The Effect of Leptin Hormone Levels In Type(II) Diabetic Nephropathy Patients

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Abstract

Type 2 diabetes Nephropathy complication is one of the most commonest metabolic disorders that becomes an advanced serum level of hormone altered. The objective is to study the effect of leptin levels in Type 2 diabetes nephropathy (D.N) complication and healthy subject.

This study was done in National Diabetes Center (NDC), AL-Mustansriya University; on a total (64) individuals whose age were ranged from (45-60) years, of which (38) patients of type 2 diabetes nephropathy, and (26) healthy (controls).

The collected data, information concerning the individuals used in the present study were: age, sex, body mass index (BMI) and blood samples to estimate serum leptin levels, fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), serum creatinine, blood urea, and micral tests (urinary microalbumin to creatinine ratio).

The mean FPG, HbA1c and Micral tests of type 2 diabetes nephropathy (D.N) showed statistical significant with healthy control; on the other hand the data shows significant increases in leptin level in type 2 diabetes nephropathy (D.N) (urinary microalbumin to creatinin ratio ranged 30-300 mg/g) compared with healthy control.

No significant correlation was present between serum leptin and both serum creatinine and blood urea, so there wasn’t any correlation between BMI and serum leptin levels. In conclusion the results showed that serum leptin level was elevated in type 2 diabetes nephropathy (D.N) because impaired increase with progression of renal disease in diabetic nephropathy.

Introduction

Type 2 diabetes mellitus: called non insulin dependsed diabetes mellitus (NIDDM) accounts for 90% of the population with diabetes in this type. There are varying degrees of insulin resistance or insulin secretary defects (1). Complication of diabetes occurs after many years of uncontrolled hyperglycemia (2). The consequences of diabetes are nephropathic disease, which lead to chronic renal failure (CRF)(3). Diabetic Nephropathy (D.N) is a progressive kidney disease caused by angopathy of capillaries in the kidney glomeruli. It is characterized by nephrotic syndrome and long standing diabetes mellitus and is a primary cause for dialysis in many western countries (4). In diabetic nephropathy measurement microalbuminuria test results may aid clinicians in the detection of patient at risk of developing kidney damage (5,6).

Leptin is a 16KD protein hormone of 167 amino acids which plays a key role in regulation food intake and energy expenditure, including the regulation of appetite and increase of metabolism (7,8). Human kidney plays a substantial role in leptin removal from plasma by taking up and degrading the peptide. Renal leptin net balance and urinary leptin excretion were detected by Lineweaver-Burk analysis. This analysis indicated that renal leptin uptake followed saturation kinetics with an apparent Michaelis-Menten constant of 10.9 ng/ml. Renal leptin uptake could be 80% of all leptin removal from plasma, generally leptin was undetectable in urine (9) about 20-30% of patients with type1 or type2 diabetes develop evidence of nephropathy, and such patients currently starting of dialysis (10). Furthermore, Hyperglycemia also activate protein kinase c, may contribute to renal diseases and vascular complications of diabetes (9), and also familiar or genetic factor plays a role in diabetic
nephropathy (3). In addition previously described direct and indirect effects of leptin on the kidney include natriuretic effects, an increase in sympathetic nervous activity, and stimulation of reactive oxygen species. These findings collectively suggest that the kidney is a target organ for leptin and that this hormone might play an important role in renal pathophysiology (11).

**Materials and Method**

This study was carried out in National Diabetes Center (NDC), AL- Mustansiriya University; on a total (64) individuals, (30 females and 34 males) aged (45-60) years. Thirty-eight patients Type 2 diabetes nephropathic (urinary microalbumin to creatinine ratio was range 30-300 mg/g), (26) healthy controls. Data collection about age, sex and body mass index(BMI). Blood samples from the individuals were taken for laboratory investigation: which included, Fasting Plasma Glucose (FPG), Glycated Hemoglobin (HbA1c), blood urea, serum creatinine and determination leptin level in serum; (DGR instruments GmbH, Germany, ELISA KIT)(12), and Micral tests; supplied by Bayer Healthy Care, V.S.A(13). Analysis of data was carried out by using SPSS(statistical package for social sciences).

**Results and Discussion**

A total of 64 individuals (38 patients and 26 control) were examined successfully without any healthy problems. Diabetes is the most common cause of renal failure, and there is an account for more than 40 percent of new cases who have development of kidney problems in people with diabetes (14). Leptin hormone, which is secreted from adipocytes has a role in the regulation of appetite and energy expenditure. This protein is produced by adipocrine, pancreas and other organs by activating the transmembrane receptor and is cleared from plasma mainly by the kidney (15). The results showed that the serum leptin levels in the Type 2 diabetes nephropathy (urinary microalbumin to creatinin ratio 30-300 mg/g) significantly were higher $p < 0.05$ (Table-1) compared with healthy controls and this result agrees with Chan-Wb et al. (17) and Fruehwared-Schultes et al. (16), they found significant elevated levels of serum leptin in Type 2 diabetes nephropathy (D.N) compared with non diabetic controls. The human kidney plays a substantial role in leptin removal from the plasma by absorbing and degrading the peptide (18). Increasing albumin level in urin (microalbuminuria) is considered as key characteristics of diabetic nephropathy (16). Table(2) showed that there was a significant positive correlation of FPG, HbA1c $p < 0.05$ in Type 2 diabetes nephropathy (D.N) compared with healthy control subjects, serum leptin level did not correlate with FPG and HbA1c ($r=0.343$, $r=0.315$) respectively (table-3), these results agreed with Fu-Me chung et al. (19). He found that there was no correlation between leptin level and FPG, HbA1c, which indicate that leptin is not affected by the degree of glycemic control, while Pistrosh et al. (20) found that patients with Type 2 diabetes had high levels of FBG and HbA1c, compared with healthy control. Such increase may be due to insulin resistance in Type 2 diabetic nephropathy patients in which leptin reduces insulin secretion and enhances hematopoesis (21). There was a significant positive correlation of BMI in Type 2 diabetic nephropathy compared with control $p < 0.05$ (Table-2) but there wasn’t any significant correlation between BMI and leptin level in Type 2 diabetic nephropathy as shown in(table-3). This correlation may be explained by the presence of additional factor which would increase the impaired degradation by the affected kidney (22). Hyperliptenimia may play a role in the decreased BMI (anorexia and malnutrition) that usually accompanied chronic renal failure. Furthermore, there were no significant correlation between serum creatinine and blood urea levels with serum leptin levels in Type 2 diabetic nephropathy (19), but both creatinine and urea levels increase in Type 2 diabetes; this may be due to renal impairment in Type 2 diabetic nephropathy (23). In conclusion the results showed that serum leptin level was elevated in
type 2 diabetes nephropathy (D.N) because impaired would increase with the progression of renal disease in diabetic nephropathy.

References
### Table 1: Serum leptin levels in Type 2 Diabetic Nephropathy and control

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Type 2 (D.N)</th>
</tr>
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<tbody>
<tr>
<td>Leptin (ng/ml)</td>
<td>10.60+3.17</td>
<td>20.18+4.40</td>
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</table>

### Table 2: The mean of BMI, FBG, and HbA1c in Type 2 Diabetes Nephropathy (D.N) and controls

<table>
<thead>
<tr>
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<th>Control n=26</th>
<th>Type 2 (D.N) n=38</th>
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<tbody>
<tr>
<td>BMI (Kg/m)</td>
<td>25.01+3.40</td>
<td>28.99+6.69</td>
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<tr>
<td>FPG (mg/dl)</td>
<td>77.19+2.25</td>
<td>177.62+50.20</td>
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<tr>
<td>HbA1c (%)</td>
<td>4.18+0.12</td>
<td>9.23+2.48</td>
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</table>

### Table 3: The correlation coefficient (r) between BMI, FBG, and HbA1c with serum leptin levels (control & diabetic nephropathy)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Type 2 (D.N)</th>
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<tbody>
<tr>
<td></td>
<td>Leptin (ng/ml)</td>
<td>Leptin (ng/ml)</td>
</tr>
<tr>
<td>BMI r</td>
<td>0.380</td>
<td>0.392</td>
</tr>
<tr>
<td>BMI p</td>
<td>0.055</td>
<td>0.120</td>
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<td>FBG r</td>
<td>0.259</td>
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<tr>
<td>FBG p</td>
<td>0.201</td>
<td>0.101</td>
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<tr>
<td>HbA1c r</td>
<td>0.256</td>
<td>0.315</td>
</tr>
<tr>
<td>HbA1c p</td>
<td>0.207</td>
<td>0.164</td>
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تأثير مستوى هرمون اللبتيين لدى مرضى السكري النوع الثاني والمصاحب باعتلال الكلى

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الخلاصة

يعد داء السكري النوع الثاني والمصاحب باعتلال الكلى من الأمراض الشائعة الذي يعزى إلى عمليات ليست غير طبيعية محدث تغيرات في مستويات معظم الهرمونات. تم دراسة تأثير مستوى هرمون اللبتيين عند مرضى السكري (النوع الثاني) والمصابب باعتلال الكلى ومدى علاقته بالمعايير السكرية الأخرى، إذ أجريت الدراسة على (64) فردًا، تراوحت أعمارهم بين (45-60) سنة، (38) مريضاً مصابين من مرضى السكري النوع الثاني والمصابب باعتلال الكلى، ومعدّل كتلة الجسم، واعتلال الكلى، ومستوى قياس لغرض قياس مستوى هرمون اللبتيين وقياس الكلبوز، والهيموغلوبين المشتركي، والبوريا، والكليتين وكذلك قياس فحص مكرر (نسبة الإثيدومين إلى الكرياتينين في البول) بين النتائج وجود قيمة إحصائية في فحص السكر الصائم والهيموغلوبين المشتركي، وفحص مكرر عند مرضى السكري النوع الثاني والمصاحب باعتلال الكلى مقارنة مع مجموعة الأصحاء، وكذلك بين الدراسة ارتفاع مستوى اللبتيين عند مرضى السكري النوع الثاني والمصاحب باعتلال الكلى التي كانت (نسبة الإثيدومين إلى الكرياتينين في البول تتراوح بين 30-300 ملغم/غم) مقارنةً مع الأصحاء. كذلك، عدم وجود علاقة ترابطية بين مستوى اللبتيين وكم من مستوى الكرياتينين والبوريا في مصل الدم، ولم يلاحظ وجود علاقة ترابطية بين معدل كتلة الجسم ومستوى اللبتيين.

تستنتج من هذه الدراسة أن مستوى هرمون اللبتيين يرتفع عند مرضى السكري النوع الثاني والمصاحب باعتلال الكلى نتيجة لضعف الكلى تدريجيًا على التجزئة والتحليل عند مرضى السكري.