Study of Visfatin Level and Its Relation to Some Histopathological Changes of Placentae in Preeclampsia

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Abstract

The objective of the present study was to measure the serum level of visfatin in preeclamptic Egyptian pregnant women and the possible relation of visfatin level to each of the measured insulin resistance, body mass index and histopathological changes of the placenta included in this study.

The study population consisted of 30 preeclamptic patients and 30 matched healthy pregnant women during the third trimester.

The present study results revealed that preeclamptic mothers had a significant increase in insulin resistance value than normal pregnant women with no significant difference in this value between mild and severe preeclamptic sub-groups. Regarding visfatin level, there was a highly significant increase in visfatin level in preeclamptic women compared with healthy controls and also increase in severe than mild preeclamptic sub-groups. Correlation analysis presented a significant negative correlation between maternal visfatin levels versus HOMA-IR among preeclamptic group, but no relation had been found between visfatin levels and body mass index among preeclamptic mothers. Histopathological examination of placentae revealed that infarctions, atherosis, hyalinized areas and Tenny Parkers changes were significantly increased in preeclamptic group than control group. The present study did not find any correlations between visfatin levels versus histopathological changes in placentae among preeclamptic mothers.

Hypervisfatinemia may be one of the possible etiologies of preeclampsia. Visfatin might be part of a feedback mechanism improving insulin sensitivity. Preeclamptic placentae exhibited definite histopathological changes which may be attributed to the vascular insufficiency of placenta.

Keywords: Visfatin, Preeclampsia, Insulin resistance, Placenta, Infarction
1. Background

Preeclampsia (PE), a hypertensive disorder in pregnancy is believed to be one of the leading causes of maternal and fetal morbidity and mortality worldwide [1]. It is a classical triad of hypertension, proteinuria and edema, defined as “a new onset of elevated blood pressure of 140/90 mm Hg or more, recorded on two separate occasions at least 6 hours apart and in the presence of at least 0.3 g of protein in a 24-hour urine, arising after the 20th week of gestation in a previously normotensive patient, and resolving completely between 6-12 weeks after delivery” [2].

In developing nations, the incidence of the disease is reported to be 4-18%, with hypertensive disorders being the second most common obstetric cause of stillbirths and early neonatal deaths in these countries [3]. There is compelling evidence that complications of pregnancy such as preeclampsia and intrauterine growth restriction (IUGR) are associated with maternal cardiovascular disease in the future. Both pregnancy disorders are characterized by a disturbed placental function and are associated with insulin resistance [4].

Insulin resistance in pregnancy and preeclampsia is mainly attributed to placental hormones [5] and increased maternal adiposity [6]. Adipose tissue represents an active endocrine organ that releases a large number of bioactive mediators (adipokines) that signal to organs of metabolic importance including brain, liver, skeletal muscles, and the immune system thereby modulating hemostasis, blood pressure, lipid and glucose metabolism and inflammation. These adipokines include adiponectin, leptin, omentin, resistin, retinol binding protein, tumor necrosis factor-α, interleukin-6, vaspin, chemerin and visfatin [7].

Besides regulating maternal energy metabolism and insulin sensitivity in normal pregnancy, adipokines have been implicated in preeclampsia. Increasing number of studies reported the role of these proteins in the deleterious insulin resistance associated with preeclampsia; however, these reports are characterized by some inconsistency and contradictions [8].

A cross sectional study demonstrated that the maternal serum visfatin levels were significantly increased in women with mild preeclampsia and even more increased in women with severe preeclampsia [9]. However, the exact opposite was reported by Hu et al. [10], indicating that further studies are necessary to evaluate the potential role of visfatin as a marker for preeclampsia.

The aim of the present study was to measure the serum level of visfatin in preeclamptic Egyptian pregnant women and the possible relation of visfatin level to each of the measured insulin resistance, body mass index and histopathological changes of the placenta included in this study.

2. Patients and Methods

2.1 Patients

This study was conducted in the departments of Obstetrics and Gynecology in Benha, Mansoura Universities Hospitals and Biochemistry Department Medical Research Institute, Alexandria University and included sixty pregnant women. A written and verbal consent has been obtained from all participants in the study according to the Instructions and Guidelines of the Ethics Committee of the Medical Research Institute, Alexandria University. They were divided into two groups:

Group I: Consists of thirty pregnant women with no obstetric or medical complications of pregnancy, no medications were given during pregnancy apart from tonics and iron, single viable pregnancy, Gestational age (37-40) weeks and spontaneous delivery of the placenta.

Group II: Consists of thirty preeclamptic women diagnosed according to its type as:

Mild preeclampsia: after 20 weeks pregnant women with blood pressure greater than 140 systolic or 90 diastolic, 0.3 g of protein in 24-hour urine sample or persistent 1+ protein measurement on urine dipstick and there are no other signs of problems with the mother or the baby.

Severe preeclampsia: after 20 weeks pregnant women with very high blood pressure (greater than 160 systolic or 110 diastolic), greater than 5 g of protein in a 24-hour sample, very low urine output, signs of central nervous system problems (severe headache, blurry vision, altered mental status), signs of liver problems (nausea and/or vomiting with abdominal pain), at least twice the normal measurements of certain liver enzymes on blood test, thrombocytopenia, signs of respiratory
problems (pulmonary edema, bluish tint to the skin) and severe fetal growth restriction.

Exclusion criteria will include patients with combined chronic diseases e.g. diabetes mellitus, autoimmune disease, thyroid, heart, chest, kidney, liver diseases and patients with preexisting chronic hypertension or taking hormonal replacement.

2.2 Methods

All subjects included in this study were asked for complete history (personal, menstrual, obstetrical, past history and drug history) and subjected to clinical and obstetrical examination. During fasting condition, urine and blood samples were collected from each case. Five milliliters blood from each case was taken and allowed to clot for 30 minutes before centrifugation for 15 minutes at 1000 x g. Serum collected and stored in three aliquots at -20° C.

Biochemical studies:
1- Proteinuria using urinary albumin creatinine ratio (ACR) that expressed as milligram of albumin excreted per gram of urinary creatinine [11].

Creatinine levels [12]: Quantitative determination of urinary creatinine was performed according to the manufacturer’s instructions (Diamond Diagnostics) with detection limit 0.09 mg/dL.

Albumin levels [13]: Quantitative determination of urinary albumin was measured turbidimetry as to manufacturer’s instructions (Biosystems S.A. Costa Brava 30, Barcelona, Spain).

2- Insulin resistance using homeostasis model assessment of insulin resistance (HOMA-IR) [14].

\[
\text{HOMA-IR} = \frac{\text{fasting insulin (µIU/mL) \times fasting glucose (mmol/L)}}{22.5}
\]

Fasting glucose levels [15]: It was measured using enzymatic colorimetric glucose oxidase method (kit purchased from spin react, Spain) with detection limit from 1 mg/dL to linearity limit 500 g/dL.

Insulin levels [16]: Concentration of insulin was measured using ELISA method according to the manufacturer’s instructions (RayBiotech Inc., USA, Cat#: EIA-VIS-1).

Pathological studies:

The collected placentae were fixed in 10% formalin solution and sent for histopathological examination to detect any pathologic abnormalities as infarctions, atheros, hyalinized areas and Tenny-Parkers changes.

Statistical analysis:

Quantitative variables were expressed as the mean, standard deviation and range and analyzed using unpaired t-test in parametric data (SD (standard deviation) <50% mean) where Mann Whitney Wilcoxon U test was used instead of unpaired t-test in non-parametric data (SD >50% mean).

Qualitative variables were expressed as number and percentage and analyzed using Chi-square test. Fisher exact test was used instead of chi-square when one or more expected cell ≤ 5 and all hypothesis tests were two-tailed with statistical significance assessed at the p-value ≤ 0.05.

3. Results

The present study results did not find any significant differences in maternal age and parity between healthy control and whole preeclamptic groups or between mild and severe preeclamptic sub-groups (Table 1).

Results also showed a significant decrease in the gestational age in whole preeclamptic group than normal controls with no significant difference between mild and severe preeclamptic sub-groups. It was found a significant increase in body mass index in preeclamptic group than control group and this increase found more in severe preeclamptic sub-group than mild one (Table 1).

Results about the maternal blood pressure presented a significant increase in both systolic and diastolic blood pressure in whole preeclamptic group compared with control group and increase in both of them found more in severe preeclamptic sub-group than mild one (Table 1).
Table 1: Clinical characteristics in control and preeclamptic groups

<table>
<thead>
<tr>
<th>variables</th>
<th>Controls (n=30)</th>
<th>Whole PE (n=30)</th>
<th>Mild PE (n=13)</th>
<th>Severe PE (n=17)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>22-36</td>
<td>20-35</td>
<td>20-35</td>
<td>23-32</td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>27.27±3.57</td>
<td>27.50±3.09</td>
<td>27.77±3.70</td>
<td>27.29±2.64</td>
<td>P1 = 0.787</td>
</tr>
<tr>
<td></td>
<td>P2 = 0.667</td>
<td>P3 = 0.976</td>
<td>P4 = 0.684</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primiparous</td>
<td>11 (36.66%)</td>
<td>17 (56.67%)</td>
<td>6 (46.15%)</td>
<td>11 (64.71%)</td>
<td></td>
</tr>
<tr>
<td>Multiparous</td>
<td>19 (63.33%)</td>
<td>13 (43.33%)</td>
<td>7 (53.85%)</td>
<td>6 (35.29%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>P1 = 0.121</td>
<td>P2 = 0.559</td>
<td>P3 = 0.064</td>
<td>P4 = 0.310</td>
<td></td>
</tr>
<tr>
<td>Gestational age at delivery (weeks)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>37-41</td>
<td>34-39</td>
<td>35-38</td>
<td>34-39</td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>38.80±1</td>
<td>37.07±1.26</td>
<td>36.92±1.11</td>
<td>37.18±1.38</td>
<td>P1 &lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>P2 = 0.224</td>
<td>P3 = 0.0001</td>
<td>P4 &lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>22.6-33</td>
<td>24.6-34</td>
<td>24.6-29.4</td>
<td>26.8-34</td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>26.38±1.99</td>
<td>28.70±2.29</td>
<td>26.96±1.19</td>
<td>30.03±2.04</td>
<td>P1 &lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>P2 = 0.0001</td>
<td>P3 &lt;0.0001</td>
<td>P4 &lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>90-130</td>
<td>140-210</td>
<td>140-150</td>
<td>160-210</td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>113.33±9.94</td>
<td>162.33±18.79</td>
<td>145.38±5.19</td>
<td>175.29±14.41</td>
<td>P1 &lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>P2 &lt;0.0001</td>
<td>P3 &lt;0.0001</td>
<td>P4 &lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>60-85</td>
<td>90-120</td>
<td>90-99</td>
<td>100-120</td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>76.17±5.68</td>
<td>103.33±10.61</td>
<td>91.92±2.53</td>
<td>112.06±3.56</td>
<td>P1 &lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>P2 &lt;0.0001</td>
<td>P3 &lt;0.0001</td>
<td>P4 &lt;0.0001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*: Statistically significant at p ≤ 0.05
P1; p value between control and whole preeclamptic groups, p2; p value between control and mild preeclamptic groups, p3; p value between control and severe preeclamptic groups, p4; p value between mild and severe preeclamptic groups.

The study results showing also a significant increase in insulin resistance value in whole preeclamptic group compared with healthy controls but no difference in insulin resistance values had been found between mild and severe preeclamptic sub-groups. Also, albumin creatinine ratio and visfatin level were increased more in whole preeclamptic group than control group and that increase was significantly much more in severe preeclamptic sub-group than mild sub-group (Table 2).

Table 2: Biochemical measurements in control and preeclamptic groups

<table>
<thead>
<tr>
<th>variables</th>
<th>Controls (n=30)</th>
<th>Whole PE (n=30)</th>
<th>Mild PE (n=13)</th>
<th>Severe PE (n=17)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HOMA-IR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>0.97-3.82</td>
<td>1.22-4.07</td>
<td>1.22-4.07</td>
<td>1.73-3.95</td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>2.06±0.68</td>
<td>3.23±0.72</td>
<td>3.05±0.81</td>
<td>3.36±0.64</td>
<td>P1 &lt;0.0001</td>
</tr>
<tr>
<td>Albumin creatinine ratio (mg/g)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>6.9-62.1</td>
<td>157.3-398.9</td>
<td>157.3-301.9</td>
<td>300-398.9</td>
<td>P1 &lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>22.47±12.52</td>
<td>302.30±67.59</td>
<td>240.68±46.98</td>
<td>349.42±34.33</td>
<td>P2 &lt;0.0001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P3 = 0.001</td>
</tr>
</tbody>
</table>
Histopathological examination of placenta showed that infarctions, atherosis, hyalinized areas and Tenny-Parkers changes were present greater in preeclamptic placentae compared with healthy controls. Only placental infarctions increase significantly in severe preeclamptic sub-group than mild preeclamptic one (Table 3, Fig 1).

### Table 3: Microscopic examination of placenta in control and preeclamptic groups

<table>
<thead>
<tr>
<th>variables</th>
<th>Controls (n=30)</th>
<th>Whole PE (n=30)</th>
<th>Mild PE (n=13)</th>
<th>Severe PE (n=17)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placental atherosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2(6.66%)</td>
<td>15(50%)</td>
<td>6(46.15%)</td>
<td>9(52.94%)</td>
<td>P1 &lt;0.0001*</td>
</tr>
<tr>
<td>No</td>
<td>28(93.33%)</td>
<td>15(50%)</td>
<td>7(53.85%)</td>
<td>8(47.06%)</td>
<td>P2 = 0.006*</td>
</tr>
<tr>
<td>Placental infarctions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3(10%)</td>
<td>22(73.33%)</td>
<td>6(46.15%)</td>
<td>16(94.12%)</td>
<td>P1 &lt;0.0001*</td>
</tr>
<tr>
<td>No</td>
<td>27(90%)</td>
<td>8(26.67%)</td>
<td>7(53.85%)</td>
<td>1(5.88%)</td>
<td>P2 = 0.014*</td>
</tr>
<tr>
<td>Hyalinized areas</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1(3.33%)</td>
<td>9(30%)</td>
<td>2(15.38%)</td>
<td>7(41.18%)</td>
<td>P3 &lt;0.0001*</td>
</tr>
<tr>
<td>No</td>
<td>29(96.66%)</td>
<td>21(70%)</td>
<td>11(84.62%)</td>
<td>10(58.82%)</td>
<td>P4 = 0.229</td>
</tr>
<tr>
<td>Tenny-Parker changes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2(6.66%)</td>
<td>24(80%)</td>
<td>10(76.92%)</td>
<td>14(82.35%)</td>
<td>P1 &lt;0.0001*</td>
</tr>
<tr>
<td>No</td>
<td>28(93.33%)</td>
<td>6(20%)</td>
<td>3(23.08%)</td>
<td>3(17.65%)</td>
<td>P2 &lt;0.0001*</td>
</tr>
</tbody>
</table>

*: Statistically significant at p ≤ 0.05
P1; p value between control and whole preeclamptic groups, p2; p value between control and mild preeclamptic groups, p3; p value between control and severe preeclamptic groups, p4; p value between mild and severe preeclamptic groups.
Figure 1: Microscopic examination of placenta: A (Normal placenta), B (Atherosis), C (Tenny-Parker changes), D (Infarctions) and E (Hyalinized areas)

Data obtained from correlation analysis found a significant positive correlation between visfatin level versus systolic blood pressure (r = 0.536, p = 0.002) and diastolic blood pressure (r = 0.469, p = 0.009) and also a significant negative correlation between serum visfatin level versus HOMA-IR (r = -0.375, p = 0.041), but no significant correlation was found between visfatin levels versus body mass index (Fig 2).

The present study did not find any significant correlation between maternal serum levels of visfatin versus histopathological changes of placentae among pregnant women with preeclampsia.

Figure 2: Correlation between visfatin level versus systolic blood pressure, diastolic blood pressure and HOMA-IR among preeclamptic women.
A. Correlation between visfatin levels and systolic blood pressure among preeclamptic women. (r= 0.536 , p= 0.002)
B. Correlation between visfatin levels and diastolic blood pressure among preeclamptic women. (r= 0.469 , p= 0.009)
C. Correlation between visfatin levels and HOMA-IR among preeclamptic women. (r= - 0.375 , p= 0.041)
4. Discussion

The aim of the present study was based on two points: firstly, identification of adipocytokines in preeclampsia and this point was achieved by determination of maternal serum levels of visfatin in normotensive and preeclamptic pregnant women and possible correlations of visfatin to measured insulin resistance and body mass index. Secondly, possible correlation between adipocytokines and histopathologic changes in preeclamptic placentae and this point was achieved by microscopic examination of placentae and study the relation between maternal serum levels of visfatin versus some pathologic abnormalities in placentae of pregnant women complicated with preeclampsia.

Changes in endothelial function and vasoactive agents have been proposed as possible pathogenic mechanisms of preeclampsia. [18] The insulin resistance syndrome has been linked to this alteration, and hyperinsulinemia promotes oxidative stress, which is related with inactivation of nitric oxide and endothelial dysfunction. [19] There are increasing data supporting the role of insulin resistance in preeclampsia [20], although this evidence has not been seen in all studies [21]. Our research confirms the increased insulin resistance in preeclamptic women and these results in agreement with those of Stefanović et al. [22] Masuyama et al. [23] also partially in agreement with our results; they found an increase in HOMA-IR in overweight patients with late-onset preeclampsia.

Since placental oxidative stress is regarded as an intermediate event in the pathogenesis of preeclampsia [24], several studies have addressed the molecular mechanisms by which oxidative stress might lead to insulin resistance. In vitro, Reactive oxygen species (ROS) and oxidative stress lead to activation of multiple serine/threonine kinase signaling cascades, these activated kinases can act on a number of potential targets in the insulin signaling pathway, including the insulin receptor and the family of Insulin receptor substrate (IRS) proteins [25].

Visfatin, another adipocytokine, is highly expressed in visceral as compared to subcutaneous adipose tissue that promotes adipogenesis. [26] The presence of visfatin transcript in human fetal membrane has been reported [27].

In the current study, results showed a significant increase in visfatin level in preeclamptic women compared with normal pregnant women. These results were in agreement with those of Zorba et al. [28] Study results found also visfatin level increased significantly in severe preeclamptic group than mild preeclamptic group and these findings were in agreement with those of Zulfikaroglu et al. [9] Unlike our results about visfatin levels, Hu et al [10] showed a significant decrease in visfatin levels in preeclamptic women.

Reasons for these conflicting results are unclear at present but it was reported that differences in specificity of the visfatin immunoassays utilized might potentially contribute to inconsistencies observed in preeclamptic women [29].

In second half of pregnancies, a physiological insulin resistance which is characterized by hyperinsulinemia, glucose intolerance and lipid abnormalities has been documented [30]. Because dysregulation of visfatin is found in insulin resistance, visfatin may be a predisposing factor in preeclampsia [31]. Fasshauer et al. found that visfatin levels were significantly elevated in pregnancies with IUGR in third trimester [32]. Also, Adali et al. [33] reported that visfatin and leptin levels of pregnant women with preeclampsia with abnormal Doppler velocimetry were significantly higher than those with normal velocimetry, in all these studies, visfatin was found to be a part of physiological feed-back mechanism improving insulin signaling in insulin resistance-associated diseases as obesity, pregnancy-related complications and type-2 diabetes mellitus.

Regarding microscopic examination of placentae, results found a significant increase in placental atherosclerosis in preeclamptic group than control group and these results were in agreement with those of Artico et al. [34] It was suggested that oxidative stress could be a driving force also in the development of acute atherosclerosis, possibly activating the phospholipase A2 (PLA2) activity in preeclamptic decidual tissue [35].

Results also found that infarctions increased in preeclamptic group than control group and these results were in agreement with those of Artico et al. [34] Zeek et al. [36] reported that presence of placental infarctions mainly due to complete
interference with their blood supply in the decidua
or in the local state by thrombosis of a spiral
arteriole or a retroplacental haemorrhage.

Concerning Tenny-parker changes (syncytial
knots); results recorded that syncytial knots
increased in preeclamptic group than control group
and these results were in agreement with those of
Artico et al. [34] Hypertension in pregnancy causes
placental hypoxia leading to loss of large number of
parenchymal cells, which causes appearance of
syncytial knots and synthesis of fibrous tissue in
their place [37].

Regarding hyalinized areas, results of
histopathological examination of placenta recorded
also a significant increase in preeclamptic group
than control group and these results agreed with
those of Majumdar et al. [38]

Correlation analysis presented a significant
negative correlation between maternal levels of
visfatin and HOMA-IR and these findings agreed
with those of Fasshauer et al. [39]

Visfatin improves insulin receptor sensitivity
[40] and owing to its action as nicotinamide
phosphoribosyltransferase (Nampt) increases
synthesis of NAD and nicotinamide
mononucleotide, enhancing pancreatic β cells and
improving insulin production and secretion [26].

Regarding correlation between visfatin levels
and blood pressure, the present study showed that
maternal visfatin level had a significant positive
correlation with blood pressure (systolic and
diastolic) and these results agreed with those of
Zorba et al. [28]. In the study of Shutte et al, a
significant correlation was found between visfatin
and mean blood pressure and they concluded that
visfatin seems to direct its effects onto the vascular
system possibly by means of mechanisms such as
inflammation and vasoconstriction [41].

Concerning correlation between visfatin levels
and body mass index, study results showed no
correlation between them, however this adipokine
correlate strongly with the amount of visceral fat in
humans [42]. This may be supported by a recent
animal study showed that visfatin is a myokine,
secreted from skeletal muscle cells in a
hypertensive rat model [43].

The evidence that the growth of fat mass is
associated with an accumulation of adipose tissue
macrophages and T-lymphocytes has raised the
hypothesis that the development of an inflammatory
process within the growing fat mass is a primary
event involved in the genesis of systemic metabolic
and vascular alterations [44]. The fact that adipose
tissue releases a wide range of adipokines, growth
factors, enzymes and enzyme substrates linked to
vascular injury provides a plausible explanation for
the role of fat in vascular disease. Visfatin among
many other products which are TNFα, leptin,
resistin, IL-1, IL-6, IL-8, and IL-18, chimerin,
serum amyloid A, MCP-1, macrophage inhibitory
factor (MIF), aortic carboxypeptidase, heparin-
binding epidermal growth factor-like growth
factor(HB-EGF), vascular endothelial growth factor
(VEGF), transforming growth factor-beta (TGF) ,
gliotensinogen, cathepsin S, estradiol, cortisol,
mineralocorticoid releasing factor, and calcitonin
peptides are probable fat-derived prothrombotic,
proinflammatory, and proatherosclerotic agents
acting in an endocrine and/or paracrine manner.
Other adipocyte products such as adiponectin, and
interleukin-10 exert an antiatherogenic effect [45].
The results of our previous study revealed that
preeclamptic women were more insulin resistant
with a significant decrease in adiponectin level
compared with healthy controls [46].

This was also in accordance with published
data showing that body mass index is only related to
visfatin in men, but not in women [47]. Lopez-
Bermejo et al. [48], Dogru et al. [49] reported absence
of correlation between plasma visfatin and body
mass index and explained this finding by the
differential regulation of visfatin expression in the
different adipose depots. Hence, the increase in
visceral adipose tissue visfatin with obesity may be
balanced by the decrease in subcutaneous adipose
tissue visfatin, such that plasma visfatin is not
affected by increasing body mass index.

5. Conclusions

Insulin resistance may be one of the casual
pathways of preeclampsia, so improving insulin
sensitivity in high risk women before and during
early pregnancy may reduce risk of preeclampsia.
Visfatin might be part of a feedback mechanism
improving insulin sensitivity in preeclamptic
women. Hypervisfatiningemia may be one of the
possible etiologies of preeclampsia, so measuring of
this adipokine may be useful for prognosis and assessment of the severity of disease.

Preeclamptic placentae underwent definite histopathological changes seemed to be the result of insufficiency of placenta in preeclampsia.

References


35 Staff AC, Ranheim T, Halvorsen B. Augmented PLA2 activity in pre-eclamptic decidual tissue—a key player in the pathophysiology of 'acute atheros' in pre-eclampsia? *Placenta* 2003; 24(10): 965-973 [PMID: 14580379]


