SERUM VISFATIN AND LIPID PROFILES IN PATIENTS WITH TYPE II DIABETES IN COMPARISON WITH HEALTHY CONTROLS IN KHARTOUM STATE-SUDAN

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ABSTRACT

Visfatin is an adipocytokine which is secreted largely by visceral adipose tissue. It acts synergistically with insulin in increasing glucose cellular uptake, it also has an insulin-like effects through direct connection and activation of insulin receptors without any change or competition with the insulin. The aim of this study was to explore the relation of serum visfatin and lipid profile in T2DM in the context of the role of glycemic control. A total of 45 T2DM Sudanese patients and 45 healthy control subjects, matched for age, body mass index (BMI) and sex ratio, were enrolled. Analytical, hospital base case control study was conducted during the period from January to May 2015. Serum levels of visfatin, total Cholesterol, Triglyceride, HDL cholesterol, LDL cholesterol, and blood HbA1c were estimated. Serum visfatin levels was higher in T2DM patients, compared to control (3.3± 2.2), (2.0 ± 0.5) respectively (P<0.001). There was no significant difference in the mean of serum levels of visfatin in good glycemic controlled patients (3 ± 1.7in comparison with non-glycemic controlled groups (3.6 ± 2.6) (P=0.30). There was no significant difference in the mean of serum levels of visfatin between good glycemic controlled patients and nonglycemic controlled groups (3 ± 1.7) (3.6 ± 2.6) respectively (P=0.30). There was significant
correlation between serum visfatin with Triglyceride, HDL cholesterol, and insignificant correlation between serum visfatin with Total cholesterol and LDL cholesterol.

**KEYWORDS:** T2DM, Visfatin, lipid profiles, Sudanese.

**INTRODUCTION**

The incidence of Type 2 diabetes mellitus (T2DM) continues to increase dramatically in most parts of the world, and the ways to prevent or cure the disorder are limited despite enormous research efforts.\(^1\) Excess adiposity is the most important risk in the development of insulin resistance and T2DM.\(^2\) In addition to its important role in saving energy as triglycerides (TG), adipose tissue produces several proteins (adipocytokines) such as leptin, adiponectin, resistin, TNFα, IL-6 and visfatin that modulate insulin sensitivity and appear to play an important role in the pathogenesis of insulin resistance, diabetes, dyslipidemia, inflammation, and atherosclerosis.\(^3\) Visfatin is a newly discovered adipocyte hormone with a direct relationship to T2DM. This hormone is found in the cytoplasm as well as the nucleus of cells and has been identified in many tissues and organs including the brain, kidney, lung, spleen and testis but preferentially expressed in visceral adipose tissue.\(^4\) Visfatin binds to the insulin receptor at a site distinct from that of insulin and causes hypoglycemia by reducing glucose release from liver cells and stimulating glucose utilization in adipocytes and myocytes. Visfatin is up regulated by hypoxia, inflammation and hyperglycemia and down regulated by insulin, somatostatin and statins.\(^5\) Visfatin seems to modulate insulin sensitivity and appear to play an important role in the pathogenesis of insulin resistance, diabetes, dyslipidemia, inflammation, and atherosclerosis.\(^2\) Moreover, there has been increasing evidence of the association between insulin resistance and subclinical inflammation involving cytokines derived from adipose tissue or adipocytokines. Knowledge of how these adipose tissue-derived factors influence metabolic and cardiovascular disease has recently expanded, and growing evidence implicates adipocyte derived factors as major regulator of insulin resistance. Interestingly, visfatin and not adiponectin or resistin levels were associated with T2DM.\(^2\)

There are controversies regarding the association of visfatin with T2DM in published literature. Although, some studies have done in other side of world but because of high incidence of diabetes and different race and ethnicity in Sudan this study is conducted to assess serum visfatin level in patients with type II diabetes in comparison to healthy control and to the correlate it to lipid profiles in Sudanese.
MATERIALS AND METHODS
This study was a quantitative approach, analytical, hospital base case control study carried in diabetic clinics in governmental hospitals at Khartoum state during the period from January 2015 to May 2015. The study samples was comprised 45 Sudanese newly diagnosed with T2DM, in contrast, 45 healthy volunteers were involved as control group ,both groups were age and sex matched.

Subjects with underlying disease (e.g. inflammatory or infectious diseases), diabetic with complications were excluded in this study. After written or verbal consent, 5ml of fasting venous blood was drawn in plain container between 8:00 and 10:00 am. Serum was obtained for estimation of glucose, visfatin, total cholesterol, triglyceride, HDL.

Blood Samples were collected in EDTA anticoagulant containers for HbA1c estimation. Glucose, total cholesterol, triglycerides, HDL were measured by enzymatic method using spectrophotometer, HbA1c was measured by Chromatographic – spectrophotometric method. LDL was calculated using (Friedwald equation). Serum visfatin was measured by sandwich Enzyme Linked-Immunosorbent Assay using Microplate Enzyme Immunoassay analyzer.

Statistical Package for Social Science (SPSS version 20) computer software was used for data analysis. We was used independent T-test and chi-square test for comparison and Spearman’s Correlation test for estimate correlation (significance levels was set at P<0.05).

RESULT
Serum mean of Visfatin level was higher in patients with T2DM as compared to control group (p<0.001) Table (1).The percent of diabetic patients with good glycemic control was 48.8%, and Non glycemic control was 51.2%. Serum level of Visfatin wasn’t significantly different in patients with glycemic control and non-glycemic controlled diabetic patients (P = 0.30) Table (2).There was a significant correlation between T.G and HDL with serum visfatin level. There was no correlation between serum total cholesterol and LDL cholesterol with serum visfatin level Figure (1) (2) (3) and (4).
Table 1: Shows the Baseline Characteristics and Biochemical Measures of the Test Group and The Control Group.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Test group N = 45</th>
<th>control group N = 45</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender ( male )</td>
<td>22 (49.9%)</td>
<td>24 (53.3%)</td>
<td>0.3</td>
</tr>
<tr>
<td>Age (years)</td>
<td>41 ± 9 (20 - 79)</td>
<td>41 ± 12.2 (23 – 70)</td>
<td>0.1</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>29.6 ± 5.2 (18.7 – 41.7)</td>
<td>23.4 ± 4 (16.1 – 34.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Family history (Yes)</td>
<td>32 (72.7%)</td>
<td>10 (22.7%)</td>
<td></td>
</tr>
<tr>
<td>Exercise (Yes)</td>
<td>7 (12.9%)</td>
<td>36.3%</td>
<td></td>
</tr>
<tr>
<td>FBG (mg/dl)</td>
<td>189.5 ± 77.4 (77 – 408)</td>
<td>89.5 ± 14.4 (65– 124)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>S.total Cholesterol (mg/dl)</td>
<td>221.7 ± 58 (111– 350)</td>
<td>177 ± 43.2 (160–279)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>S.Triglyceride (mg/dl)</td>
<td>158.7 ± 52.9 (69 – 269)</td>
<td>140.3 ± 85.3 (70 – 370)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>39.8 ± 10.2 (19–69)</td>
<td>44.7 ± 13.0 (23–78)</td>
<td>0.050</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>150.2 ± 57.1 (44 – 233)</td>
<td>97.7 ± 24.2 (55–161)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Visfatin (ng/dl)</td>
<td>3.3 ± 2.2 (1-11.6)</td>
<td>2.0 ± 0.5 (1-3.2)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

- The table shows the mean ± SD, minimum and maximum values, probability (p value).
- T-test used for the comparison.
- P- Value < 0.05 considered significant.

Table 2: Comparison of the Means of FBG, TC, TG, LDLc, HDLc and Visfatin Between Glycemic Control and Non-Glycemic Control Among Test Group.

<table>
<thead>
<tr>
<th></th>
<th>Glycemic control N = 22</th>
<th>Non glycemic control N = 23</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBG (mg/dl)</td>
<td>170.4 ± 72.9 (77-323)</td>
<td>207±78.8 (100- 408)</td>
<td>0.12</td>
</tr>
<tr>
<td>TC (mg/dl)</td>
<td>209 ±48.1 (112 -307)</td>
<td>232.7±13.6 (137 -300)</td>
<td>0.19</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>154.2 ±56.7 (69 -246)</td>
<td>162.8±10.5 (104 -269)</td>
<td>0.59</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>136.2±46.1 (44 -209)</td>
<td>163.1±63.9 (71 -268)</td>
<td>0.15</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>42.8±9.8 (30 -69)</td>
<td>37.1±9.8 (20 -49)</td>
<td>0.062</td>
</tr>
</tbody>
</table>
The table shows the mean ± SD, minimum and maximum values, probability (p value).

- T-test used for the comparison.
- P-Value < 0.05 considered significant.

| Visfatin (ng/dl) | 3±1.7 (1 - 4.6) | 3.6±2.6 (1.9 - 11.6) | 0.30 |

Figure 1: Ascotter Plot Shows the Relationship between Serum Visfatin (Ng/ML) & the TC (Mg/Dl). (R = 0.1, P = 0.15)

Figure 2: Ascotter Plot Shows the Relationship between Serum Visfatin (ng/ml) & TG (mg/dl). (r = 0.08, P = 041)
DISCUSSION

Regarding to the contraverseries about the relationship between visfatin and lipid profiles in T2DM patients, in previous studies some of them showed that visfatin levels were significantly lower in subjects with diabetes and related this result to pioglitazone use through a short period as in a study published in Albany in USA in 2012 visfatin were strongly correlated with resistin and CRP, and negative correlate with BMI, TG and glucose. It concluded that visfatin may be a marker of subclinical inflammatory state.\(^6\)
While in a case control study done in Tehran 2012, serum visfatin level was investigated in 64 women consisting of 32 Diabetic patient and 32 age matched healthy control and they found that the average visfatin was significantly higher in diabetic than control and the mean values of anthropometric indexes and lipid profile were not significantly different between the groups. They conclude that there is an inverse relationship between circulating level of visfatin and fasting blood glucose and refer the cause of increase visfatin either due to more accumulation of as dipocyte and/ or faster differentiation and consequently synthesis and more secretion of serum levels to the patient or as mechanism to compensate insulin deficiency or inefficiency so that it can regulate blood glucose.[7]

Also in a study carried out in Romania 2011, in which the correlation of visfatin with the lipid metabolism is studied in diabetic and obese patients, in their study the mean values of visfatin were higher in diabetic group as compared to obese and control. They obtained negative correlation of visfatin with TG in diabetic patients. In case of visfatin against HDLc, there were obtained negative correlation in diabetic and obese patients and positive correlations in the control group.[8]

More over in the year of 2010 an Egyptian study found that there was an elevation of visfatin in diabetic patients, visfatin and vaspin were significantly correlated with each other and with other biochemical parameter, and visfatin positively correlated with TG, TC and did not show correlation with HbA1c, it conclude that vaspin and visfatin might play an important role in the pathogenesis T2DM.[9]

In our study, we found that serum visfatin concentrations was significantly higher in the diabetic group compared with the control group (table 1) and this was agree with Gligor et. al.[8], H.O. El-Mesallamy et. al.[9], Berndt et. al.[10], and Varma et. al.[11], and disagree with S. Yaturu et. al.[6] this may be due to pioglitazone use through a short period.

Elevated visfatin/Nampt levels in patients with T2DM could have more than one possible explanation: may be due to impairment of visfatin/Nampt signaling in target tissues[12], being insulin mimetic, the increased plasma visfatin/Nampt concentrations could be a compensatory mechanism in response to hyperglycemia[13], or being an adipokine with proinflammatory properties, these elevated levels could be attributed to the chronic state of low-level inflammation in T2DM in which adipose tissue plays a pivotal role.[14]
Our findings showed no significant different between the mean serum visfatin levels among diabetic patients with good glycemic control (HbA1c < 7.5%) compared with Non glycemic controlled patients (HbA1c > 7.5%) (p= 0.30). (Table 2).

Our findings showed a significant positive correlation between visfatin and TG (p=0.001), and negative correlation with HDL (p= 0.002) and no significant correlation with TC and LDL (p=0.15, 0.065) respectively (figure 1, 2, 3, 4.). This result was agree with the result of Gligor et al [8], H.O. El-Mesallamy et al.[9] and Hajianfar, et al.[15]. The cause of increase TG can be due to dysfunction of lipase enzyme, which analyzes the chylomicrons.[15]

CONCLUSION
This study concluded that visfatin was significantly higher in diabetic patients as compared to healthy individuals. Visfatin was positive correlated with TG and negative correlated with HDL.

REFERENCES
1. Arner P. Visfatin-a true or false trail to type 2 Diabetes Mellitus. J Clin Endocrinol Metab., 2006; 91: 28-30.


