). Furthermore, plasma resistin concentrations were higher in type 2 diabetic obese patients than in non-diabetic obese subjects (P < 0.01), whereas no such difference was found between overweight and normal-weight controls.

Conclusion. – These results suggest that variations in resistin concentrations are not directly related to susceptibility to type 2 diabetes. However, it may be that resistin plays a role in the pathogenesis of obesity and insulin resistance, both of which could, indirectly, contribute to the development of type 2 diabetes.

Keywords: Resistin; Type 2 diabetes; Obesity; Insulin resistance; Jordan

Résumé

Corrélation des concentrations plasmatiques de résistine avec l’obésité et l’insulinorésistance chez des diabétique de type 2.

But. – Évaluer les relations entre concentrations plasmatiques de résistine, obésité et insulinorésistance dans le diabète de type 2 (DT2).

Méthodes. – Une étude cas-témoins a été réalisée à partir d’un échantillon de la population jordanienne qui comprenait 140 patients atteints de DT2 et 125 témoins.

Résultats. – Les concentrations plasmatiques de résistine étaient plus élevées chez les DT2 que celles des témoins (P < 0.01). Les marqueurs d’adiposité (indice de masse corporelle et tour de taille), d’insulinorésistance, la glycémie à jeun, l’HbA1c, l’urée et la pression artérielle étaient plus...
élevés chez les diabétiques que chez les témoins. Lorsque les patients diabétiques ont été répartis par tranches d’âge de dix ans, les concentrations plasmatiques de résistine augmentaient selon l’âge avec une proportion significative dans le groupe de plus de 60 ans (P < 0.01). De même, il y avait une association significative entre la résistine et l’âge selon l’âge. Des corrélations positives entre les concentrations plasmatiques de résistine et l’âge, l’urée, la créatinine, l’insulinémie, l’indice de masse corporelle, le tour de taille, la masse grasse et le HOMA ont été mises en évidence grâce au test de Pearson. Les concentrations plasmatiques de résistine étaient plus élevées chez les DT2 obèses que chez les obèses non diabétiques (P < 0,01), alors qu’il n’y avait pas de différence chez les témoins de poids normal et obèses.

Conclusions. — Ces résultats suggèrent que les variations des concentrations plasmatiques de résistine ne sont pas directement impliquées dans la susceptibilité au DT2. Ils suggèrent néanmoins que la résistine pourrait jouer un rôle dans la physiopathologie de l’obésité et de l’insulinorésistance, et contribuer indirectement au développement du DT2.

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Mots clés : Résistine ; Obésité ; Diabète de type 2 ; Résistance à l’insuline ; Jordanie

1. Introduction

Type 2 diabetes mellitus is a multistage process that begins as insulin resistance, characterized by inability of the body to use its own insulin properly, and ends with exhaustion of the insulin-producing pancreatic β cells, thereby leading to hyperglycaemia. Several factors are implicated in the development of type 2 diabetes, including obesity, family history, physical inactivity and inherited factors [1]. However, obesity is considered the most important risk factor for the disease, as obese individuals are seven times more likely to develop type 2 diabetes than are normal-weight individuals [2]. In addition, central obesity is strongly correlated with insulin resistance in type 2 diabetic patients [3].

Adipose tissue is a highly active endocrine organ that secretes a range of hormones known as ‘adipocytokines’ [4]. One of these adipokines is a cysteine-rich protein called ‘resistin’, formed initially in humans as a propeptide consisting of 108 amino acids prior to losing a signal peptide of 16 amino acids to become a dimer (92 amino acids) or a hexamer (276 amino acids) connected by disulphide bridges [5]. Although, initially, resistin was found to be adipose-specific in rodents [6], it was later shown that, in humans, it is expressed by many other tissues, including preadipocytes, endothelial cells and vascular smooth muscle cells, and is particularly abundantly expressed in macrophages [7]. Indeed, Degawa-Yamauchi et al. [8] showed the expression of resistin in adipose tissue from obese patients.

However, the role of resistin in response to obesity and insulin resistance in type 2 diabetic patients is still obscure [9]. Several studies have reported increased resistin levels in association with obesity and insulin resistance in type 2 diabetes [8,10,11], whereas other studies have failed to detect any change in resistin levels under such conditions [12,13]. Yet other studies found that circulating resistin levels are involved in promoting adiposity, but had no effect on the degree of insulin resistance [14]. These observations suggest that the role of resistin in the pathogenesis of diabetes remains controversial.

To clarify this controversy, there is clearly a need for more data from different ethnic groups, as serum resistin levels might reflect the impact of genetic or environmental factors on resistin expression and, thus, be subject to ethnic variations [15].

The prevalence of diabetes in Jordan is 9.8% — corresponding to that of the world’s population — and is considered to be relatively high; it also shows a progressively rising profile [16]. The age-standardized prevalence of diabetes in Jordan increased from 13.0 to 17.1% over a period of 10 years, and the rate of increase was greatest in those aged ≥ 60 years. Thus, Jordan is not far from being in the increasing dangerous zone of diabetes in this part of the world.

For this reason, the present study was undertaken to investigate the effects of obesity and insulin-resistance markers in Jordanians with type 2 diabetes, and to evaluate the relationship between these markers and plasma levels of resistin.

2. Subjects and methods

2.1. Patients

A total of 140 type 2 diabetic patients were selected according to the criteria published by the American Diabetes Association [1]. The present study also included 125 non-diabetic control subjects, who were age- and gender-matched to the diabetic patients, but had no history of any pathological conditions. Written informed consent was obtained from all study participants, and the local institutional review board approved the study.

2.2. Quantification of body fat

Lean body mass (LBM) was calculated as follows: in men, LBM (kg) = 0.32810 × weight (kg) + 0.33929 × height (cm) − 29.5336; in women, LBM (kg) = 0.29569 × weight (kg) + 0.41893 × height (cm) − 43.2933 [17].

2.3. Pancreatic β-cell secretion, insulin resistance and hepatic insulin sensitivity

Pancreatic β-cell secretory capacity was estimated by the β-cell index [index of β-cell secretory force, homoeostasis model assessment (HOMA) β-cell index] using the formula proposed by Hosker et al. [18]. The rate of insulin resistance was evaluated by the HOMA devised by Matthews et al. [19] and calculated using the formula described by Bonora et al. [20]. Insulin resistance (IR) was expressed as: IR = fasting serum insulin (μU/mL) × fasting plasma glucose (mmol/L)/22.5. Hepatic insulin sensitivity (HIS) was assessed using the following formula: HIS = k/[FPG (mg/dL) × fasting insulin (μU/mL)], wherein k = 22.5 × 18 = 405.
Table 1
Means ± SEM of various parameters in type 2 diabetics and controls.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>Control (n = 125)</td>
<td>0.061</td>
</tr>
<tr>
<td></td>
<td>Diabetic (n = 140)</td>
<td></td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>51.81 ± 1.04</td>
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<tr>
<td></td>
<td>54.36 ± 0.88</td>
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<tr>
<td>Waist circumference (cm)</td>
<td>29.84 ± 0.43</td>
<td>0.109</td>
</tr>
<tr>
<td></td>
<td>30.89 ± 0.47</td>
<td></td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>98.09 ± 1.03</td>
<td>0.0001*</td>
</tr>
<tr>
<td></td>
<td>103.90 ± 1.04</td>
<td></td>
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<tr>
<td>Fasting blood glucose (mmol/L)</td>
<td>0.906 ± 0.005</td>
<td>0.0001*</td>
</tr>
<tr>
<td></td>
<td>0.937 ± 0.005</td>
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<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.50 ± 0.05</td>
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<tr>
<td></td>
<td>10.10 ± 0.32</td>
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<tr>
<td>HbA₁c (%)</td>
<td>5.94 ± 0.06</td>
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<tr>
<td></td>
<td>7.70 ± 0.14</td>
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<tr>
<td>HDL (mmol/L)</td>
<td>4.87 ± 0.09</td>
<td>0.209</td>
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<td></td>
<td>5.08 ± 0.13</td>
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<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.90 ± 0.11</td>
<td>0.05</td>
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<tr>
<td></td>
<td>2.70 ± 0.21</td>
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<tr>
<td>LDL (mmol/L)</td>
<td>0.97 ± 0.02</td>
<td>0.05</td>
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<tr>
<td></td>
<td>0.90 ± 0.02</td>
<td></td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>3.26 ± 0.08</td>
<td>0.901</td>
</tr>
<tr>
<td></td>
<td>3.27 ± 0.08</td>
<td></td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td>4.91 ± 0.16</td>
<td>0.981</td>
</tr>
<tr>
<td></td>
<td>5.78 ± 0.21</td>
<td></td>
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<tr>
<td>Insulin (µU/mL)</td>
<td>72.0 ± 1.9</td>
<td>0.105</td>
</tr>
<tr>
<td></td>
<td>78.6 ± 3.4</td>
<td></td>
</tr>
<tr>
<td>Resistin (ng/mL)</td>
<td>10.38 ± 0.56</td>
<td>0.061</td>
</tr>
<tr>
<td></td>
<td>11.94 ± 0.60</td>
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<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>6.34 ± 0.17</td>
<td>&lt;0.0001*</td>
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<td></td>
<td>7.82 ± 0.29</td>
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<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>131.7 ± 1.5</td>
<td>0.0004*</td>
</tr>
<tr>
<td></td>
<td>138.6 ± 1.2</td>
<td></td>
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<tr>
<td>Lean body mass (kg)</td>
<td>52.79 ± 0.69</td>
<td>0.614</td>
</tr>
<tr>
<td></td>
<td>52.32 ± 0.62</td>
<td></td>
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<tr>
<td>Body fat (kg)</td>
<td>30.61 ± 0.80</td>
<td>0.199</td>
</tr>
<tr>
<td></td>
<td>32.20 ± 0.91</td>
<td></td>
</tr>
<tr>
<td>HOMA (β-cell index)</td>
<td>2.17 ± 0.11</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td></td>
<td>1.47 ± 0.08</td>
<td></td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>2.55 ± 0.14</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5.46 ± 0.37</td>
<td></td>
</tr>
<tr>
<td>Hepatic insulin sensitivity</td>
<td>0.60 ± 0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.30 ± 0.02</td>
<td>&lt;0.0001*</td>
</tr>
</tbody>
</table>

Lean body mass (kg) = 0.32810 × weight (kg) + 0.33929 × height (cm) – 29.5336.
HOMA = 20 × FI/FPG – 3.5, where FI (µU/mL) = fasting insulin and FPG (mg/dL) = fasting plasma glucose.
Insulin resistance = fasting serum insulin (µU/mL) × FPG (mmol/L)/22.5.
Hepatic insulin sensitivity = k(FPG (mg/dL) × FI (µU/mL)), where k = 22.5 × 18 = 405.

* Statistically significant difference.

2.4. Biochemical assays

Blood samples were obtained in the morning after an overnight fast. A commercially available ELISA kit (BioVendor Laboratory Medicine Inc., Brno, Czech Republic) was used to measure human resistin in plasma according to the manufacturer’s instructions. The assay is based on the detection of circulatory homodimeric resistin by rabbit polyclonal antihuman resistin antibody. Human insulin was measured with an insulin kit (Roche Diagnostics, Indianapolis, IN, USA) using a cobas immunoassay analyzer (Roche Diagnostics). Glucose, glycated haemoglobin (HbA₁c), urea, creatinine, cholesterol, triglycerides and high-density lipoprotein (HDL) were measured in plasma by standard methods using the Roche Chemistry Analyzer and Roche kits (Roche Diagnostics). All samples were assayed in duplicate, and the mean of the paired results was determined.

2.5. Statistical analysis

Data were expressed as means ± SEM. Analyses that involved two variables were carried out by Student’s t test, while multiple comparisons were performed using ANOVA followed by post-hoc tests. The SPSS 15.0 statistical software package (SPSS Inc., Chicago, IL, USA) was used for all statistical evaluations. P values < 0.05 were considered significant.

3. Results

Diabetic patients showed significantly (P < 0.05) higher levels of resistin, fasting blood glucose (FBG), HbA₁c, triglycerides, HDL and urea in comparison to control subjects (Table 1). Also, diabetic patients had higher values of waist circumference (WC), waist-to-hip ratio (WHR), systolic and diastolic blood pressure, HOMA β-cell index, IR and HIS. Some parameters, such as BMI, total cholesterol, creatinine and insulin, were markedly increased in the diabetic group, although the increase was not statistically significantly different from that in the controls. No differences were detected in levels of low-density lipoprotein (LDL), LBM and body fat (BF) between the two groups. However, proportions of serum resistin were almost 14% higher in the diabetics than in the controls.

On comparing male and female type 2 diabetic patients with their corresponding healthy controls (Table 2), WC and systolic blood pressure values were significantly different in women, but not in men. However, no statistically significant gender differences were detected in any other parameters, such as resistin, WHR, FBG, HbA₁c, triglycerides, urea, diastolic blood pressure, HOMA, IR and HIS (Table 2).

Patients with type 2 diabetes and their matching controls were further subdivided into four age groups of 10-year intervals (Table 3). Below the age of 40 years, the diabetes group showed no significant differences in serum levels of resistin compared with the healthy control group. However, as the age of the diabetics increased, resistin levels also began to increase.
Resistin (ng/mL) 6.34 ± 0.32
Body fat (kg) 28.7 ± 1.3
Insulin (μU/mL) 12.1 ± 3.1
TG (mmol/L) 2.14 ± 0.17
Body mass index (kg/m²) 28.5 ± 0.52
Waist circumference (cm) 98.6 ± 1.3
HbA1C (%) 5.84 ± 0.04
HDL (mmol/L) 0.87 ± 0.03
Waist-to-hip ratio 0.86 ± 0.02
LDL (mmol/L) 1.09 ± 0.10
TC (mmol/L) 4.83 ± 0.17
HbA1c (%) 5.49 ± 0.22
FBG (mmol/L) 2.14 ± 0.11
Urea (mmol/L) 6.00 ± 0.60
Creatinine (μmol/L) 8.56 ± 0.85
Insulin resistance 0.86 ± 0.60
Lean body mass (kg) 58.0 ± 5.55
Age (years) 50.3 ± 0.18
Resistin (ng/mL) 0.19 ± 0.13
HOMA (IR) 0.54 ± 0.04
HOMA (β-cell index) 2.26 ± 0.17
Insulin resistance < 0.0001
HIS 0.44 ± 0.13
HIS < 0.0001

Data are expressed as means ± SEM.

FG: fasting blood glucose; TC: total cholesterol; TG: triglycerides; HDL/LDL: high-/low-density lipoprotein; SBP/DBP: systolic/diastolic blood pressure; HIS: hepatic insulin sensitivity.

* Statistically significant difference.

The table shows the effect of gender on various clinical parameters in type 2 diabetic patients and controls. It indicates that significant differences were observed in the parameters measured between males and females. For instance, FBG, HbA1C, HOMA, IR, and HIS were significantly higher in diabetic patients compared with controls, and these differences were more pronounced in males than in females.

Table 3: Effect of age on various parameters in type 2 diabetic patients and their matched controls.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>&lt;40 years Controls (n=16)</th>
<th>40–49 years Controls (n=36)</th>
<th>50–59 years Controls (n=37)</th>
<th>&gt;60 years Controls (n=49)</th>
<th>Diabetics (n=77)</th>
<th>Diabetics (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBG (mmol/L)</td>
<td>&lt;0.001 *</td>
<td>&lt;0.001 *</td>
<td>&lt;0.001 *</td>
<td>&lt;0.001 *</td>
<td>&lt;0.001 *</td>
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<tr>
<td>HbA1C (%)</td>
<td>&lt;0.05 *</td>
<td>&lt;0.01 *</td>
<td>&lt;0.01 *</td>
<td>&lt;0.001 *</td>
<td>&lt;0.001 *</td>
<td></td>
</tr>
<tr>
<td>Urea (mmol/L)</td>
<td>NS</td>
<td>NS</td>
<td>&lt;0.01 *</td>
<td>&lt;0.01 *</td>
<td>&lt;0.01 *</td>
<td></td>
</tr>
<tr>
<td>Resistin (ng/mL)</td>
<td>NS</td>
<td>NS</td>
<td>&lt;0.049 *</td>
<td>&lt;0.049 *</td>
<td>&lt;0.01 *</td>
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<tr>
<td>WC (cm)</td>
<td>&lt;0.01 *</td>
<td>&lt;0.05 *</td>
<td>&lt;0.01 *</td>
<td>&lt;0.01 *</td>
<td>&lt;0.01 *</td>
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<tr>
<td>WHR</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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</tr>
<tr>
<td>SBP (mmHg)</td>
<td>NS</td>
<td>NS</td>
<td>&lt;0.01 *</td>
<td>&lt;0.01 *</td>
<td>&lt;0.01 *</td>
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<tr>
<td>DBP (mmHg)</td>
<td>NS</td>
<td>NS</td>
<td>&lt;0.01 *</td>
<td>&lt;0.01 *</td>
<td>&lt;0.01 *</td>
<td></td>
</tr>
<tr>
<td>HOMA (β-cell)</td>
<td>NS</td>
<td>NS</td>
<td>&lt;0.001 *</td>
<td>&lt;0.001 *</td>
<td>&lt;0.001 *</td>
<td></td>
</tr>
<tr>
<td>HOMA (IR)</td>
<td>&lt;0.01 *</td>
<td>&lt;0.001 *</td>
<td>&lt;0.01 *</td>
<td>&lt;0.01 *</td>
<td>&lt;0.01 *</td>
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</tr>
<tr>
<td>HIS</td>
<td>&lt;0.01 *</td>
<td>&lt;0.01 *</td>
<td>&lt;0.05 *</td>
<td>&lt;0.01 *</td>
<td>&lt;0.01 *</td>
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</tr>
</tbody>
</table>

NS: not significant; FBG: fasting blood glucose; WC: waist circumference; WHR: waist-to-hip ratio; SBP/DBP: systolic/diastolic blood pressure; HOMA: homeostatic model assessment; IR: insulin resistance; HIS: hepatic insulin sensitivity.

* Statistically significant difference.

Significantly higher levels of resistin were observed in diabetic patients compared with controls. The most significant resistin increase was observed in patients aged >60 years. Also, a particular increase in blood urea and HOMA was observed in the diabetic patients as their age increased to >50 years. In fact, all of the investigated diabetic age groups exhibited significant increases in levels of FBG, HbA1C, HOMA, IR and HIS compared with the healthy controls.

Patients with type 2 diabetes were also divided into three groups according to BMI: normal weight; overweight; and obese. Serum resistin levels in the diabetics were significantly increased (P<0.001) in those who were obese compared with the controls (Table 4), whereas no statistically significant differences were detected in either the overweight or normal-weight diabetic patients.

Resistin plasma levels in the diabetics were strongly associated with age (r=0.16, P<0.05), urea (r=0.44, P<0.001) and creatinine (r=0.46, P<0.0001). Positive correlations were also observed between resistin and obesity markers such as BMI (r=0.19, P<0.05), BF (r=0.19, P<0.05) and WC (r=0.22, P<0.01). Similarly, positive correlations were found between resistin and parameters of IR rate such as insulin (r=0.19, P<0.05) and HOMA (r=0.24, P<0.005). In contrast, plasma

Table 2: Effect of gender on various clinical parameters in type 2 diabetic patients and controls.
resistin levels showed no significant correlation with FBG, HbA1c, total cholesterol, triglycerides, HDL, LDL, systolic and diastolic blood pressure, LBM, WHR and IR.

### 4. Discussion

The present study data revealed significantly higher levels of plasma resistin in type 2 diabetic patients compared with healthy control subjects, with an overall difference in levels of around 14% in the two tested groups. This finding is consistent with several other studies linking resistin and type 2 diabetes [12,21,22], but contradicts other reports that failed to detect any considerable levels of resistin in such patients [5,23]. In the present study, our Jordanian diabetics were also characterized by high WC, WHR and HOMA (β-cell index) values, as well as an increase in plasma levels of glucose, HbA1c, and triglycerides, with a decrease in plasma HDL.

Analysis of the gender effect showed that male diabetic patients had no significant differences in systolic blood pressure, WC and HDL values in comparison to the male controls. On the other hand, changes in female diabetic patients’ parameters, including resistin, were consistent with the parameters seen in the whole Jordanian diabetic group. Indeed, several studies have suggested significant gender differences in plasma concentrations of resistin [10,23,24], although other reports [12,25] — in agreement with our present study — could not verify such a finding.

However, growing older appears to be a major factor in determining levels of serum resistin in type 2 diabetics. Patients who were ≤40 years of age had similar levels of plasma resistin as their corresponding controls. However, patients aged >60 years had a highly significant increase in resistin values compared with their corresponding controls. This observation may be explained by the development of obesity and IR with ageing [26]. The importance of the age factor on levels of plasma resistin in diabetic patients may have been overlooked in the past, and could partly explain some of the controversial data regarding plasma resistin levels in such patients [5,13,23].

The present study also demonstrated a significant relationship between diabetics’ age and IR as expressed by HOMA, IR and HIS markers. Similarly, the observed association of resistin with serum insulin and HOMA values shown by Pearson’s analysis confirms the role of resistin in IR (Table 5). This finding of a link between plasma resistin and IR in Jordanian type 2 diabetics is contrary to previous reports of other diabetic ethnic groups, such as the Japanese [12] and Pima Indians of Arizona [27]. However, such differences are probably due to ethnic variations or to technical discrepancies that may require further investigations involving a wider range of different ethnic groups and the use of standardized assessment methodology.

The data from Pearson’s analysis also showed positive correlations between circulating resistin and obesity markers as conveyed by BMI, WC and BF values (Table 5). The latter observation was further substantiated by the detection of a positive correlation between serum resistin and obese — but not overweight or normal-weight — type 2 diabetic patients. This finding is in agreement with a study of resistin levels in Saudi diabetics by Al-Harithy and Al-Ghamdy [28] that showed no correlation in lean subjects, but a highly significant correlation with BMI, WHR and WC in diabetic women. However, our present finding contradicts another Saudi report by Al-Daghri et al. [29] that failed to find a positive correlation between resistin levels and BMI in diabetic Saudi patients.

An increase in human obesity can raise serum resistin levels [8,30] and is directly correlated with IR [10,31], while medical treatment resulted in declines in both serum resistin and obesity [32]. Lazar [7] proposed that communication between adipocytes and macrophages might lead to hyperresistinaemia, as human resistin is mainly expressed in macrophages. In addition, there is genetic evidence to support a relationship
between human resistin protein and obesity or IR [33]. Overall, these data favour a possible link between human plasma resistin levels, obesity, IR and type 2 diabetes, despite being clearly inconsistent with other observations [12,13,23].

The present study data also revealed a significant increase in blood urea in diabetics compared with non-diabetics, especially when these patients were older in age (> 50 years). This finding was clearly demonstrated by Pearson’s analysis, which showed a positive correlation between resistin and old age and urea, as well as creatinine, in type 2 diabetic patients. Altogether, they support earlier reports of an association of high plasma resistin with a decrease in glomerular filtration rate [34] and progressive impairment of renal function, as well as chronic kidney disease [35]. Moreover, it signifies the potential role of resistin as a biomarker for renal complications in type 2 diabetes.

There was a significant increase in blood pressure in diabetics, and hypertension remains a high-risk factor even for older, non-diabetic, subjects, which makes any comparison of the blood pressure effect in relation to age parameters somewhat meaningless. This may partly explain the failure to obtain a relationship between systolic and diastolic blood pressure values with increasing age in Jordanian diabetics, or any significant correlation between blood pressure and plasma resistin levels in such patients. Evidently, resistin possesses a proinflammatory action in humans, allowing it to play an important role as a vasoactive factor that directly affects endothelial function and vascular homeostasis [36]. This particular property of resistin may be linked to the risks of nephropathy and atherosclerosis that are encountered as common complications of type 2 diabetes [6,37].

The lack of association between serum resistin and blood glucose or HbA1c in diabetic patients is consistent with previous data [6]. Taken together, this suggests an indirect role of resistin on the development of type 2 diabetes most likely by aggravating the inherent incompetence of insulin metabolism.

Several studies have shown that the production of other adipokines, such as leptin and adiponectin, is altered in type 2 diabetes and might be involved in IR pathophysiology [38]. In addition, certain variations in leptin and adiponectin genes have been implicated in successful ageing (ageing without age-related diseases) in the Jordanian population [39]. However, the contribution of these adipokines to the development of obesity and IR in type 2 diabetes was not investigated in the present study, although it will be the subject of future research.

In conclusion, the present findings suggest that resistin may be implicated in the pathogenic mechanisms through which increased adiposity leads to the development of IR and type 2 diabetes in the Jordanian population. Furthermore, resistin could serve as a biomarker for renal and other vascular complications associated with type 2 diabetes, particularly in older-aged patients.

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References


