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Assessment of Serum Apelin Level in Acne Vulgaris Patients: a pilot case-control study

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Abstract

Background: **Acne vulgaris (AV) is a disorder of the pilosebaceous unit, mainly affecting the neck, trunk, face, and arms. Key factors include increased sebaceous gland secretion, follicular hyperproliferation, androgen activity, inflammation, and Propionibacterium acnes colonization. Recent studies highlight insulin resistance and adipokines in acne pathogenesis. Apelin, a new adipokine, is linked to insulin resistance.** ***Aim*****: To measure serum apelin levels in acne vulgaris patients and its correlation with disease severity.** ***Subjects and Methods:*** **This is a case control study including thirty-Six randomly chosen acne patients and 36 healthy controls. Acne patients were classified by severity (mild, moderate, severe) using the Global Acne Grading System (GAGS). Serum apelin levels were measured by enzyme-linked immunosorbent assay, and insulin resistance was estimated using the Homeostasis Model Assessment for Insulin Resistance (HOMA-IR).** ***Results:*** **Apelin levels were significantly higher in acne vulgaris patients. However, no significant difference in apelin levels was found across varying acne severity. Insulin levels and HOMA-IR were significantly higher in acne patients compared to controls, indicating insulin resistance. Apelin levels correlated positively with HOMA-IR, fasting glucose, and insulin levels. Conclusion: Serum apelin may contribute to acne vulgaris pathogenesis by promoting insulin resistance. Larger studies are needed to confirm its role.**

Key Words: Acne vulgaris, Apelin, insulin resistance.

Introduction

Acne vulgaris is a disease of the pilosebaceous unit that often appears from puberty to young adulthood. The most important pathogenic factors of AV are high sebaceous gland secretion, hyperproliferation of follicle, high action of androgen, inflammation and Cutibactrium acnes colonization [(1)].

Globally, AV is regarded as one of the most common skin conditions [(2)]. It is estimated to impact roughly 10% of the world's population, making it the eighth most common disorder worldwide. AV is most popular in postpubertal teenagers especially with the disease's more severe forms [(3)].

Apelin, one of the adipocytokines, was discovered for the first time in 1998. Apelin has been found to do many biologically diverse actions in different organs. It attaches itself to the G protein-coupled receptor family member known as the APJ receptor [(4)]. Apelin is linked to obesity and insulin resistance, according to data gathered from both clinical and basic research contexts. It increases the use of glucose, reduces the release of insulin, and inhibits catecholamine-mediated lipolysis [(5)].

Insulin resistance is a disorder in the different biological units in the body that makes them less responsive to insulin [(6)]. Recent data draw attention to the action of insulin resistance and adipocytokines on the pathogenesis of AV [(7)].

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Therefore, the purpose of this study was to find out serum apelin level in AV patients in Ismailia and how it related to the severity of the condition.

Methods

An analytical case control study included 36 patients with acne vulgaris (group I), who were recruited from the Dermatology Outpatient Clinics using simple randomization method and 36 apparently healthy individuals (age and sex matched) from controls from blood donors who served as a control (group II). The 2013 Helsinki Declaration standards were followed in the conduct of this study. Both the local Institutional Review Board and the Research Ethics Committee (No.#4514) granted their approval. Before being enrolled in this trial, all patients gave their informed permission.

Patients of both genders with age above 18 years old with acne vulgaris were included. Exclusion criteria were patients who had concomitant inflammatory disease, cardiovascular disease, autoimmune diseases, or received isotretinoin treatment in the last 6 months; patients with chronic dermatological diseases as psoriasis and atopic dermatitis; pregnant and lactating females and diabetic patients

Diagnosis of AV based on history and clinical findings including presence of comedones, erythematous papule, pustule, or nodule. Every patient had a thorough history taken as well as a general and dermatological examination. The global acne grading system (GAGS) was used to classify the acne patients into mild, moderate, and severe categories. The sum of the six geographic sub-scores determines the overall severity score. In each region, the factor is multiplied by the most strongly weighted lesion (1 for ≥ one comedone, 2 for ≥ one papule, 3 for ≥ one pustule, and for ≥ one nodule). The factors are two for the forehead and cheeks, one for the chin and nose, and three for the chest and upper back. Surface area, pilosebaceous unit density, and distribution were taken into consideration while determining the regional parameters. Scores between 1 and 18 were classified as mild, scores between 19 and 30 as moderate, scores between 31 and 38 as severe, and scores greater than 38 as very severe [8].

Assessment of serum apelin level and Insulin resistance:

The assessment of serum level of apelin was done by enzyme-linked immunosorbent assay (ELISA) by Human Apelin (AP) ELISA Kit, Shanghai Sunred Biological Technology Company, made in china (2021). Fasting glucose level was tested by Enzymatic Colorimetric Method. Serum insulin level was tested by insulin ELISA kits (Catalog No. BDIN31-BA). The Homeostasis Model Assessment for Insulin Resistance (HOMA-IR) index, which was calculated using the following formula, was used to quantify insulin resistance: Fasting insulin (μU/mL) × fasting glucose (mmol/L)/22.5.

Statistical analysis

The statistical package for social science software, version 25.0 (Armonk, NY: IBM Corp.), was used to analyse the data. Numbers and percentages were used to describe categorical data. The normality of the distribution was confirmed using the Kolmogorov-Smirnov test. The mean ± standard deviation was used to represent data that was normally distributed. The data was analysed using the Pearson coefficient, F-test (ANOVA), Student t-test, and Chi-square test. P-values were deemed significant if they were less than 0.05.

Results

A case-control study including 36 acne vulgaris patients (group I) and 36 apparently healthy volunteers as a control (group II) with matched age and gender was done in Dermatology Outpatient Clinics. Most of the patients 33(91.7%) were females, as were the majority of the control group. The patients' mean ± SD age was 22.56 ± 3.84 years, while the mean ± SD age of the control group was 23.36 ± 4.26 years. There were insignificant differences between patients and controls as regard each of age and sex. GAGS score of the disease ranged from 2.0 to 41.0 with a mean ± SD of 15.58 ± 9.97, with

25(69.4%) patients had mild acne, 7(19.4%) had moderate acne, 2(5.6%) had severe acne and 2(5.6%) had very severe acne. Twenty-four (66.7%) of patients had progressive course and 12(33.3%) had relapsing course. Nineteen (52.8%) patients had a family history of acne.

The difference in fasting glucose levels between the two groups was insignificant. Serum level of fasting glucose in AV patients ranged from 70.0 – 164.0 mg/dL, and in the control group, ranged from 70.0 – 219.0 mg/dL. The serum level of insulin in AV patients ranged from 3.90 – 10.0 mIU/ml, and in the control group, ranged from 1.30 – 6.20 mIU/ml.AV patients had statistically significantly higher HOMA-IR levels (Table 1).

Table 1: Comparison between the two studied groups according to Fasting glucose, insulin, HOMA-IR test and apelin

	Patients (n = 36)	Control (n = 36)	U	p
Fast glucose level (mg/dl)				
Min. – Max.	70.0 – 164.0	70.0 – 219.0	533.0	0.194
Mean ± SD.	94.61 ± 21.30	90.36 ± 23.89		
Median (IQR)	93.50 (76.0 – 107.0)	89.50 (80.0 – 94.50)		
Insulin level (mIU/ml)				
Min. – Max.	3.90 – 10.0	1.30 – 6.20	85.50*	<0.001*
Mean ± SD.	6.11 ± 1.87	2.45 ± 1.27		
Median (IQR)	5.60 (4.70 – 7.10)	1.95 (1.70 – 2.40)		
HOMA test				
Min. – Max.	0.70 – 3.85	0.60 – 1.30	455.0*	0.029*
Mean ± SD.	1.34 ± 0.71	0.91 ± 0.21		
Median (IQR)	1.15 (0.72 – 1.83)	0.88 (0.71 – 1.10)		
Apelin level (pg/ml) Min. – Max. Mean ± SD. Median (IQR)	210.0 – 411.0 274.08 ± 56.08 260.0 (222.0 – 312.0)	40.0 – 312.0 90.08 ± 75.24 60.0 (55.0 – 73.50)	81.50*	<0.001*

IQR: **Inter quartile range** SD: **Standard deviaton.**
U: Mann Whitney test. HOMA-IR**: Homeostatic Model Assessment of Insulin Resistance.**
p: p value for comparing between the studied groups *****: Statistically significant at p ≤ 0.05

Serum level of apelin in AV patients ranged from 210.0 – 411.0 pg/mL, and in the control group, ranged from 40.0 – 312.0 pg/mL.Serum apelin levels were statistically significantly elevated in AV patients compared to controls (Table 1). There was statistically insignificant difference between apelin levels and disease severity (p=0.110). HOMA-IR levels in patients with mild AV ranged from 0.70 – 3.85, moderate AV ranged from 0.72 – 1.64, severe AV ranged from 0.70 – 0.80, and in patients with very severe AV ranged from 2.0 – 2.20. There was no statistically significant difference between HOMA-IR levels and disease severity (Table 2). Serum apelin exhibited a significant and strong direct correlation with HOMA-IR levels, fasting glucose levels, and insulin levels (Table 3). So, when the insulin resistance or fasting glucose alone or insulin alone increased, the level of Serum Apelin will also increase.

Table 2: Relation between AV severity and HOMA-IR levels in patients group (n = 36).

HOMA test	Acne severity				H	p
	Mild (n= 25)	Moderate (n= 7)	Sever (n= 2)	Very sever (n= 2)		
Min. – Max.	0.70 – 3.85	0.72 – 1.64	0.70 – 0.80	2.0 – 2.20	4.71	0.194
Mean ± SD.	1.36 ± 0.79	1.22 ± 0.38	0.75 ± 0.07	2.10 ± 0.14		
Median	1.10	1.20	0.75	2.10		

SD: Standard deviation. H: H for Kruskal Wallis test.
p: p value for comparison between the studied categories

Table 3: Correlation between Apelin level and HOMA test with different parameters in patients group (n = 36).		
	Apelin level (pg/ml)	
	r_s	p
HOMA test	0.553	<0.001*
Age (years)	0.010	0.952
GAGS	-0.075	0.663
Fast glucose	0.601*	<0.001*
Insulin	0.512*	0.001*

rs: Spearman coefficient.
*: Statistically significant at p ≤ 0.05

Discussion

AV is a multifactorial inflammatory disease. Androgen mediated heightened sebum production, follicular hyperkeratinization, colonization by Propionibacterium acnes and inflammation are the main pathogenic factors [(1)]. The adibocytokine apelin and insulin resistance, which could influence AV,thought to be connected together. Apelin enhances glucose utilization, reduces insulin production, and inhibits lipolysis mediated by catecholamines[(5)]. Higher insulin like growth factor –1 levels are connected to greater levels of fascial sebum secretion and may encourage increased androgen production [(9)]. To detect the association between Apelin and AV, 36 AV patients and 36 controls were recruited in this study. The study reported that 52.8% of AV patients had positive family history, this came in agreement with Sorour et al. 2018 and Bhate and Williams 2013 who found that Family history was more frequent in the group with AV which demonstrated the genetic role in AV pathogenesis. There is a significant difference in insulin serum levels and HOMA-IR values between patients and controls. They are higher in AV patients which reflected the vital role of insulin resistance in pathophysiology of AV, and this came in parallel with Sharma et al. 2019, Nagpal et al. 2016 and Emiroğlu et al. 2015 who discovered that patients with AV exhibited significantly higher fasting insulin levels, HOMA-IR scores, and, as a result, greater states of insulin resistance compared to the controls. Contradictory to these results, Balta et al. 2015 revealed that insulin resistance may not be a significant factor in the pathophysiology of acne, as no notable differences in fasting blood sugar, insulin levels, or HOMA-IR values were observed between AV patients and controls.

HOMA-IR levels in this study did not differ significantly between acne cases of different severity grades, this came in parallel with Singh and Shri 2022 who found that insulin resistance was present in patients with AV, but no direct correlation was found between the severity of acne and insulin resistance. In contrast with these results, Jain et al. 2022 found that HOMA-IR levels were positively associated with the severity of acne. In this study, patients with AV exhibited significantly elevated serum apelin levels (P < 0.001), this came in parallel with Sorour et al. 2018 who assessed apelin13 level in AV patients and found that the mean level of serum apelin13 in AV patients was significantly high in comparison with controls. Apelin 13 is an active form of native apelin assessed in this study. Serum levels of apelin in this study did not differ significantly between acne cases of different severity grades.

High serum Apelin levels in this study had significant direct strong correlation with HOMA-IR levels, fasting glucose level and insulin levels. The elevations of serum apelin levels in insulin resistant subjects have been previously reported by Li et al. 2006. According to Daviaud et al. 2006, elevated apelin concentrations in type 1 diabetes may be an effort to overcome insulin resistance and make up for its absence. Therefore, the rise in serum apelin levels in an insulin resistant state may be a compensatory mechanism of the body.

Conclusion

Serum apelin levels were significantly elevated in patients with AV, independent of the severity. Acne vulgaris is linked to a state of insulin resistance as HOMA-IR increased in all acne vulgaris patients and serum Apelin had significantly strong correlation with HOMA-IR levels. So Apelin may have a role in AV pathogenesis by its action in insulin resistance.

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