Serum Desnutrin Level and Acne Severity

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ABSTRACT

The role of metabolic factors in pathophysiology of acne is highly controversial. A potential role for various factors such as desnutrin has been suggested in the pathogenesis of acne. The aim of this study was to measure the serum levels of desnutrin and insulin and estimate insulin resistance (HOMA-IR), in acne patients in comparison to normal controls, and evaluate the relationship of these levels to severity of acne, in order to investigate the role of these factors in the pathogenesis of acne. The present study included 60 acne patients and 20 healthy controls. Full history and clinical assessment of acne severity were performed for patients. Body mass index was calculated for patients and controls. Serum samples were collected from patients and controls after fasting for 10 hours for estimation of laboratory parameters (fasting blood sugar, insulin, triglycerides, LDL, HDL and total cholesterol). The homeostasis model assessment of insulin resistance (HOMA-IR) was used to calculate insulin resistance. Desnutrin levels were determined by enzyme-linked immunosorbent assay (ELISA). The results of this study revealed no significant difference in desnutrin, fasting blood sugar, insulin and HOMA-IR between acne patients and controls. No statistically significant difference was detected between patients with mild, moderate and severe acne regarding BMI, laboratory parameters. The present study couldn’t prove a significant relation between serum desnutrin, insulin and HOMA-IR levels in acne patients.

Keywords: Acne, Insulin resistance (HOMA-IR), Desnutrin

INTRODUCTION

Acne vulgaris is a common disorder of pilosebaceous unit affecting adolescents. Most cases of acne present with pleomorphic variety of lesions, consisting of comedones, papules, pustules and nodules (1).

There are many factors involved in the pathogenesis of acne such as follicular hyperkeratinization, abnormal follicular desquamation, increase in sebum production, bacterial proliferation, inflammation and genetic role (2). However, acne may also be a common component of many systemic diseases or syndromes which are also usually linked to insulin resistance (3).

IR is defined clinically as the inability of a known quantity of exogenous or endogenous insulin to increase glucose uptake and utilization in an individual as much as it does in a normal population. It causes an insufficiency in insulin-stimulated glucose transport in the skeletal muscle and fat tissue, as well as a suppression of glucose production in the liver (4).

In 2004, three laboratories independently identified the same novel TAG lipase named desnutrin, ATGL and phospholipase A2, leading to re-evaluation of the classic model of lipolysis (5,6,7). Desnutrin/ATGL is predominantly expressed in adipose tissue and exhibits high substrate specificity for TAG (5,7).

It has been reported that desnutrin is inhibited by insulin secretion and increased lipolysis due to extended fasting. Suppression of desnutrin lipase activity by insulin has been reported to contribute to the development of obesity, hyperlipidemia and insulin resistance (8).

Since insulin/IGF-1 receptors are expressed in epidermal keratinocytes, hyperinsulinemia may lead to an increased proliferation of basal keratinocytes within the FPSU duct inducing failure of terminal differentiation of follicular corneocytes, thus actively participating in acne pathogenesis. Furthermore, insulin also stimulates the synthesis of androgens, leading to high sebum production, a recognized correlate of acne severity (9).
METHODS

The present study is cross sectional study performed on 60 acne patients and 20 healthy controls during the period from February 2016 to November 2016 in Dermatology Clinic, Faculty of Medicine, Fayoum University. The number of patients recruited was calculated based upon the least prevalence of acne as with (8).

Inclusion Criteria:

Any Patient presented to the Dermatology Clinic, Faculty of Medicine, Fayoum University with acne vulgaris > 18 years old is recruited to participate in the study after obtaining an informed consent. Full history was obtained and Exclusion Criteria included patients having systemic disease (Diabetes, hypothyroidism or hyperthyroidism), pregnancy, malignancy and systemic drug or alcohol abuse.

Informed Consent:

Objective of the study and steps were explained clearly to every patient.

Examination: The weight and height for each patient were measured and body mass index (BMI) was calculated:

\[ BMI = \frac{\text{Weight (In kg)}}{(\text{Height (In Meters)})^2} \]  

(10).

Dermatological examination: of the distribution, type of lesions and severity of acne:

Mild
Moderate
Severe
Comedones and papules
Comedones, papules and pustules
All of the above plus nodules and cysts

(11).

Blood collection:

Five ml blood samples were collected after fasting for 10 h for analysis of serum glucose, insulin, lipid profile (TG, Cholesterol, HDL and LDL) and desnutrin. Insulin resistance index (HOMA-IR) levels were calculated according to the formula: (serum glucose/18 x insulin)/22.5. Levels above 3 were considered as indicators of insulin resistance (12).

Data collected were statistically analyzed to estimate the relationship between acne patients and controls regarding clinical data. BMI and laboratory parameters (FBS, Insulin, HOMA-IR, lipid profile and desnutrin) to detect if those factors really affect acne severity whether positively or negatively.

The serum level of desnutrin was measured by ELISA kit provided by Kono biotec ELISA (KN2059Hu) and serum insulin was measured by ELISA using Calibotech Human Insulin kit. This kit provides a method for the quantitative measurement of insulin in human serum. Blood glucose level was measured using glucose PAP on flexor 200 autoanalyzer.

The Statistical analysis was performed using SPSS software version 18 in windows 7. The data obtained in the study were expressed as means± SD. In-dependent student t-Test and one way ANOVA test were used to compare quantitative data of independent groups. Chi square test was used to compare qualitative groups. Bivariate pearson correlation test to test association between variables. The level p < 0.05 was considered the cut-off value for significance.

RESULTS

The present study included 60 patients with acne vulgaris and 20 healthy individuals as controls group. The patients are divided into four groups mild, moderate, severe and patients who received netlook for 6 months. The patients group included 46 females (57.5%) and 34 males (42.5%), their ages ranged from 16 to 29 years (mean ±SD: 20.65±3.25).

There was no statistically significant difference between our five study groups (patients with mild, moderate, severe acne, control and patients on netlook) as regards laboratory parameters (FBS, Insulin, Desnutrin and HOMA-IR).

Regarding lipid profile, our study showed that there was no statistically significant difference between the five study groups as regards triglyceride and HDL levels. There is no statistically significant correlation with p>0.05 between serum desnutrin level and any of patients' variables (age, BMI, Insulin, FBS, TG, Cholesterol, HDL and LDL).

There was no statistically significant difference between patients with mild, moderate and severe acne as regards BMI (p value>0.05).

Table-1. Comparison between acne severity and laboratory parameters.

<table>
<thead>
<tr>
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<th>Mild n=15</th>
<th>Moderate n=15</th>
<th>Severe n=15</th>
<th>Isotretinoin n=15</th>
<th>Control n=20</th>
<th>p-value</th>
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<tbody>
<tr>
<td>FBS (mg/dl)</td>
<td>73.9±22.9</td>
<td>64.8±13.5</td>
<td>73.3±20.1</td>
<td>81.1±19.2</td>
<td>73.3±20.1</td>
<td>0.069</td>
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<tr>
<td>Insulin (uiU/ml)</td>
<td>1 (0.1-4.6)</td>
<td>0.9 (0.1-7)</td>
<td>0.6 (0.1-2.4)</td>
<td>0.7 (0-4.5)</td>
<td>1.3 (0-7.2)</td>
<td>0.305</td>
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<tr>
<td>Desnutrin (ng/ml)</td>
<td>63±17.6</td>
<td>67.9 (26.8-133)</td>
<td>72.8 (12.5-486)</td>
<td>63.5 (12.5-118.8)</td>
<td>61.3 (12.5-565)</td>
<td>0.733</td>
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<td>HOMA-IR</td>
<td>0.153/0.012-0.882</td>
<td>0.131 (0.012-1.2)</td>
<td>0.099 (0.015-0.526)</td>
<td>0.153 (0.005-0.986)</td>
<td>0.217 (0.019-1.4)</td>
<td>0.300</td>
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DISCUSSION

This study included 15 patients (18.75%) with mild acne, 15 patients (18.75%) with moderate acne and 15 patients (18.75%) with severe acne, 15 patients (18.75%) received Netlook for 6 month duration and 20 healthy controls (25%).

In our study there was no statistically significant difference between patients and controls regarding Desnutrin levels (p> 0.05) and also we didn’t find a correlation between serum glucose, insulin and desnutrin levels (r=0.002, p>0.05), (r=0.199, p>0.077) respectively.

This is in contradistinction to what was observed by Demir and colleagues (8), who observed significant higher levels of desnutrin in patients with acne than in controls. Also he found that serum glucose, insulin and HOMA-IR levels were significantly higher in patients group than controls. However, evaluation of patients and controls for insulin resistance revealed that only six patients (24%) had insulin resistance while none of the control subjects had IR. But similar to our study, there was no significant difference between patients and controls regarding age, sex and BMI (p>0.05).

He reported that pathological high levels of serum fatty acids have been reported to cause hyperinsulinemia and insulin resistance. However, insulin resistance may be caused by dysregulation of lipolysis rather than increased lipolysis. No other studies mentioned such a relation.

Also his finding may be due to the frequent consumption of carbohydrates of high glycemic index with worldwide adoption of western diet in this population leading to acute hyperinsulinemia which influences follicular epithelial growth, keratinization and sebaceous secretion. Acne begins about the same time as the preadolescent increase in plasma insulin (13,14).

The present study revealed no significant difference between patients and controls regarding BMI. Similar results have been demonstrated by Kaymak and colleagues (15), who observed that there was no significant difference in BMI (p value >0.05) between 49 Turkish university students with acne and 42 control subjects.

Similarly, Ismail and colleagues (16) studied 44 acne patients and 44 controls aged 18-30 years and revealed no significant difference between the two groups regarding BMI.

Also, Lu and Hsu (17) reported that BMI is negatively associated with the number of acne lesions in Taiwanese women with moderate to severe post-adolescent acne.

However, in other studies, BMI has been identified as a risk factor for the development of acne. In a study conducted by Tsai and colleagues (18) on 3,274 school children, they reported significantly higher BMI in subjects

<table>
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<th>Table-2. Lipid profiles of the study patients.</th>
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<tr>
<td>Cholesterol (mg/dl)</td>
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<td>TG (ulU/ml)</td>
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<td>LDL (mg/dl)</td>
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<td>HDL (mg/dl)</td>
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Figure-1. Serum desnutrin level in study patients.
with acne than those without acne although similar to our study they revealed no significant correlation between BMI and severity of acne (p>0.05). The risk of moderate to severe acne was reduced in their patients with lower body mass index.

Also, Di Landro and colleagues (19) have recently reported that acne risk was reduced in Italian adolescents and young adults with lower BMI.

Halvorsen and colleagues (20) observed an association between increased BMI and acne in female Norwegian adolescents.

In our study all participants were subjected to estimation of fasting blood sugar and insulin levels and calculation of HOMA-IR.

Regarding serum insulin level, there was no significant difference between patients and controls groups with (p> 0.05).

Similar to our result Kaymak and colleagues (15) found that insulin level in their study in the acne group was not different from the control group, and they suggested that insulin does not play a major role in pathogenesis of acne in that sample.

In contrast with our result Abulnaja and colleagues (21) found in their study, the levels of serum insulin in obese subjects with acne were significantly higher than obese subjects without acne (p< 0.01) and the levels of insulin in the obese subjects with or without acne was significantly higher than the non-obese subjects with or without acne (p< 0.05).

Our study showed that acne is not associated with insulin resistance. In addition, there were no significant differences between fasting blood glucose or fasting insulin levels, or HOMA-IR indices, and acne severity.

These results are similar to Balta and colleagues (22) who showed that post-adolescent acne is not associated with insulin resistance. In addition, there were no significant differences between fasting blood glucose or fasting insulin levels, or HOMA-IR indices, and acne severity.

Also Kaymak and colleagues (15) reported that serum glucose, insulin levels, and HOMA-IR indices in younger patients with acne vulgaris and control subjects did not differ significantly, which represents a set of findings similar to those in the present study. In addition, Kaymak and colleagues (15) did not find any statistically significant association between acne severity and insulin resistance.

Cetinozman and colleagues (23) evaluated androgens and insulin sensitivity markers before and after treatment with isotretinoin in women with severe post-adolescent acne. They reported that all parameters were similar in patients and controls at baseline. Isotretinoin therapy increased BMI and triglyceride levels without any effect on androgens or insulin sensitivity. As a result, these authors reported that severe acne itself is not associated with hyperandrogenemia or insulin resistance.

Ertugrul and colleagues (24) also reported that three months of isotretinoin treatment did not change insulin sensitivity in patients with acne vulgaris.

By contrast with these studies, Del Prete and colleagues (25) who found in their study that the male subjects with acne had a significant increase in the insulin resistance (IR) compared with the control subjects (p = 0.016) and even in their study the subjects with acne and BMI <24.9 there was significant increase of IR (p = 0.05).

Also Smith and colleagues (13) reported fasting blood glucose, insulin levels, and HOMA-IR indices to be elevated in young males with acne vulgaris compared with healthy controls.

These inverse correlations may be attributed to that insulin resistance increased immediately at the onset of puberty and gradually decline until the third decade to near pre pubertal with improvement of insulin sensitivity (13,26).

Regarding serum HDL levels we did not find any statistically significant difference in serum HDL levels between subjects with and without acne. Similar results were reported by Balta and colleagues (22) did not find any statistically significant difference in serum HDL-C levels between subjects with and without post-adolescent acne.

In accordance with previously mentioned studies, we found no statistically significant difference in serum triglyceride levels between acne patients and control subjects. These differences may reflect the effects on serum lipid concentrations of dietary habit, socioeconomic status, smoking habit, and racial and genetic factors.

The present study couldn’t prove a significant relation between serum desnutrin, insulin and HOMA-IR levels in acne patients.

The major limitations of the present study concern its comparatively small study population. In addition, as well as not having used a validated tool to measure the diet and calculating the exact glycemic index and measured its relationship with acne.

Conflicts of Interest

Authors declare that there is no conflict of interests regarding the publication of this paper.

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increased in alopecia areata patients. *Cutaneous and Ocular Toxicology;* 32(2): 102–106.


