

Original Research Article

Role of insulin-like growth factor 1 in pathogenesis of acne vulgaris: relation to acne severity and body mass index

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ABSTRACT

Background: Acne vulgaris is a multifactorial skin disease. A potential role for insulin-like growth factor-1 (IGF-1) has been suggested in the pathogenesis of acne. Several studies have shown that elevated levels of serum IGF-1 correlate with overproduction of sebum and acne. **Objective:** Measurement of the serum level of IGF-1 in acne patients in comparison to normal controls and evaluating the relationship of these levels to severity of acne and body mass index (BMI), in order to investigate the role of this factor in the pathogenesis of acne.

Methods: Fifty-four patients with acne vulgaris and 42 healthy controls were included. History taking, dermatological examination, clinical assessments of acne severity, calculation of BMI were performed for patients. Blood samples were collected from all participants for estimation of serum IGF-1 level using enzyme linked immunosorbant assay.

Results: There was a significantly higher serum IGF-1 level in acne patients ($p < 0.05$) than controls. Authors didn't find a relation of significance between elevated serum IGF-1 level and degree of acne severity and BMI ($p > 0.05$). There was a significant positive correlation between serum IGF-1 level and age of the patients.

Conclusions: There is a significantly higher serum IGF-1 in acne patients than controls not related to acne severity and BMI. That is adding to the scientific evidence of IGF-1 role in pathogenesis of acne vulgaris.

Keywords: Acne vulgaris, Acne severity, Body mass index, IGF-1, Pathogenesis

INTRODUCTION

Acne vulgaris is a chronic inflammatory disease of pilosebaceous unit (PSU). The pathogenesis of acne is complex and multifactorial, as there are many pathophysiologic events; increased sebum production, hyper cornification of the pilosebaceous duct, colonization with *Propionibacterium acnes* (*P. acnes*) and inflammation.^{1,2}

There is increasing evidence supporting the interplay of growth hormone (GH), insulin and IGF-1 signaling during puberty, which may play a causal role in

pathogenesis of acne through influencing adrenal and gonadal androgen metabolism. The highest incidence of acne occurs when IGF-1 levels peak.^{3,4} GH stimulates the liver to produce IGF-1, and both i.e. GH and IGF-1 are important in maintenance of epidermal homeostasis.^{5,6} Accordingly, elevated levels of GH and IGF-1 may be involved in the pathogenesis of acne. IGF-1 is more stable and reflects cumulative level of GH, and thus it is more suitable for serum sampling.⁷

IGF-1 is a polypeptide hormone that has almost the same molecular properties of insulin, and it plays an important role in regulating cellular proliferation and

differentiation.^{8,9} In sebaceous gland organ cultures, IGF-1 induced sebaceous lipogenesis, by the induction of Sterol Response Element-Binding Protein-1 (SREBP-1), which preferentially regulates genes of fatty acid synthesis. IGF-1 is important for lipid synthesis in sebocytes and for keratinocyte proliferation.^{6,10} Several studies have shown that elevated levels of serum IGF-1 correlate with overproduction of sebum and acne.^{11,12}

Aim of the study was to investigate the possible role of IGF-1 in the pathogenesis of acne vulgaris through assessment of 1) serum levels of IGF-1 in acne patients in comparison to controls, 2) relation of IGF-1 levels to acne severity and BMI.

METHODS

This case control study included 54 patients with acne vulgaris, their ages ranged from 13-30 years and 42 healthy volunteers served as controls. Patients were recruited from the Dermatology Outpatient Clinic of Fayoum University Hospital during the period from April 2017 to February 2018. Exclusion criteria included history of any systemic disease and systemic treatment for acne during the last 6 months. Full medical history was obtained from all patients (age, sex, disease duration, family history) and from controls.

Dermatological examination was performed for all patients to diagnose acne and determine distribution, type and grade of acne severity and Body Mass Index (BMI)

was calculated for all participants. Authors applied the grading system of, and classified acne lesions to mild, moderate and severe grades.¹³ Blood samples were collected from patients and controls and drawn into serum separator tubes and centrifuged at 3000 xg after clot formation for 10 minutes to separate serum. Serum IGF-1 levels were estimated using Assay Max Human IGF-1 Enzyme-Linked Immunosorbent Assay (ELISA) Kit (Catalog No. EI1001-1). Serum IGF-1 was considered elevated when its level >170 ng/ml and BMI was considered elevated if >25.^{14,15} The study was approved by the Ethical Committee; Faculty of Medicine, Fayoum University, and signed informed consents were obtained from all participants.

Statistical analysis

Statistical analysis was performed using Chi-square test or Fisher's exact test and two-tailed test. p values <0.05 were considered statistically significant.

RESULTS

This study included 54 patients with acne vulgaris (20 mild, 20 moderate and 14 patients with severe acne), aged 13-30 years (mean±SD: 18.74±3.18) who were attending the Dermatology outpatient clinic of Fayoum University Hospital. Of these, 40(74%) were females and 14(26%) were males and family history of acne vulgaris was found in 33(61%) patients. The study, also, included 42 age and sex matched controls (Table 1).

Table 1: Demographic and clinical data in both study groups.

		Patients (n=54)	Controls (n=42)	P value
BMI	Mean ± SD	21.95±4.06	20.78±2.84	0.355
	Weight in kilograms / (height in meter) ²	Range	16.2-38.1	
Family history	+ve	33 (61.1%)	-	
	-ve	21 (38.9%)		
Acne grades	Mild	20 (37.05%)	-	
	Moderate	20 (37.05%)		
	Severe	14 (25.9%)		
IGF-1 ng/mg	Mean±SD	148.15±98.80	87.14±49.74	0.029*
	Range	32-460	28-200	

*p<0.05 is statistically significant

In acne patients, BMI values ranged between 16.2-38.1 (mean±SD: 21.95±4.06) and in the control group, BMI values ranged between 14.7-24.9 (mean±SD: 20.78±2.84) with no statistically significant differences between both groups as regards BMI (p>0.05).

Serum IGF-1 levels in acne patients group ranged between 32-460 IU/ml (mean±SD: 148.15±98.80) and in the control group, serum IGF-1 levels ranged between 28-200 IU/ml (mean±SD: 87.14±49.74). There was a

significant higher serum level of IGF-1 in acne patients as compared to controls (p<0.05; Figure 1). Serum levels of IGF-1 in patients with mild acne (mean±SD: 166.80±118.69), moderate acne (mean±SD: 140.80±96.14) and severe acne (mean±SD: 132.0±69.34), didn't show a statistical significant difference regarding IGF-1 level (p>0.05). Thus, there was no significant statistical relation between elevated serum level of IGF-1 and different grades of acne severity in acne patients (p>0.05). Regarding relation of IGF-1 level and BMI,

there was no statistically significant relation found between serum level of IGF-1 and BMI in acne patients (p value >0.05).

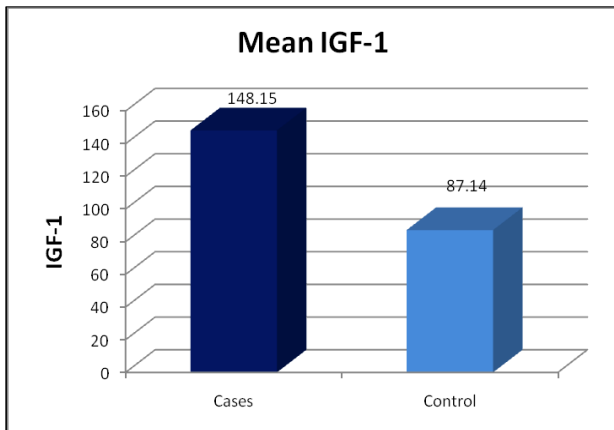


Figure 1: Mean IGF-1 in both study groups.

DISCUSSION

The present study revealed a significantly higher serum IGF-1 level in acne vulgaris patients in comparison to normal controls ($p=0.029$), with no statistically significant relation between the elevated serum IGF-1 level and acne severity or BMI ($p>0.05$).

Sebum production is one of the critical factors in the pathogenesis of acne. Maximal sebum production begins during puberty, which coincides with the peak incidence of acne, when serum IGF-1 and GH levels reach their peak in midpuberty.^{16,17}

IGF-1 induces keratinocyte proliferation *in vitro* and *in vivo*; it mediates its effects through IGF-1R, which is activated and phosphorylated in skin keratinocytes, in response to IGF-1 stimulation, in a differentiation-dependent manner as proved by.¹⁸ In addition, 19 reported that IGF-1 can also increase lipid production in sebocytes *in vitro* via the activation of IGF-1R through multiple pathways.

These results were in agreement with the findings of other studies that revealed a statistically significant higher IGF-1 level in acne patients than controls ($p<0.001$) and there was also no statistically significant difference between patients with mild, moderate and severe acne regarding IGF-1 level ($p>0.05$).^{7,20}

In contrast to these results, studied 49 patients with acne and 42 controls, and revealed no significant difference between patients and controls regarding serum IGF-1 levels.²¹ Also, reported high serum IGF-1 level in severe acne patients when compared with mild, moderate acne patients, and healthy controls ($p=0.0001$).²²

The factors that are known to cause variation in the levels of GH and IGF-1 in the circulation including: genetic

make-up, the time of day, age, sex, exercise status, stress levels, nutrition level and BMI, disease state, race, estrogen status, as reported by.²³

These results revealed a non-significant relation between IGF-1 level and family history ($p>0.05$), which may contradict the possible role of genetic factor in affecting the level of IGF-1. However, this finding may be due to the limited sample size of the present study. In the current study there was no significant difference between patients with acne and normal controls as regarding sex, and there was no significant correlation between IGF-1 level and sex of the patients ($p>0.05$). These results were in agreement with.^{4,6,7} However, this finding was not consistent with the results of studies conducted by.^{24,25}

Regarding BMI in this study, the statistical difference between acne patients' group and normal controls was insignificant. In addition, there was no significant correlation between IGF-1 level and BMI in patients with acne. These results were in agreement with findings of.^{20-22,26} However, unlike previous studies, BMI has been identified as a risk factor for the development of acne, in a study conducted by.²⁷

CONCLUSION

In conclusion, the serum IGF-1 level is significantly elevated in patients with acne vulgaris. There is no relation between IGF-1 level and acne severity and BMI. There is growing scientific evidence in support of the role of IGF-1 in pathogenesis of acne vulgaris, for further investigation.

Recommendations

Well-designed studies on larger scales are required to further explore the role of IGF-1 in the pathogenesis of acne vulgaris, and to elaborate the relation between IGF-1 and acne severity and its treatment, and to study IGF-1 gene polymorphism. It is necessary to estimate serum androgens, blood glucose level and diet in acne vulgaris patients and correlate them to IGF-1 levels. Physicians should conduct routine serum IGF-1 evaluation in resistant cases with acne vulgaris.

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