Elevated Serum Leptin In Non-Obese Females With Acne Vulgaris. A Case Control Study

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ABSTRACT

Background: The majority of those who suffer from acne vulgaris are adolescents. In the preteen years, acne commonly occurs before a girl's menstrual period. About 85% of teens have acne, but it may also afflict people of all ages and last far into adulthood. Strong evidence supports the participation of follicular hyperkeratinization, hyperactivity of the epidermal keratinocytes contain acne vulgaris, and acne both have adipocytes that have upregulated mTORC1 signalling, which is directly linked to central nervous system (CNS) and peripheral tissues. The placenta, ovaries, skeletal muscles, the stomach, and bone marrow may be little of it, with white adipose tissue producing the bulk of it (11,12).

The leptin receptors enhance the pleiotropic effects of leptin because of its widespread distribution. Leptin's attachment to its receptor begins several signal transduction pathways, which in turn governs a variety of cell processes inside the body, such as metabolism and immune response. Leptin might alter skin diseases pathophysiology and, as a result, skin illnesses and systemic autoimmune diseases (13).

According to studies, up to half of women in their 20s, 26% in their 30s, and 14% in their 40s still experience symptoms. Adult acne has been claimed to affect 54–82.1 % of women and 17.9–40 % of males (8). More adult women suffer from acne, particularly active professional women in their 20s to 40s. In comparison to teenage acne, adult-induced acne is often mild to moderate in intensity and manifests as more inflammatory lesions and fewer comedones (9).

Acne's root causes are not entirely understood. Endogenous and exogenous variables, such as genetic predisposition, hormone concentrations, food, smoking, stress, and UV light exposure, can cause acne or make it worse (10).

Leptin, a 167 amino acid protein with a molecular weight of 16 kDa, is released by adipose tissue and controls the energy balance, neuroendocrine function, metabolism, immune system, and other systems in the central nervous system (CNS) and peripheral tissues. The placenta, ovaries, skeletal muscles, the stomach, and bone marrow may be little of it, with white adipose tissue producing the bulk of it (11,12).

The leptin receptors enhance the pleiotropic effects of leptin because of its widespread distribution. Leptin's attachment to its receptor begins several signal transduction pathways, which in turn governs a variety of cell processes inside the body, such as metabolism and immune response. Leptin might alter skin diseases pathophysiology and, as a result, skin illnesses and systemic autoimmune diseases (13).
We designed this case control study to compare leptin levels between acne patients and healthy controls, as well as comparing its levels between adolescent patients with acne and adult acne patients.

PATIENTS AND METHODS
This case-controlled study included a total of 63 non-obese females with body mass index (BMI) <30, 42 patients with variable degrees of acne vulgaris and 21 age-compatible healthy controls attending at Helwan University (Badr) Hospital-Dermatology Clinic. This study was conducted from August 2020 to July 2021. We included non-obese females, between 18 and 45 years, complaining of acne and they were divided into two groups; Group A: 21 adolescent female patients aged between 18-25 years with acne vulgaris, and Group B: 21 post-adolescent female patients aged between 25-45 years with acne vulgaris. The groups were subdivided into three subgroups according to severity into mild, moderate and severe. The sample size was calculated using Open Epi program version 3 and according to a previous study done in Al Menofya University who mentioned that the serum leptin level in mild group 5.80 ± 0.67 and in moderate group 6.12 ± 0.93 and in severe group 23.29 ± 25.99 with average serum leptin in cases group of 11.74 ± 9.19 while in control group it was 5.12 ± 1.29 and by changing the power of the test to 80%, the confidence interval to 95%, and the proportion of the control group to the cases group to 1:3. The 63 subjects needed for the study's overall sample size (21 controls and 42 cases) plus two subgroups of 21 cases each will make up the cases group.

We excluded male patients, obese patients with body mass index > 29.9), patient with any systemic diseases as diabetes mellitus, patients with any diagnosed auto-immune disease or other dermatological diseases, patient with history of systemic isotretinoin treatment or hormonal contraception, and pregnant or lactating women.

All patients underwent history taking, general and dermatological examination to assess the severity of acne vulgaris and to exclude the presence of other diseases. The BMI of patients with acne vulgaris and control groups was calculated and the cutoff for exclusion of obese patients was BMI > 29.9. Venous blood samples were drawn from the participants to assess serum leptin level and random blood sugar (RBS). Blood sampling was performed from 9 am to 12 pm to overcome the confounding effect of diurnal variation of leptin.

Serum leptin level measurements were performed with Leptin Human ELISA kit with double antibody sandwich ELISA technique using kits provided by Jiaxing Korain Biotech Co., Ltd (China). The test was performed according to the manufacturers’ directions. In an ELISA plate reader, absorbance was measured at 450 nm, and the findings were assessed using a standard curve. In ng/mL, serum L levels were reported. The standard curve ranged from 0.05 ng/ml to 10 ng/ml.

Ethical approval:
The Faculty of Medicine at Helwan University gave its ethical approval for this investigation [Approval number: 53-2020 on 28/7/2020]. After receiving all the facts, all the patients gave their signed approval. The Helsinki Declaration was upheld throughout the course of the investigation.

Statistical Analysis
SPSS version 22 for Microsoft Windows was used for all statistical calculations. Quantitative data were statistically reported using mean±standard deviation (SD) and range. The Student t-test for independent samples was used to compare two groups of regularly distributed data. Using LSD as a post-hoc for multiple 2-group comparisons, an ANOVA test was utilised to assess normally distributed numerical variables across more than two groups. Serum leptin levels were investigated using multivariate linear regression analysis for significant independent variables. P values lower than 0.05 were regarded as significant.

RESULTS
This case control study included 42 non-obese females with variable degrees of acne vulgaris and 21 controls. Cases were subdivided into 2 equal groups: Group A: 21 adolescent female patients aged between 18-25 years. Group B: 21 post-adolescent female patients aged between 25-45 years. Group C consisted of 21 age compatible controls who did not have any systemic illness, acne, or drug history (Table 1).

Table (1): Demographic data and characteristics of the studied groups

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Acne cases</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>18-43</td>
<td>18-44</td>
</tr>
<tr>
<td>Sex</td>
<td>Female No.</td>
<td></td>
</tr>
<tr>
<td>Female No.</td>
<td>42</td>
<td>21</td>
</tr>
</tbody>
</table>

Serum leptin was significantly higher among acne cases than controls (Table 2). However, with more stratification of the groups, no statistically significant difference was found in serum leptin levels between adolescent and adult cases (Table 3).

Table (2): Comparison between acne cases and control group regarding S. leptin

<table>
<thead>
<tr>
<th>Serum leptin</th>
<th>Acne cases Mean ± SD</th>
<th>Control group Mean ± SD</th>
<th>t. test</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.295±0.0735</td>
<td>0.233±0.0483</td>
<td>3.272</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Table (3): Comparison of the examined groups' S. leptin levels

<table>
<thead>
<tr>
<th>Serum Leptin</th>
<th>Adolescent patients</th>
<th>Adult patients</th>
<th>Adolescent controls</th>
<th>Adult controls</th>
<th>F. test</th>
<th>P. value</th>
<th>LSD (least significant difference)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>0.31± 0.07</td>
<td>0.27± 0.06</td>
<td>0.25± 0.05</td>
<td>0.21± 0.03</td>
<td>6.364</td>
<td>0.001</td>
<td>P1=0.159, P2=0.079, P3=0.131</td>
</tr>
</tbody>
</table>

P1= between adolescent patients and adult patients
P2= between adolescent patients and adolescent Controls
P3= between adult patients and adult Controls

No significant association was found between serum leptin and acne severity in either adolescent or adult groups (P value was 0.823 and 0.394 respectively). The regression model was adjusted for potential confounders; age, metabolic risk factors (RBS and BMI) and serum leptin. No evidence of significant effect was found on serum leptin among any of the groups (acne patients and healthy controls) (Table 3 and Table 5).

Table (4): Regression of variables in controls

<table>
<thead>
<tr>
<th>Unstandardized Coefficients</th>
<th>B</th>
<th>Standard Error</th>
<th>P. value</th>
<th>LowerCI</th>
<th>Upper CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leptin</td>
<td>0.310</td>
<td>0.128</td>
<td>0.026</td>
<td>0.041</td>
<td>0.579</td>
</tr>
<tr>
<td>Age</td>
<td>-0.002</td>
<td>0.002</td>
<td>0.132</td>
<td>-0.006</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.001</td>
<td>0.005</td>
<td>0.906</td>
<td>-0.010</td>
<td>0.009</td>
</tr>
<tr>
<td>Random blood sugar</td>
<td>0.000</td>
<td>0.001</td>
<td>0.996</td>
<td>-0.002</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Table (5): Regression of variables in patients

<table>
<thead>
<tr>
<th>Unstandardized Coefficients</th>
<th>B</th>
<th>Standard Error</th>
<th>P. value</th>
<th>Lower CI</th>
<th>Upper CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leptin</td>
<td>0.409</td>
<td>0.122</td>
<td>0.002</td>
<td>0.162</td>
<td>0.657</td>
</tr>
<tr>
<td>Age</td>
<td>-0.003</td>
<td>0.002</td>
<td>0.073</td>
<td>-0.006</td>
<td>0.000</td>
</tr>
<tr>
<td>BMI</td>
<td>0.000</td>
<td>0.004</td>
<td>1.000</td>
<td>-0.008</td>
<td>0.008</td>
</tr>
<tr>
<td>Random blood sugar</td>
<td>0.000</td>
<td>0.001</td>
<td>0.616</td>
<td>-0.002</td>
<td>0.001</td>
</tr>
</tbody>
</table>

DISCUSSION

In the current study; serum leptin was statistically higher among acne cases than healthy controls with no significant difference in serum leptin within acne cases between adult and adolescent age groups.

Our study yielded similar results to that obtained by Sallam et al. (14) who found that both obese and non-obese acne patients had significantly higher serum leptin levels in cases compared to controls. We contend that these findings are consistent with Dreno (15) theory that leptin is a novel mediator in inciting inflammation and altering the lipid profile in sebocytes, and that there may be a link between the development of inflammatory acne and food intake.

In contrast to the current findings, both Ozuguz et al. (16) and Kaynak et al. (17) discovered no statistically significant difference in leptin levels between the groups of people with good skin and people with acne vulgaris. Ozuguz et al. (18) also recruited non-obese patients. Also, a study of college students aged 19–34 years discovered no change in leptin levels between patients with and without acne (19).

The differences between our study and the studies mentioned above may be because our study only included non-obese adolescent and post-adolescent females, excluding obese females to avoid the confounding effect of obesity on serum leptin levels. Their patients were adolescent males and females. Another plausible explanation might be that severe and moderate types of acne vulgaris were included in the current investigation, which would have prevented a substantial increase in serum leptin levels among acne vulgaris patients. Further study on big sample sizes must be done because such a change may also be the result of a smaller sample size.

According to Karadag et al. (19), basal leptin levels in the acne group were considerably lower than those in the control group. After isotretinoin treatment, leptin levels decreased significantly. They suggested that isotretinoin may affect leptin levels. On the other hand, Cemil et al. (20) showed that isotretinoin may exercise its anti-inflammatory activity by boosting blood leptin levels in a study associating leptin as one of the variables driving anti-inflammatory rule. Therefore, leptin may have a double rule that justifies the opposing points of view that leptin levels are
elevated after an acute infection and in cases of chronic inflammation, suggesting that leptin may actively participate in the immune system and host defence, and leptin can be either pro- or anti-inflammatory in adipose tissue.

According to our findings, serum leptin levels didn’t show any significant association with acne severity. That agrees with Sallam et al. (14), who reported a non-significant variation in relation to the serum leptin levels among the four studied acne groups (mild, moderate, severe, and very severe).

LIMITATIONS
The research population was constrained to a lower sample size, and it employed a cross-sectional approach. Additionally, the association between acne and the degree of glycemic index may be underestimated or overestimated when utilising the random blood sugar.

CONCLUSION
We found that acne vulgaris in non-obese females was associated with elevated serum leptin level compared to healthy controls. Our result supports the hypothesis that leptin may have a significant role in the pathogenesis of acne, especially in females. According to our findings, this association was not severity related.

REFERENCES