Relationship between skin tags, leptin hormone and metabolic disturbances

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Abstract

**Background:** Skin tags are small skin colored to dark brown sessile or pedunculated papillomas commonly occurring on the neck, axillae and the eye lids, less often on the trunk and groin. Many theories were existing to explain the occurrence of skin tags, some authors reported that skin rubbing, skin aging and a familial predisposition are causes for skin tags, while others described hormonal imbalances and hyper-insulinemia as contributing factors. The association of skin tags with many diseases as obesity, acromegaly, Crohn's disease and diabetes mellitus was proposed.

**Objectives:** Assessment of serum leptin, atherogenic lipids, HbA1C and fasting blood glucose levels in patients with skin tags trying to find a correlation between skin tags and the metabolic profile.

**Patients and methods:** 50 persons were included in this study, they were divided into 2 groups, the first group included 30 patients (each with 3 or more skin tags) and the second group was age and sex matched 20 apparently healthy volunteers with no skin tags as control. Patients and controls were subjected to full history taking, dermatological examination, measurement of body mass index and assessment of fasting glucose level, HbA1C, cholesterol, triglycerides, HDL, LDL and serum leptin level which was measured by using Solid Phase Sandwich ELISA.

**Results:** Highly significant difference was found of the fasting blood glucose, HbA1C,
serum cholesterol, LDL and VLDL between patients and controls while serum TG and HDL were higher in patients than controls but did not reach the statistical significance. As regard the serum leptin level we found a highly significant difference between patients and control.

**Conclusion:** Skin tags are associated with increased serum leptin, hyperglycemia, increased HbA1C, dyslipidemic lipid profile and obesity.

**Introduction**

Skin tags are small skin colored to dark brown sessile or pedunculated papillomas commonly occurring on the neck, frequently seen in the axillae and the eye lids, less often on the trunk and the groin. Both sexes are equally affected [1].

Histopathologically, they are composed of loose collagen fibers and dilated capillaries [2]. Skin tags are generally ignored but they may represent a cosmetic concern. Occasionally, they become irritated or necrotic and then they become painful.

In the last years, the finding of multiple skin tags has been associated with abnormality of glucose metabolism especially type II diabetes [3], and may be considered a diagnostic clue to impaired carbohydrate metabolism.

Atherogenic lipid profile is thought to be strongly associated with atherosclerosis and cardiovascular diseases and skin tags were found in association with atherogenic lipid profile [4]. Also, skin tags are cutaneous finding of metabolic disorder that comprise metabolic syndrome (obesity, hypertension, dyslipidemia, insulin resistance and hyperglycaemia)[5].

Leptin is a 16KDa protein, is a product of obese gene (Ob), produced by adipocyte including those of subcutaneous tissue. It is involved in the regulation of appetite and energy expenditure[6].

Obesity and aging can lead to increased leptin concentration due to dysfunctional leptin signaling and not associated with reduced food intake and subsequent weight loss, i.e. leptin resistance. This metabolic disturbance may have broad physiological consequences affecting all body tissues including the skin.

**Patients and Methods**

Fifty persons were included in this study, with age ranged from 27 - 56 years old. They were divided into two groups, the first group included 30 patients (each with 3 or more skin tags) and the second group was age and sex matched 20 apparently healthy volunteers with no skin tags as controls.

The patients were selected randomly from Out Patients Clinic of Dermatology, Zagazig University Hospitals in the period between January and June 2011. We excluded from
our study: patients receiving any drug that could alter leptin level as sympathomimetics, antipsychotics and retinoids. Patients receiving any drug that could alter blood lipids (e.g. statins), pregnant females and patients with thyroid function disorders were also excluded.

Methods

All patients and controls were subjected to the following:

Full history taking:

Including history of previous disease as diabetes mellitus and thyroid disease, current pregnancy, any medication known to alter leptin, glucose metabolism or blood lipids, smoking and special habits.

General examination:

For detection of any systemic diseases and measurement of blood pressure.

Dermatological examination:

Including total body examination to detect any associated skin disease, location and number of the skin lags.

Measurements of body mass index (BMI):

BMI was calculated by the following equation:

$$\text{BMI} = \frac{\text{Weight in kg}}{(\text{Height in meters})^2}$$

[7]

Laboratory tests:

- Collection of samples:

Venous blood (10ml) was taken after twelve hours fasting, samples centrifuged at 4000rpm for 10 minutes, serum samples were used for measuring fasting blood glucose level, HbAlc lipid profile parameters including cholesterol, triglycerides (TG), HDL, LDL and the rest of the samples were stored at - 80°C till the time of assay of leptin when they thawed just before analysis. The following values were considered normal as:

- Fasting blood glucose (FBG): 80 - 120mg/dL
- Cholesterol total < 200mg/dL
- Triglycerides < 150mg/dL
- HDL > 40mg/dL in men.
- and > 50mg/dL in females.

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- LDL < 100mg/dL
- HbAlc < 6.5% [8]

- Assessment of leptin levels:

Measured by Solid Phase Sandwich ELISA using a Commercial Kit (DGR leptin Sandwich ELISA E1A - 2395, USA).

- Statistical analysis:

They were done using Statistical Program for Social Science (SPSS) version 12 as follow:

- Description of quantitative variables mean, SD and range.
- Description of qualitative variables as number and percentage.
- Unpaired T-test to compare quantitative variables between two groups.
- Analysis variance (ANOVA) was used to compare qualitative data of three or more groups.
- Post HOC test was used in conjunction with ANOVA to determine which specific group pair(s) is statistically different from each other.
- Chi-square test was used to compare qualitative variables between groups.
- Fisher exact test was used instead of Chi-square when one expected cell was less than five.
- Spearman correlation test was used to rank different variables versus each other positively or inversely.

(p) Values > 0.05 was considered insignificant.

(p) Values < 0.05 was considered significant.

(p) Values < 0.01 was considered highly significant.

Results

The results of this study are illustrated in the following tables:
### Table (1): Characteristic of the study groups

In table (1) there were statistically non significant differences between patients and controls as regards gender and age distribution, while a highly significant difference in BMI was found between patients and controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>ST patients</th>
<th>Controls</th>
<th>t</th>
<th>(X²)</th>
<th>P</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>30</td>
<td>20</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Gender:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>22</td>
<td>13</td>
<td>0.01</td>
<td>0.9</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Age (years):</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>30-56</td>
<td>27-36</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>43.6 ± 7.96</td>
<td>39.1 ± 8.6</td>
<td>1.71</td>
<td>0.09</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>BMI:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>25.9 - 46</td>
<td>25 – 33.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>32.8 ± 4.46</td>
<td>28.5 ± 2.97</td>
<td>3.41</td>
<td>0.001</td>
<td>H Sig</td>
<td></td>
</tr>
</tbody>
</table>

Table (1): Characteristic of the study groups

In table (1) there were statistically non significant differences between patients and controls as regards gender and age distribution, while a highly significant difference in BMI was found between patients and controls.
In Table (2) fasting blood glucose and HbA1C were found to be highly significantly different between patients and controls with high levels in patients.

**Table (2): Fasting glucose and HbA1C**

<table>
<thead>
<tr>
<th>Variable</th>
<th>ST patients</th>
<th>Controls</th>
<th>t</th>
<th>P</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>30</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F.B.G.:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>76 - 350</td>
<td>81 - 110</td>
<td>2.84</td>
<td>0.006</td>
<td>H Sig</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>155.7 ± 85</td>
<td>92 ± 9.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbA1C:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>5.2 – 11.4</td>
<td>4.8 – 6.5</td>
<td>3.39</td>
<td>0.0014</td>
<td>H. Sig.</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>10.94 ± 1.75</td>
<td>5.36 ± 0.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Variable</td>
<td>ST patients</td>
<td>Controls</td>
<td>t</td>
<td>P</td>
<td>Sig.</td>
</tr>
<tr>
<td>--------------</td>
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<td>-------</td>
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<td>------</td>
</tr>
<tr>
<td>Number</td>
<td>30</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholesterol:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>150 - 252</td>
<td>155 - 181</td>
<td>2.64</td>
<td>0.011</td>
<td>Sig</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>184.4 ± 27.5</td>
<td>164.8 ± 9.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>80 – 189</td>
<td>93 – 181</td>
<td>0.2</td>
<td>0.83</td>
<td>NS</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>122.5 ± 35.7</td>
<td>120.2 ± 33</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>30 – 50</td>
<td>33.5 – 45.6</td>
<td>0.55</td>
<td>0.58</td>
<td>NS</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>39.7 ± 4.9</td>
<td>38.9 ± 45.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>95 – 175</td>
<td>86 – 157</td>
<td>2.2</td>
<td>0.03</td>
<td>Sig.</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>123.8 ± 24.4</td>
<td>106.3 ± 25.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VLDL:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>17.6 – 40</td>
<td>17.6 – 29</td>
<td>3.75</td>
<td>0.001</td>
<td>H. Sig.</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>28.9 ± 6.6</td>
<td>21.8 ± 4.5</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table (3):** Lipid profile in patients and controls

In table (3) the serum cholesterol, LDL and VLDL levels were significantly higher in patients than controls, while serum TG and HDL levels were higher in patients than controls but did not reach the statistical significant.
Regarding serum leptin, the highest levels were found in the patients with a statistically highly significant difference between the groups as in table (4).

<table>
<thead>
<tr>
<th>Variable</th>
<th>ST patients</th>
<th>Controls</th>
<th>t</th>
<th>P</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>30</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leptin:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>13.9 - 111</td>
<td>4 – 38.5</td>
<td>4.28</td>
<td>0.011</td>
<td>H. Sig</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>44.5 ± 23.1</td>
<td>16.5 ± 13.9</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table (4):** Leptin level among study groups

The comparison of serum leptin levels between patients as regards the gender reveals a significantly difference between females and males as in table (5).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Females</th>
<th>Males</th>
<th>t</th>
<th>P</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>22</td>
<td>8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leptin:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>18.5 - 111</td>
<td>13.9 – 42.2</td>
<td>2.41</td>
<td>0.02</td>
<td>Sig</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>50.2 ± 23.9</td>
<td>28.8 ± 10.8</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table (5):** Relation between leptin and gender
Table (6): Correlation between leptin and other parameters

Table (6) shows a significant correlation between serum leptin levels and the mean BMI with no significant correlations with other laboratory findings in patients with skin tags.

Discussion

Skin tags are very common benign dermal connective tissue neoplasm. They usually occur as small, soft, pigmented or skin colored growth. Despite the high incidence of skin tags, data about their etiopathogenesis are scarce in the medical literature [9].

Because the main etiology of skin tags is still obscure, Mc Coy 2008 [10] proposed some risk factors that increase the chance to develop skin tags as obesity pregnancy, polycystic ovarian syndrome, acromegaly, insulin resistance, obesity, type II diabetes, Crohn's disease, skin shaving, irritation and aging. Skin tags may be due to infection with human papilloma virus.

In the last years, skin tags was found to be associated with abnormalities of glucose metabolism especially type II diabetes mellitus, hyperinsulinemia and atherogenic lipid profile [4], and also coexist in association with the components of metabolic syndrome [5].

Insulin is a hormone that promotes tissue growth and stimulates glucose uptake in the tissues at an intensity that varies from one individual to another, when insulin resistance is present the cells are less responsive to the effect of this hormone and to compensate, the pancreas begins to produce a greater amount of insulin (i.e. insulin resistance) [11].

Chronic hyperinsulnemia results in increased circulatory levels of insulin growth factor-1 (IGF-1). Free IGF-1 is a potent mitogen for virtually all of the body's tissues including the skin [12].

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Leptin hormone may be related to the pathophysiology of insulin resistance in both non-insulin dependent diabetes and obesity via inhibition of insulin receptor kinase activity and inhibition of phosphorylation of insulin receptor substrate [13].

In our study, the two groups (patients and controls) were evaluated according to the age, sex, BMI, fasting blood glucose level, HbA1C, lipid profile and serum leptin level. We found significant association between skin tags and increased BMI, increased fasting blood glucose level, increased HbA1C in agreement with the results obtained by Tamega 2010 [14] and in apposition with Gorpelloglu's results in 2009 [7], who found no correlation between the presence of skin tags and these findings.

Comparing lipid profile in patients with skin tags and controls in our study showed statistically significant differences between both groups as regard serum cholesterol, LDL, VLDL levels with higher values in patients than controls. These results were going on line with Gorpelloglu's 2009 [7] who found association between skin tags and increased serum cholesterol and LDL.

Assessment of serum leptin level in the present work, revealed that the mean serum leptin level was significantly increased in patients than controls. In contrast to Gorpelloglu et al., 2009 [7] who found non significant difference of serum leptin levels between patients and controls.

The increased serum leptin level in patients with skin tags than controls can be explained by the proliferative effect of leptin in agreement with El-Safoury et al., 2010 [15] who also found an increased tissue leptin level in skin tags so, leptin may be involved in the pathogenesis of skin tags through its proliferative effect. This is further supported by Frank et al., 2000 [16] who investigated the beneficial effect of leptin on keratinocytes in rodents. Moreover, direct proliferative effects of leptin on mouse and human keratinocytes have also been reported [12].

The proliferative effect of leptin may be due to its angiogenic effect and induction of cellular proliferation as evidenced by El-Safoury et al., 2010 [15] who reported higher level of tissue leptin in small skin tags compared to large ones, which may correspond to increased proliferative potential of developing small skin tags compared to more stable larger lesions. These results provided further support to the proliferative effect of leptin.

In this study, we found that females had a significantly higher serum leptin level than males. This may be due to the increase in the total fat mass in female bodies and also due to the effects of sex hormones [17]. Serum leptin level in skin tags patients is strongly correlated with BMI [18]. Our results going with these results, but in contrast Gorpelloglu et al., 2009 [7] found a non significant difference between groups as regard gender distribution.

The relation between increased BMI and increased serum leptin level may be related to leptin secretion by adipocytes and leptin receptors deficiency at the level of hypothalamus and hyper leptinaemia.
There was no correlation between serum leptin level and lipid profile, glucose and HbA1C in our patients in agreement with Pop et al., 2009 [19] who found no correlation between HDL, cholesterol and leptin.

**Conclusion and recommendations**

The positive correlation between serum leptin levels, fasting blood glucose, HbA1C and the presence of skin tags in our study threw bright light that patients with skin tags must be investigated for the presence of metabolic abnormalities which are proved to be cardiovascular risk factors. Increased serum leptin levels in patients of skin tags reflect the proliferative and angiogenic effect of leptin which may have its role in the stimulation of growth of different cell types or by stimulation of epidermal growth factors production. Further studies including measuring serum leptin level and epidermal growth factors in patients with skin tags both in skin keratinocytes and skin tags is highly recommended for better understanding of the role of leptin and its relation to many metabolic and endocrinal abnormalities. We may propose that skin tags may be one of the important skin markers of metabolic disorders and may attract physicians and dermatologist for further investigation as it is proved to be not just a cosmetic problem.

**References**


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