The Egyptian Journal of Hospital Medicine (July 2023) Vol. 92, Page 5604- 5607

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

Bakr Mohamed Elzawahry[1], Nermeen Ibrahim Bedair[2], Yasmine Mohamed Amrousy[3], Mahmoud Adel Attia*[4]

[1]Department of Dermatology, Faculty of Medicine, Cairo University, Egypt

[2]Departments of Dermatology, Andrology, Sexual Medicine and STDs and [3]Clinical Pathology, Faculty of Medicine, Helwan University, Egypt

[4]Cairo Hospital of Dermatology, Egyptian Ministry of Health, Cairo, Egypt

***Corresponding author:** Mahmoud Adel Attia, **Mobile:** (+20) 01064598309, **E-mail:** mahmoud.adel91@gmail.com

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 sebaceous glands, colonisation of Propionibacterium acnes and yeast, and inflammation in the complicated etiology of acne.

Objective: To evaluate leptin level in non-obese females with acne vulgaris.

Patients and Methods: This was a cross sectional study that was conducted in Helwan University (Badr) Hospital-Dermatology Clinic on 42 non-obese females with variable degrees of acne vulgaris, and 21 age compatible controls from people without any systemic disease, acne lesions, or medication. This study was conducted from August 2020 to July 2021.

Results: The current study demonstrated that the mean value of serum (S.) leptin was statistically higher among acne cases than control group (0.295; 0.233) P= 0.002. There was a non-statistically significant difference between severity in acne groups regarding S. leptin.

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.

Keywords: Serum Leptin Level - Non-Obese Females - Acne Vulgaris.

INTRODUCTION

A typical chronic inflammatory condition of the pilosebaceous unit is acne vulgaris. About 80% of young adults and adolescents are affected, and older persons are being diagnosed with it more often [(1)].

It has been proposed that acne vulgaris is a cutaneous manifestation of the mTORC1-driven metabolic disorders, which also include type 2 diabetes, obesity, and cancer. The Western diet, particularly its high hyperglycemic load and milk consumption, may activate the mTORC1 signalling pathway, which is mediated by insulin-like growth factor 1 (IGF-1) [(2)].

Because epidermal keratinocytes contain insulin/insulin-like growth factor 1 receptors, insulin elevation may increase basal keratinocyte proliferation in the follicular sebaceous unit duct, impairing the terminal differentiation of follicular corneocytes and contributing to acne pathogenesis [(3)]. Visceral obesity and acne both have adipocytes that have up-regulated mTORC1 signalling, which is directly linked to enhanced lipogenesis and inflammation. The over activation of mTORC1 caused by nutritional excess is a key factor in acne [(4)].

The severity of acne in boys was shown to be connected with pubertal maturity. Fifty percent of boys aged 10 and 11 had more than 10 comedones [(5)]. Acne was seen in 78% of females between the ages of 8 and 12 in another research [(6)]. There are only 1% of men and 5% of women that have acne by the time they are 40 years old [(7)]. Adult women are more likely to have symptoms, and they are more severe, than adult men. 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 make very 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)].

Received: 15/01/2023
Accepted: 16/03/2023

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

			Acne cases	Control group
Age (years)	**Range**		18-43	18-44
	Mean ± SD		26.17± 7.75	25.95± 7.30
Sex	**Female**	**No.**	42	21

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

		Acne cases	Control group	t. test	P. value
Serum leptin	**Mean ± SD**	0.295± 0.0735	0.233± 0.0483	-3.272	<0.001

Table (3): Comparison of the examined groups' S. leptin levels

		Adolescent patients	Adult patients	Adolescent controls	Adult controls	F. test	P. value	LSD (least significant difference)
Serum Leptin	**Mean ± SD**	0.31± 0.07	0.27± 0.06	0.25± 0.05	0.21± 0.03	6.364	0.001	P1=0.159 P2=0.079 P3=0.131

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 by any of the variables on serum leptin among any of the groups (acne patients and healthy controls) (Table 4 and Table 5).

Table (4): Regression of variables in controls

	Unstandardized Coefficients		P. value	LowerCI	Upper CI
	B	Standard Error			
Leptin	0.310	0.128	0.026	0.041	0.579
Age	-0.002	0.002	0.132	-0.006	0.001
BMI	-0.001	0.005	0.906	-0.010	0.009
Random blood sugar	0.000	0.001	0.996	-0.002	0.002

Table (5): Regression of variables in patients

	Unstandardized Coefficients		P. value	Lower CI	Upper CI
	B	Standard Error			
Leptin	0.409	0.122	0.002	0.162	0.657
Age	-0.003	0.002	0.073	-0.006	0.000
BMI	0.000	0.004	1.000	-0.008	0.008
Random blood sugar	0.000	0.001	0.616	-0.002	0.001

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 **Kaymak *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 [18].

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

1. **Gold M, Baldwin H, Lin T (2018):** Management of comedonal acnevulgaris with fixed-combination topical therapy. J Cosmet Dermatol., 17(2):227-231.
2. **Melnik B (2018):** Acne vulgaris: The metabolic syndrome of the pilosebaceous follicle. Clinics in Dermatology, 36(1):29–40.
3. **Napolitano M, Megna M, Monfrecola G (2015):** Insulin resistance and skin diseases. Scient World J., 15: 479354. doi: 10.1155/2015/479354.
4. **Melnik B (2015):** Linking diet to acne metabolomics, inflammation, and comedogenesis: an update. Clinical, Cosmetic and Investigational Dermatology, 15: 371-388.
5. **Thielitz A, Goldberg D, Berlin A (2012):** Acne and rosacea—epidemiology, diagnosis and treatment. DOI:10.1007/s00403-012-1234-4.
6. **Spencer E, Ferdowsian B (2009):** Diet and acne: a review of the evidence. International Journal of Dermatology, 48(4): 339–347.
7. **Dawson A, Dellavalle R (2013):** Acne vulgaris. BMJ., 346 (5): f2634. doi: 10.1136/bmj.f2634.
8. **Fisk W, Lev-Tov H, Sivamani R (2014):** Epidemiology and Management of Acne in Adult Women. Curr Derm Rep., 3:29–39.
9. **Dreno B, Thiboutot D, Layton A *et al.* (2014):** Large-scale international study enhances understanding of an emerging acne population: adult females. J Eur Venereol., 29: 1096–1106.
10. **Ramos-e-Silva M, Ramos-e-Silva S, Carneiro S (2015):** Acne in women. Br J Dermatol., 172: 20–26
11. **Park H, Ahima R (2015):** Physiology of leptin: energy homeostasis, neuroendocrine function and metabolism. Metabolism, 64(1): 24–34.
12. **Aydin S (2018):** Gestational diabetes and peptides in breast milk, nutrition and diet in maternal diabetes. Pp: 367-383. DOI:10.1007/978-3-319-56440-1_29
13. **Münzberg H, Morrison C (2015):** Structure, production and signaling of leptin. Metabolism, 64: 13–23.
14. **Sallam M, Al Sohafy M, Abdel Salam D (2021):** Serum leptinand adiponectin in obese and non-obese patients with acne vulgaris. The Egyptian Journal of Hospital Medicine, 85(1): 2845-2851.
15. **Dreno B (2017):** What is new in the pathophysiology of acne, an overview, European Academy of Dermatology and Venereology, 31(5): 8–12.
16. **Ozuguz P, Kacar S, Asik G *et al.* (2017):** Evaluation of leptin, adiponectin, and ghrelin levels in patients with acne vulgaris. Human and Experimental Toxicology, 36(1): 3-7.
17. **Kaymak Y, Adisen E, Ilter N *et al.* (2007):** Dietary glycemic index and glucose, insulin, insulin-like growth factor-I, insulin-like growth factor binding protein 3, and leptin levels in patients with acne. J Am Acad Dermatol., 57(5): 819–823.
18. **Kwon H, Yoon J, Hong J *et al.* (2012):** Clinical and histological effect of a low glycaemic load diet in treatment of acne vulgaris in Korean patients: a randomized, controlled trial. Acta Derm Venereol., 92: 241–246.
19. **Karadag A, Ertugrul D, Takci Z *et al.* (2015):** The effect of isotretinoin on retinol-binding protein 4, leptin, adiponectin and insulin resistance in acne vulgaris patients. Dermatology, 230(1): 70-74.
20. **Cemil B, Havva H, Gulfer O *et al.* (2016):** Effects of isotretinoin on body mass index, serum adiponectin, leptin, and ghrelin levels in acne vulgaris patient. Postepy Dermatol Alergol., 33(4): 294–299.