SERUM VISFATIN IN RELATION TO SOME PARAMETERS OF IRON METABOLISM IN EGYPTIAN SUBJECTS WITH ALTERED GLUCOSE TOLERANCE

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Received 19/4/2012– Accepted 17/6/2012

ABSTRACT

Visfatin is an adipokine mainly synthesized and secreted in visceral fat. Visfatin was found to have important proinflammatory and immunomodulating properties. The aim of the present work was to clarify the relation between plasma visfatin, some parameters of iron metabolism and insulin resistance in altered glucose tolerance patients and its relation to obesity.

Eighty subjects were included in this study; 60 diabetic patients, and 20 healthy subjects, sex and age matched, used as controls (Gr.I). The patients were divided into: Gr. II impaired glucose tolerance (IGT); Gr. III (type I); Gr. IVa (obese type II) and Gr.IVb (non obese type II). The following biochemical parameters were estimated in this study: serum visfatin, plasma fasting and postprandial glucose, glycated hemoglobin (HbA1c), serum insulin, HOMA, HOMAβ, QUICKI, serum total cholesterol, LDL-C, HDL-C, triacylglycerols (TGs), as well as serum ferritin, sTFR and TNF-α.

Results indicated a significant positive correlation between serum visfatin and each of FPG (in IGT patients) and serum ferritin (in type I), but it was correlated negatively with sTFR/log ferritin (in type I) and serum sTFR (in obese type II diabetics). Serum ferritin level showed a significant positive correlation with BMI, waist to hip ratio, HDL-C (in non obese type II), and with TNF-α (in type II diabetics). No correlation was detected between ferritin and HOMA-

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all patients.
As a conclusion, serum visfatin was correlated to some parameters of iron metabolism in type I and in obese type II diabetics. Visfatin was also correlated with FPG in IGT group, its increase may be due to hyperglycemia itself and at the same time it may induce progression of inflammatory condition. This study did not show an association of serum visfatin with insulin resistance or obesity.
This as adapted from Ph.D theses is submitted to Ain Shams University by Doaa M. Ibrahim

Key Words: Serum visfatin, insulin, ferritin, sTFR

INTRODUCTION

Diabetes mellitus is one of the most common chronic diseases in nearly all countries, and continues to increase in numbers and significance, as changing lifestyles lead to reduced physical activity and increasing obesity.

Shaw et al., (2010) recorded that about 285 million people worldwide are diabetics, while it will be 439 million in 2030. The authors added that in Egypt ~10.4% are diabetics (2010), expected to be 12.8% in (2030).

Adiposity is the most important risk in the development of insulin resistance and type 2 diabetes mellitus. Adipose tissue produces several proteins (adipocytokines) such as leptin, adiponectin, resistin, tumor necroses factor alpha (TNF-α), and interleukin-6 (IL-6), that modulate insulin sensitivity and appear to play an important role in the pathogenesis of insulin resistance, diabetes, dyslipidemia, inflammation, and atherosclerosis (Fantuzzi., 2005).

Visfatin was rediscovered by Fukuhara et al., (2005) as an adipokine that is mainly synthesized and secreted in visceral fat hence, the name visfatin. Surprisingly, visfatin was shown to activate its target cells by binding to the insulin receptor, although at a site distinct from insulin, and to exert a variety of insulin-mimetic effects including enhancing glucose uptake, inhibiting hepatocyte glucose release and insulin-like effects in the insulin-transduction pathway (Xie et al., 2007). On the other hand, visfatin was found to have an important proinflammatory and immunomodulating properties (Dahl et al., 2007) and also found to function as nicotinamide phosphoribosyl transferase (Nampt), the rate-limiting enzyme in the
NAD biosynthetic pathway from nicotinamide in mammals (Garten et al., 2009).

Body iron level may be altered in adults at high-risk of type 2 diabetes, including people with obesity and prediabetic states; impaired fasting glucose (IFG) and impaired glucose tolerance (IGT). Iron-induced oxidative stress which associated with elevated body iron levels may play a pathogenic role in chronic diseases (Fernandez-Real et al., 2002).

Ferritin is a sensitive clinical tool commonly used to assess body iron stores, it is also an acute phase reactant that is affected by other factors, including systemic inflammation (Fernandez-Real et al., 2002).

Circulating soluble transferrin receptor (sTfR) has been proposed as a novel marker of iron status that is less affected by the presence of inflammation (Cotton et al., 2000).

MATERIALS AND METHODS

1. Subjects

Eighty subjects were included in this study: 20 healthy subjects used as controls (Gr.I). Sixty diabetic patients were recruited from Out-Patients Clinic, Ain Shams Hospital. They were enrolled in the present study after obtaining informed consent. These patients were divided into: 15 IGT (GrII), 15 type I (Gr III), 30 type II subdivided into 15 obese (GrIVA) and 15 non obese (Gr IVB). Exclusion criteria were sustained hypertension, heart failure, peripheral vascular disease, acute or chronic infections, cancer, hepatic and renal disease. Diabetic patients with acute illness, myocardial infarction, unstable angina or stroke were also excluded from this study. Before inclusion, all the patients and control subjects underwent careful physical examination and detailed laboratory investigations to exclude any condition that may interfere with glucose tolerance. Standing height and body weight were measured in light indoor clothing without shoes. Body mass index (BMI) and waist to hip ratio were calculated.

2. Biochemical parameters:

Blood samples were collected between 08:00 and 08:30 a.m. after 12 hours fasting. Serum was separated and stored at -80°C. Fasting and postprandial plasma glucose (FPG&PPPG) were determined enzymatically according to the method of (Trinder, 1969) using Spinreact diagnostic kits (San Antonio, Claret, Texas). Glycated
Hemoglobin (HbA1c) was measured on a DCA 2000 analyser with dedicated reagent cartridges supplied by Bayer, Elkhart, USA (Trivelli et al., 1971). Serum visfatin levels were determined by ELISA method (Human visfatin ELISA kit, Alpco Diagnostics, Samal et al., 1994). Total cholesterol (TC) was measured colorimetrically as described by (Allain, 1974), triacylglycerols (Wahlefeld, 1974), HDL-C (Lopes-Virella, 1977). LDL-C level was calculated by Friedwald’s formula. Reagents were obtained from Stanbio, North Main Street, Boerne, Texas (Gama-Trade). Soluble transferrin receptor (sTFR) and ferritin level were determined by ELISA technique using commercial kit (DiaMED Euro Gen) (Beguin, 1993), and (Monobind, Inc.) (Jandal, 1996) respectively. Tumor necrosis factor alpha (TNF-α) was measured by ELISA technique using commercial kit (AviBion) (Beutler, 1987), and serum insulin by ELISA technique using commercial kit (BioSource International, Inc.) (Flier et al, 1979).

HOMA was calculated by the formula: HOMA = fasting glucose (mg/dl) x fasting insulin (µU/ml)/405 (Matthews et al., 1985) and HOMA-β by the equation: [20 x fasting plasma insulin (mU/l) / (FPG (mmol/l) - 3.5)] (Matthews et al., 1985). The quantitative insulin sensitivity check index (QUICKI) was calculated as 1/ {log (fasting insulin) +log (fasting glucose)} (Katz et al., 2000). Oral glucose tolerance test (OGTT) was carried out as described by (Harris, 1995).

Statistical analysis was performed using Student’s t-test and the differences between the groups were tested for significance by one-way ANOVA test. For correlation, Pearson’s test was used and the level of significance was at p<0.05.

RESULTS

Fasting and post prandial plasma glucose levels, ferritin, triacylglycerols, visfatin and tumour necrosis factor-α levels showed a significant increase while HDL-C concentration showed a significant decrease in all subjects with altered glucose tolerance compared to the control group. Results are represented in Tables (1-3). HbA1c level showed a significant elevation in type I DM, obese and non obese type II DM patients compared to the control and IGT groups. Insulin showed a significant elevation in IGT and obese type II DM patients compared to the control group. HOMA-IR index (insulin resistance) was significantly increased while QUICKI and HOMAβ index were
**Table (1):** Glycated hemoglobin (HbA\textsubscript{1c}), fasting and postprandial plasma glucose (FPG&PPPG), waist/hip, insulin, HOMA, QUICKI, and HOMA β in IGT, type I and type II diabetic patients.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>HbA\textsubscript{1c} (%)</th>
<th>FPG (mg %)</th>
<th>PPPG (mg %)</th>
<th>Waist/hip</th>
<th>Insulin (µIU/ml)</th>
<th>HOMA</th>
<th>QUICKI</th>
<th>HOMA β</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control Mean ± S.D</td>
<td>5.07±0.82</td>
<td>89.4±7.5</td>
<td>111.9±9.4</td>
<td>0.89±0.04</td>
<td>10.8±3.55</td>
<td>2.49±0.9</td>
<td>0.34±0.02</td>
<td>149.65±34.7</td>
</tr>
<tr>
<td></td>
<td>IGT Mean ± S.D</td>
<td>5.6±3.4</td>
<td>111.7±10.3</td>
<td>147.8±27.4</td>
<td>0.88±0.05</td>
<td>14.5±3.8</td>
<td>4.04±1.1</td>
<td>0.31±0.01</td>
<td>111.3±38.5</td>
</tr>
<tr>
<td></td>
<td>Type I DM Mean ± S.D</td>
<td>7.21±0.5*</td>
<td>175.87±37.4</td>
<td>206.9±37.8</td>
<td>0.87±0.05</td>
<td>N.D.</td>
<td>N.D.</td>
<td>N.D.</td>
<td>N.D.</td>
</tr>
<tr>
<td></td>
<td>Obese Type II DM Mean ± S.D</td>
<td>8.3±0.98*</td>
<td>192.1±46.3</td>
<td>250.3±56.5</td>
<td>0.93±0.03</td>
<td>17.07±6.1</td>
<td>7.96±3.29</td>
<td>0.28±0.01</td>
<td>52.7±24.6</td>
</tr>
<tr>
<td></td>
<td>Non obese Type II DM Mean ± S.D</td>
<td>8.4±1.2*</td>
<td>183.47±47.7</td>
<td>247.6±60.8</td>
<td>0.88±0.03</td>
<td>13.2±2.9</td>
<td>5.93±1.8</td>
<td>0.29±0.01</td>
<td>46.1±21.7</td>
</tr>
</tbody>
</table>

*: P<0.05 vs. control

N.D. Not determined.
**Table (2):** Lipid profile in IGT, type I and type II diabetic patients.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>TC (mg %)</th>
<th>TGs (mg %)</th>
<th>HDL-C (mg %)</th>
<th>LDL-C (mg %)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control Mean+ S.D</td>
<td>177.4±13.8</td>
<td>83±18.06</td>
<td>54.3±10.01</td>
<td>106.4±16.8</td>
</tr>
<tr>
<td></td>
<td>IGT Mean+ S.D</td>
<td>184.9±33.2</td>
<td>116.87±24.7</td>
<td>43.7±10.95*</td>
<td>118.7±33.4</td>
</tr>
<tr>
<td></td>
<td>Type I DM Mean+ S.D</td>
<td>178.5±18.9</td>
<td>106.1±43.2*</td>
<td>33.4±4.97*</td>
<td>121.2±19.1</td>
</tr>
<tr>
<td></td>
<td>Obese Type II DM Mean+ S.D</td>
<td>219.27±40.24</td>
<td>168.7±41.8*</td>
<td>35.8±8.6*</td>
<td>152.2±44.1*</td>
</tr>
<tr>
<td></td>
<td>Non obese Type II DM Mean+ S.D</td>
<td>199.4±19.8*</td>
<td>154.2±26.6*</td>
<td>35.3±4.6*</td>
<td>134±20.4*</td>
</tr>
</tbody>
</table>

*: P<0.05 vs. control  
N.D. Not determined.

**Table (3):** sTFR, ferritin, sTFR/log ferritin, visfatin and TNFα in IGT, type I and type II diabetic patients.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>sTFR (µg /ml)</th>
<th>Ferritin (ng /ml)</th>
<th>sTFR/Log ferritin</th>
<th>Visfatin (ng /ml)</th>
<th>TNFα (pg /ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control Mean+ S.D</td>
<td>1.1±0.36</td>
<td>28.1±7.88</td>
<td>0.25±0.08</td>
<td>8.05±2.58</td>
<td>2.87±0.35</td>
</tr>
<tr>
<td></td>
<td>IGT Mean+ S.D</td>
<td>1.02±0.4</td>
<td>75.07±28.9*</td>
<td>0.21±0.08</td>
<td>13.63±6.8*</td>
<td>3.72±0.29*</td>
</tr>
<tr>
<td></td>
<td>Type I DM Mean+ S.D</td>
<td>0.89±0.23*</td>
<td>44.7±23.3*</td>
<td>0.2±0.06</td>
<td>14.47±2.85*</td>
<td>3.42±0.22*</td>
</tr>
<tr>
<td></td>
<td>Type II DM Obese Mean+ S.D</td>
<td>0.96±0.26</td>
<td>76.5±26.45*</td>
<td>0.2±0.05*</td>
<td>18.2±5.16*</td>
<td>4.7±0.47*</td>
</tr>
<tr>
<td></td>
<td>Non obese Type II DM Mean+ S.D</td>
<td>0.8±0.2*</td>
<td>40.3±13.1*</td>
<td>0.18±0.05*</td>
<td>14.47±3.56*</td>
<td>3.9±0.34*</td>
</tr>
</tbody>
</table>

*: P<0.05 vs. control  
N.D. Not determined.
Table (4): Pearson’s correlation coefficient (r) between serum visfatin and biochemical parameters in the patient groups.

<table>
<thead>
<tr>
<th>Groups Parameters</th>
<th>Visfatin</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IGT</td>
<td>Type I</td>
</tr>
<tr>
<td>FPG</td>
<td>0.63*</td>
<td>-0.08</td>
</tr>
<tr>
<td>Ferritin</td>
<td>-0.04</td>
<td>0.52*</td>
</tr>
<tr>
<td>sTFR/log ferritin</td>
<td>0.20</td>
<td>-0.55</td>
</tr>
<tr>
<td>sTFR</td>
<td>0.18</td>
<td>-0.21</td>
</tr>
</tbody>
</table>

* Correlation is significant at the 0.05 level.

N.B. 1- Visfatin is positively correlated with FPG in IGT group and ferritin in type I.
2- Visfatin is negatively correlated with sTFR in type II obese and sTFR/ log ferritin in type I diabetics.

Table (5): Pearson’s correlation coefficient (r) between serum ferritin and biochemical parameters in the patient groups.

<table>
<thead>
<tr>
<th>Groups Parameters</th>
<th>Ferritin</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IGT</td>
<td>Type I</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.15</td>
<td>0.47</td>
</tr>
<tr>
<td>HDL-C</td>
<td>0.19</td>
<td>0.13</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>-.01</td>
<td>0.27</td>
</tr>
<tr>
<td>TNF-α</td>
<td>0.92*</td>
<td>0.12</td>
</tr>
<tr>
<td>HOMA</td>
<td>-0.39</td>
<td>-</td>
</tr>
</tbody>
</table>

* Correlation is significant at the 0.05 level.

N.B. 1- Ferritin is positively correlated with BMI, waist to hip ratio, HDL-C in non obese type II and TNF-α in type I diabetics
2- No correlation between ferritin and HOMA.

HOMA-IR index in type II diabetics was significantly elevated while QUICKI and HOMA β were significantly reduced compared to IGT group.
Total cholesterol and LDL-C concentrations showed a significant elevation in obese and non obese type II DM patients compared to the control group. The elevation in total cholesterol was significant in obese type II diabetics compared to each of IGT group, type I DM and non obese type II DM.
Serum total cholesterol and triacylglycerols showed a significant
elevation in obese type II DM patients compared to both IGT and type I DM groups.
HDL-C showed a significant decrease in type I DM and type II diabetic patients compared to the IGT group.
Serum ferritin levels were significantly reduced in type I and non obese type II diabetic groups compared to the IGT group as well as obese type II DM group.
Serum sTFR levels were significantly decreased in the type I and non obese type II DM groups compared to the control group. In addition, sTFR level was significantly reduced in non obese type II DM group compared to the IGT group.
sTFR/log ferritin ratio was significantly decreased in obese and non obese type II DM groups compared to the control group.
Serum TNF-α showed a significant decrease in IGT, type I DM and non obese type II DM groups compared to obese type II DM group.
Also, TNF-α level significantly decreased in IGT group compared to non obese type II DM group.
Serum visfatin decreased significantly in IGT group, type I DM group and non obese type II DM group compared to obese type II DM group.

In the present study, correlation between each of serum visfatin, soluble transferrin receptor (sTFR), ferritin, tumor necrosis factor alpha (TNF-α) and other biochemical parameters in the patients groups are illustrated in tables (4&5).

**DISCUSSION**

The present study was carried out to find the relationship between visfatin, some parameters of iron metabolism and insulin resistance in impaired glucose tolerance, type I, and type II diabetics.
In the present work, glycated hemoglobin showed a significant elevation in all type I and type II diabetic patients.
This result is in accordance with that observed by (Rajpathak et al., 2009 and El-Mesallamy et al., 2011).
In the current study, serum insulin level showed a significant increase in IGT and obese type II groups. These results are in line with that of findings of Wassink et al., (2007). El-Mesallamy et al., (2011) also reported a significant elevation in Egyptian obese type II patients. In contrast, Dogru et al., (2007) indicated that there was no change in
insulin level in impaired glucose tolerance group.
In the present study, HOMA (as indication of insulin resistance) level showed a significant elevation in IGT group and in all type II diabetics.
This result is consistent with that recorded by De Luis et al., (2009).
Also El-Mesallamy et al., (2011) indicated that HOMA increased significantly in obese and non obese type II diabetics. Lu et al., (2010) showed that insulin resistance was elevated in Chinese patients with type 2 diabetes, suggesting that abdominal obesity could partly explain the link between subclinical inflammation and insulin resistance.
In the course of the present study, QUICKI (as indication of insulin sensitivity) level showed a significant decrease in IGT group and in all type II diabetics. According to Lhoret et al., (2003), similar decrease in QUICKI was recorded in IGT patients. Meanwhile, Chen et al., (2005) found that QUICKI decreased significantly in type II patients.
In the current study, HOMA β (as indication of β cell function) level showed a significant decrease in IGT and in all type II patients.
Parallel results were indicated by Tutuncuog et al., (2008) who found that HOMA β decreased in IGT Turkish subjects, and also with Wang et al., (2009) for first degree relatives of patients with type II diabetes.
On the other hand, Sathiyapriya et al., (2009) found no changes in HOMA β in Indian subjects with first degree relatives of patients with type II diabetes.
In the current study, triacylglycerols level showed a significant elevation in IGT and all type I and II diabetic patients.
In this connection, El-Mesallamy et al., (2011) recorded a similar elevation in Egyptian obese and non obese type II diabetics.
Concerning total cholesterol and LDL-C levels, a significant elevation in all type II diabetic patients was demonstrated.
This result is in line with that observed by El-Mesallamy et al., (2011) and in contrast to Dogru et al., (2007) who found that there was no change in LDL-C level in IGT patients.
With regard to HDL-C level, a significant decrease in all patients was recorded. A similar decrease in HDL-C was observed by Dogru et al., (2007) in IGT group and by El-Mesallamy et al., (2011) in type II diabetics.
In the present study, serum ferritin level showed a significant elevation in IGT and in all type I and II diabetic patients.
In this connection, Fernandez-Real et al., (2007) found that ferritin concentration was the highest in type II diabetic subjects, followed by the IGT group.

The literature implies a large number of authors reported that serum ferritin predicts the development of diabetes and also increased in type II patients. Rajpathak et al., (2009) recorded that iron may play a role in the development of diabetes through several potential mechanisms. As mentioned earlier, iron is a strong pro-oxidant that catalyzes several reactions leading to the formation of reactive oxygen species (ROS) (e.g. hydroxyl radicals) and resulting in elevated oxidative stress which is proposed to contribute to an increased risk of type 2 diabetes. In addition high iron stores in the liver may induce insulin resistance by impeding its capacity for insulin extraction, thereby resulting in impaired suppression of hepatic glucose production. Similarly, iron may also impair insulin action and interfere with glucose uptake in adipocytes. Furthermore, increased muscle iron stores may enhance free fatty acid oxidation and thereby could interfere with glucose disposal. Thus, both increased glucose production and decreased glucose utilization may occur with increasing levels of body iron. Excess body iron may also cause iron deposition in the pancreatic β-cells resulting in impaired insulin secretion.

Hernandez et al., (2005) suggested that ferritin was also an acute phase reactant so that increased ferritin levels in patients with DM may reflect systemic inflammation rather than iron overload.

In the present study, serum sTFR was decreased significantly in type I and non obese type II diabetic patients, while it wasn’t changed in impaired and obese type II diabetics. This result is consistent with the findings of Abou-Shousha et al., (2006) and Fernandez-Real et al., (2007) who noticed no change in sTFR level in type II diabetic patients.

In contrast, Rajpathak et al., (2009) reported that serum sTFR was elevated in impaired glucose tolerance group. The authors demonstrated that sTFR has been proposed as a novel marker of iron status that is less affected by the presence of inflammation. It is therefore possible that sTFR levels may be associated with increased DM risk through mechanism unrelated to iron overload. It is possible that sTFR levels may increase as a compensatory mechanism for a reduction in free iron levels that may occur secondary to oxidative
stress.
In the present study, serum visfatin was significantly elevated in all altered glucose tolerance patients (IGT, type I and type II). Similar results were reported by Fernandez-Real et al., (2007) in altered glucose tolerance (IGT and type II) patients. They suggested that increased iron stores would lead to increasing visfatin synthesis. De Luis et al., (2009) indicated that visfatin increase was only in IGT patients. While, Dogru et al., (2007) found no elevation in visfatin level in IGT group.

With regard to the elevation of serum visfatin in all type II DM patients, several authors recorded the same result (El-Mesallamy et al., 2011 and Esteghamatia et al., 2011).

El-Mesallamy et al., (2011) stated that the elevation of plasma visfatin in patients with type II diabetes mellitus could have more than one possible explanation: Firstly; the elevation may suggest the impairment of visfatin signalling (hypervisfatinemia) in target tissues or the dysregulation in biosynthesis or in response to hyperglycemia, hyperinsulinemia, or adipocytokines in state of diabetes (Chen et al., 2006). Secondly; being insulin mimetic, it may be hypothesized that chronic hyperglycemia and activation of angiotensin II in diabetics persistently stimulates visfatin synthesis from adipose tissue (Kang et al., 2010) and so the increased serum visfatin concentration can respond to a compensatory mechanism aimed at ameliorating the functional consequences of insulin deficiency (Lopez-Bermejo et al., 2006). Thirdly, the discovery of visfatin/Nampt-mediated systemic NAD biosynthesis plays a critical role in maintaining glucose homeostasis. Circulating NMN functions as an essential plasma metabolite that can modulate glucose-stimulated insulin secretion (GSIS) in pancreatic beta cells. Given that fully differentiated adipocytes are natural producers of extracellular nicotinamide phosphoribosyl transferase (eNAMPT), adipose tissue may regulate beta cell function through secretion of eNAMPT and extracellular biosynthesis of NMN. So it could be considered as a compensatory mechanism for β-cell functioning (Imai and Kiess, 2009).

Finally, being an adipokine with pro-inflammatory properties (Moschen et al., 2007), the elevated levels of visfatin could be attributed to the chronic state of low-level inflammation in T2DM in which adipose tissue plays a pivotal role. Also Kang et al., (2010) suggested that the plasma concentration of visfatin was elevated when
inflammatory conditions exist. Overall, these findings suggest that the activation of visfatin synthesis in a diabetic environment induces Nuclear factor kappa B (NF-kB) activation and leads to activation of pro-inflammatory cytokines and systemic inflammation in cultured adipocytes. So the interaction between visfatin and inflammation in adipocytes shown in this study could provide a new physiologic role of visfatin in the pathogenetic mechanism of systemic inflammation in diabetic patients.

In the present study, serum TNF-α was elevated in IGT, and all type I and type II patients. With respect to IGT patients, Konukoglu et al., (2008) reported that hyperglycemia associated with increased circulating cytokine concentrations and fasting TNF alpha concentrations seem to be more associated with IGT. In contrast, Choi et al., (2004) showed no significant difference in plasma TNF-α between normal and impaired glucose tolerance groups.

Concerning type I diabetic patients, Gordin et al., (2008) reported that acute hyperglycaemia induces an inflammatory response in patients with type 1 diabetes and also Alexandraki et al., (2008) suggested that the high levels of proinflammatory cytokines that have been reported in patients with a recent diagnosis of type I might imply that the systemic inflammation is more prominent during the early stages of type I diabetes mellitus.

The increase in serum TNF-α in type II patients in the present study is in agreement with the findings of Mishima et al., (2001) who recorded that TNF-α was elevated in obese type II diabetic men and it may play an important role in insulin resistance associated with obesity and/or diabetes mellitus in humans.

Chen et al., (2007) suggested that elevated serum TNF-α in newly diagnosed type II diabetics was due to severe hyperglycemia via oxidative stress and correlated to β cell function and insulin resistance. Mavridis et al., (2008) reported that serum TNF-α was elevated in type II diabetic patients due to the presence of systemic, low-grade inflammation. With respect to correlations between parameters in the present work, serum ferritin level showed a significant positive correlation with BMI, waist to hip ratio, insulin, sTFR and TNF-α in all type II diabetic patients. While, Rajpathak et al., (2009) reported that ferritin was correlated only with BMI, waist to hip ratio and
HDL-C in non obese diabetics.

In type I diabetic patients, serum ferritin was correlated positively with visfatin and TNF-α. But it wasn’t correlated with BMI and waist to hip ratio. This result is in agreement with that stated by (Rajpathak et al., 2009).

In the present study, serum sTFR was positively correlated with BMI, waist to hip ratio, sTFR/log ferritin and negatively with visfatin in obese type II diabetic patients; also it was correlated positively with BMI, FPG, sTFR/log ferritin and negatively with HOMA β in non obese patients. In type I patients, sTFR correlated positively with LDL-C and sTFR/log ferritin, while it was correlated negatively with QUICKI in IGT group.

In the present work, serum visfatin was positively correlated with fasting plasma glucose in impaired glucose tolerance patients, while it was positively correlated with serum ferritin and negatively correlated with the ratio of sTFR/log ferritin in type I patients.

In obese type II patients, visfatin showed a negative correlation with sTFR. This result was in harmony with the findings of (Fernandez-Real et al., 2007).

In contrast, in IGT patients visfatin showed a non significant correlation with ferritin, sTFR, TNF-α, BMI, waist to hip ratio, insulin, HOMA, quicki, HOMA β and lipid profile. This result is also in accordance with the findings of (Fernandez-Real et al., 2007). Visfatin also showed a non significant correlation with BMI, waist to hip ratio, insulin, HOMA, QUICKI, HOMA β and lipid profile in type II diabetic patients. This result is in consistent with those reported by several authors (Kang et al., 2010 and Esteghamati et al., 2011); while Sandeep et al., (2007) only found an association between visfatin and BMI.

In the current study, serum TNF-α was positively correlated with FPG and negatively with HOMA β in only non obese type II patients. In type I patients, serum TNF-α was negatively correlated with waist to hip ratio and positively with ferritin.

In conclusion, serum visfatin is correlated to some parameters of iron metabolism as ferritin and sTFR/log ferritin in type I patients and sTFR in obese type II patients. Visfatin is also correlated to FPG in IGT group. So visfatin may be increased due to hyperglycemia itself and at the same time it may induce progression of inflammatory condition.
REFERENCES


الملخص العربي

العلاقة بين الفيزانتين في مصل الدم و بعض دلالات أحيان ألم البدائل المصابين يقر في القدرة على تحمل الجلوكوز

يعتبر الفيزانتين كأدوية أثرها بارز في الأنسجة الدقيقة الموجودة في الأذهان، وقد وُجد أن الفيزانتين له بعض الخصائص المناعية المحترقة للالتهاب. يضيف هذا البحث إلى دراسة العلاقة بين الفيزانتين في مصل الدم و بعض دلالات ألم الحدود و مقاومة الإسمنولوجين في المرضى المصابين بالجلوكوز و النوع الأول والثاني داء السكر و العلاقة بالسمنة.

اشتملت الدراسة على تسعةين شخصًا: مجموعة ضابطية تتكون من 50 شخصاً من الأشخاص (مجموعة 1)، و 60 مريضاً بدأ السكر خصوصاً إلى أربع مجموعات: 15 مصاباً بحالة في مستوي الجلوكوز (مجموعة 2)، 15 مصاباً بدء السكر من النوع الأول (مجموعة 3)، 15 مصاباً بدء السكر من النوع الثاني وبنية (مجموعة 4) و 16 مصاباً بدء السكر من النوع الثاني غير البيناء (مجموعة 5).

وقد تم عمل القياسات الكيميائية الحيوية الآثارية: الفيزانتين بمضاء الدم، الجلوكوز الصائم، القافط، الهيموجلوبين السكري، الإسمنولوجين، الهيمو، هيموفيليا، التهيمن، الفيروين، مستقبل الترارسينيغين الذائب ومستقبل الترارسينيغين الذائب/تروغينغوفين الفيروين بمضاء الدم، بالإضافة إلى عامل الورم الترمي-ألفا. أشارت النتائج إلى وجود علاقة معينة بين الفيزانتين والجلوكوز الصائم (في المصابين بحالة في مستوي الجلوكوز (في الفيزانتين و مستقبل الترارسينيغين الذائب/تروغينغوفين الفيروين بمضاء الدم، بالإضافة إلى كنهاية الجسم، نسبة العصرا إلى الأدفان، كولسترول البروتين الدهناء على الكثافة (في مرضى النوع الثاني غير البيناء)، و توجد علاقة معينة مع الفيزانتين و عامل الورم الترمي-ألفا (في مرضى النوع الأول).

أسفرت الدراسة إلى وجود ارتباط بين الفيزانتين و بعض دلالات ألم الأذى في المصابين بالجلوكوز و البدائل النوع الثاني، و توجد علاقة مع الجلوكوز الصائم (في المصابين بحالة في مستوي الجلوكوز) مما يفيد بأن زيادة الفيزانتين مرتبطة بارتفاع نسبة السكر في الدم، و في الوقت نفسه يُمناسبة بسبب الفيزانتين في تطور حالة الإسمنولوجين، و لم تسفر هذه الدراسة عن وجود ارتباط بين الفيزانتين و مقاومة الإسمنولوجين أو البيناء.