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Correlation of serum Insulin-Like Growth Factor one with acne severity

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Abstract

Background and Objectives: Acne is a common chronic inflammatory skin condition; Acne could present as inflammatory or non-inflammatory lesion. Acne can be varied in severity from patient to another, generally, it can present in mild, moderate or severe degree.

Excessive production of sebum by sebaceous glands in the skin contributes in acne formation. One of the factors associated with the production of sebum is Insulin-Like Growth Factor in serum. Current study tries to find any association between acne severity and serum Insulin-Like Growth Factor.

Method: On a sample of 40 female patients with acne, aged 14-26 years at the outpatient clinic as a cross sectional study. Serum IGF-1 level was compared to their acne severity across three groups, mild, moderate and severe acne. Global acne grading system was used to classify the acne severity.

Results: Median levels of IGF-1 were 208.09 ng/ml. Mean serum level of IGF-1 is 254.53ng/ml, 200.03ng/ml and 172.39ng/ml in severe, moderate and mild acne respectively. Acne severity strongly associated with serum level of IGF-1 which is statistically significant. No significantly association between serum level of Insulin-Like Growth Factor and the age of patients was found. Likewise, the severity degree of acne has no association with body mass index

Conclusion: There is a direct relationship between mean level of IGF-1 in patients with AV with degree of their acne severity.

Key word: Insulin growth factor-1; Acne vulgaris; Acne severity.

Introduction

Acne vulgaris is a chronic inflammatory skin illness targeting pilosebaceous follicle. It is multifactorial in origin and it can affect almost all ages but mainly it's a disease of adolescent age group. Clinically it can present with inflammatory papules and pustules, comedonal acne, nodules and less often scars[1]. The presentation varies according to acne severity. Severe acne often presents with breakouts like cysts, nodules, whiteheads and blackheads, sometimes they are painful and may leave scars afterwards. Acne vulgaris has negative impacts on psychosocial life of the patients in the form of loss of self-confidence, shame and depression even suicidal ideation among

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female patients in particular[2-3]. The pathogenesis of acne vulgaris depends on several aetiologies; mainly four factors are addressed. Firstly, excessive production of sebum, ductal occlusion by hyperkeratinazation of epidermal follicles, inflammation and overgrowth of Propionibacterium acnes (P. acnes)[4]. Acne patient have high sebum excretion rate but, this is alone doesn't cause acne, patient who had acne may continue to have high sebum excretion or patient with Parkinson disease have high sebum excretion with no acne[5]. Though, drugs which decrease sebaceous gland activity can be therapeutic for acne since, well known association between sebum and acne recognized[6]. Serum Insulin-Like Growth Factor-1 will reach its peak in adolescence like the peak incidence of AV in the same life period. Moreover, with age, serum IGF-1 levels will decrease along with a decrease in the incidence of AV, hence, the process of sebum formation somehow related to serum ILG-1[7]. Research on female patients showed that, serum ILG-1 has direct relation with growth and differentiation of sebaceous glands, as it has a mitogenic effect[8]. Because variability in serum IGF-1 level affects females more than males and the effect of IGF-1 in men is obscured by higher serum androgens effects on acne[9]. Higher metabolic rate is a pathophysiological sign of acne patients, high carbohydrate diets and fatty diets are food related triggers of higher metabolic rate and acne occurrence, thus, consumption of lower carbohydrate and fatty diets would help to control acne[10]. Insulin-Like Growth Factor-1 is an indicator of high metabolic rate, it also has a role in carbohydrate metabolism, high serum IGF-1 persistently could be a sign of acne, or even a cancer like prostatic cancer. Thus, drugs targeting a reduction in IGF-1 could decrease a risk of cancer as well as decrease in acne severity[11]. Role of IGF-1 in acne vulgaris is solely in sebum production, it also helps to regulate keratinocyte production, the effect of IGF-1 shown in researches in the pathogenesis of acne and the androgenic hormones impact on acne is due to the effect of IGF-1[12]. The Current study seeks any association between serum IGF-1 and acne severity. By confirming the hypothesis of this association, an alternative therapeutic challenge available for acne treatment as well as patient education based on association of higher glycemic diet and IGF-1 with acne severity would assist in controlling acne severity.

Patients and methods:

The current study is descriptive observational cross-sectional study tries to find the type of association between serum IGF-1 and degree of acne severity among female patients. For this research, 40 patients were enrolled. Patients with mild were 12, 16 patients with moderate and 12 patients with severe acne. Age of patients was between 12-26 years. Serum IGF-1 level was assessed and compared according severity across three groups, the consent achieved from the patients and the research approved by ethical committee of Kurdistan Board of Medical Specialties. The global acne grading system (GAGS) was used to classify the severity of AV. The data obtained from 1st of February to 1st of March, 2019 in the outpatient department of Sulaimani center for treatment of skin diseases. The inclusion criteria of samples were female patients with AV at various degree of severity after been diagnosed through their medical documents and physical examination in outpatient clinic of Sulaimani skin center. While the exclusion criteria of Samples were diabetes mellitus, polycystic ovarian disease, pregnant and breastfeeding female patients, morbid obesity, patients who receive hormonal

therapy, insulin and/or oral glucose-lowering agents and male patients.in other words, any conditions interfering with serum IFG-1 were not included in the study. History taking and clinical examination were performed at Sulaimani center for treatment of skin diseases. Sampling 2 mL of patients' serum was used to measure their serum IGF-1. After twelve hours overnight fast blood was taken. Enzyme linked immunosorbent assay (ELISA) and all laboratory assessments were performed in a single lab center, Spearman correlation is used to find correlation between body mass index BMI and serum IGF-1 with acne severity. A p-value of ≤0.05 was considered statistically significant. Data analysis was done using software program SPSS version 22.

Results

In the current study, there were 40 female cases. Their age ranges from 12 to 26 years old. Median age is 19.5 and (SD=3.44). Out of 40 cases, 12 patients had mild acne, 16 cases had moderate acne and 12 patients suffered from severe acne. Correlation between age of the patient and serum IGF-1 was not significant (p-value 0.889) by using Spearman's rank correlation. Regarding BMI of patients according to distribution of their acne severity, only 3 cases had BMI<18.5 2 cases with mild, 1 case with moderate and no cases with severe acne. Those with ideal body weight were 32 in total, 10 cases with mild, 13 with moderate and 9 cases with severe acne. Those with BMI of 25-29.9 i.e., who were overweight, were only 5 cases, 2 patients with moderate and 3 with severe acne. The comparison between acne severity and BMI revealed non-significant (P-value 0. 255) associated Table (1).

Table 1: Comparison of BMI values with acne severity.

Group	BMI			Total	p- value
	<18.5	18.5-24.9	25-29.9		
Severe	0 (0.0%)	9 (28.1%)	3 (60.0%)	12 (30.0%)	0.255
Moderate	1 (33.3%)	13 (40.6%)	2 (40.0%)	16 (40.0%)	
Mild	2 (66.7%)	10 (31.3%)	0 (0.0%)	12 (30.0%)	
Total	3 (100%)	32 (100%)	5 (100%)	40 (100%)	

Acne severity distribution in the current study divided in to three categories, mild acne category had mean serum IGF-1 of 172.3917ng/ml. moderate acne category had mean serum IGF-1 of 200.0375ng/ml. and those with severe acne had mean serum IGF-1 of 254.5250. There is strong direct association between serum IGF-1 and severity of acne (p-value 0.001) Table (2).

Table 2: Comparison of IGF (ng/ml) values by acne severity**.**

	IGF-1			
Group	**Mean**	**N**	**Std. Deviation**	**p-value**
Severe	254.53	12	57.92	0.001
Moderate	200.03	16	44.93	
Mild	172.39	12	49.88	

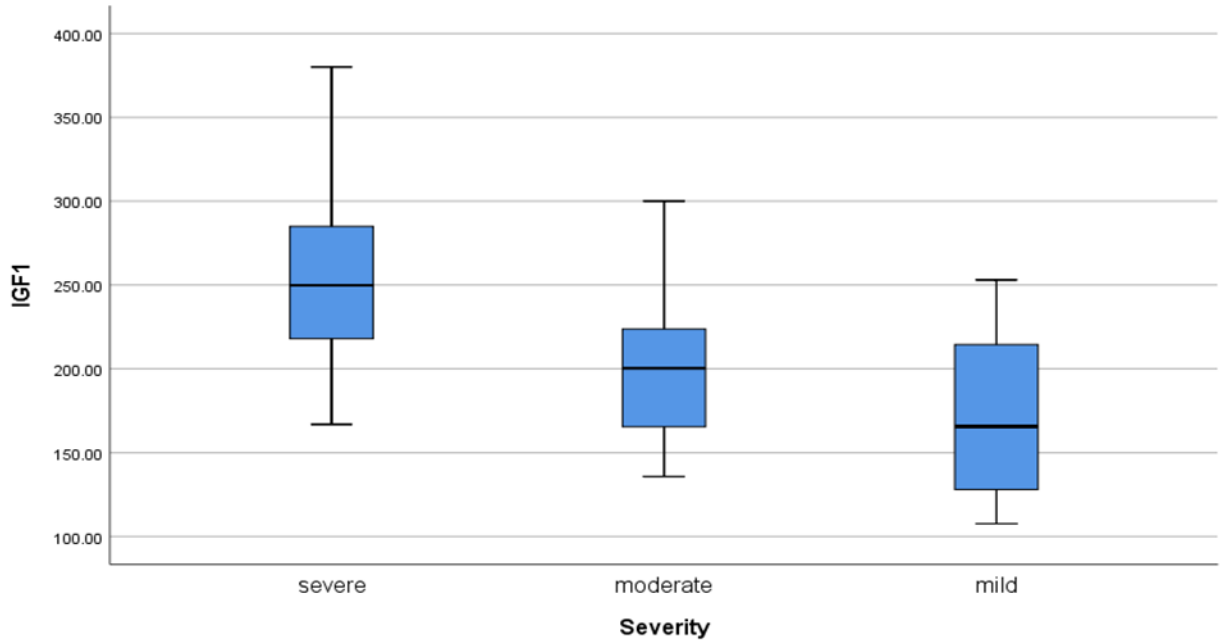

Figure 1. Relationship between serum IGF-1 level and acne severity.

Discussion

Liver is main source of production of IGF-1 and transportation in blood is via IGFBP-3. It is a polypeptide of 70-aminoacides, IGF-1 structure is similar to insulin molecule. Highest sebum excretion and acne development happen during puberty which is concomitantly the time of highest androgen, growth hormone and IGF-1 level. After puberty only androgens levels remain high while, acne usually fading hence, independent role of GH and IGF-1 in high sebum production and acne is possible[13]. Per our knowledge, this study is the first of its kind attempts to find the impact of IGF-1 on acne severity in Kurdistan Region-Iraq. Studies done in different countries confirm that IGF-1 has a role in acne formation or induce sebum secretion. One of the earliest studies done in Japan, they compared serum IGF-1 level in 31 control 82 post-adolescent women with acne. They found significant increase ($p < 0.001$) of serum IGF-1 in acne patient[14]. Female patients were compared on the basis of acne severity and their serum IGF-1 level. In the current no significant association was found between serum IGF-1 level and BMI neither with serum IGF-1 level with age. But, there was a significant relation between serum IGF-1 level and acne severity. This result is similar to those reported by a local research conducted by Saleh, who evaluated the role of GH and IGF-1 in acne severity, androgens productions and secondary hyperlipidemia. His study had no control group and participants were only males aged (18-30). Their cases were grouped into three categories. 13 mild acne, 13 moderate and 14 patients with severe acne. He noted that, IGF-1 is (440.77_+46.71ng/ml) in severe > (365.84_+16.97) in moderate and (335.98_+18.15) in mild acne subgroup which are higher than in normal males (243.23_+59.84). He concluded that, Iraqi males with acne have higher levels of IGF-1

($p < 0.0001$) and GH, they can induce androgen formation and secretion and worsening of acne together[7]. Polat conducted his study on post teenager females, looking for any link between high serum (IGF-1) and high sebum secretion and/or acne, they found higher mean serum IGF-1 level in acne patient compared to control group, nodular acne patients have even higher serum IGF-1 level then the rest of acne patients[15]. Vora et al, searching for any association between facial sebum excretion and serum IGF-1. However, their study is of small sample size16 participants (5 women, 11 men) and they didn't clarify inclusion and exclusion criteria but, they frankly found that high serum IGF-1 level may cause higher facial sebum excretion in both genders and increase acne lesion counts in women only[9]. Another study carried out by Rahaman et al, they found mean plasma IGF-1 level in acne cases was significantly higher than in non-acne controls (p-value 0.04). IGF-1 level directly associated with severity of acne (p-value 0.01). they conclude that, Plasma IGF-1 levels positively correlate with severity of acne[16]. Studies have shown that, IGF-1 level induce acne via two mechanisms, firstly through induction of sebum production by peroxidation within sebaceous cells and secondly through increasing sex hormone levels[10]. IGF-1 can stimulate lipid production in adipocytes[17]. Higher serum level of IGF-1 in acne patients compared to control group and direct correlation with acne severity can indicate that, acne patients have higher metabolism rate and nutrition related life style can contribute to acne occurrence and severity, moreover, modification of nutritional life style may have a role and recommended in acne control, like restriction of carbohydrates, proteins and calorie restrictions and intense walking exercise[8, 18]. Insulin like growth factor-1 reducing drugs like Metformin may contribute to treatment of acne[19], however this needs further study. It has been suggested that increasing the glycemic load will stimulate occurrence of AV with production of insulin-like growth factor-1 (IGF-1), a mitogen that can stimulate follicular growth[20]. Ben-Amitai, performed an interesting study on the role of (IGF-1) level on acne vulgaris in a children's centre. The study was conducted on 21 (10 males, 11 female) children with Laron syndrome which is autosomal recessive disease, characterized by congenital absence of IGF-1. They concluded that, absence of IGF-1 can prevent acne development and is fundamental for acne formation[13]. Karadag et al, were examining the effect of Isotretinoin on serum IGF-1 level, IGFBP-3 and GH. Post-adolescent patients with acne vulgaris enrolled (15 men, 32 women). Hormonal levels detected just before treatment and after 3 month of therapeutic dose of isotretinoin. They found that both IGF-1 and IGFBP-3 were significantly reduced after treatment (p-value < 0.01) while GH level didn't change. They thought that, therapeutic effect of the drug may have led to IGF-1 reduction[21]. In the study by Wulan et al, they try to find the association of serum IGF-1 and acne severity without having control group, they found that, the mean levels of IGF-1 in patients with moderate degrees of AV was higher than mild or severe AV. IGF-1 levels can vary influenced by many factors[22].

Iftikhar revealed that, IGF-1 levels were significantly different between cases and controls and between mild and severe acne, but not between mild and moderate acne[12]. In contrast to the study carried out by Saleh et al, in which they enrolled only male acne patients, in this study female patients were enlisted. There is negative relationship between serum estrogen and IGF-1 levels. Peak level of serum IGF-1 will be reached at adolescent period. In both men and women, serum level of IGF-1 decreases with time, but when estrogen level reaches the peak in premenopausal women, this coincides with the highest rate of decline in IGF-1 levels[22].

Melnik & Schmitz, reported, the PI3K / Akt pathway can be activated via high-glycaemic diets and milk consumption which can increase IGF-1 and in turn lipid formation in sebaceous glands alongside keratinocyte and adipocyte proliferation. Insulin/IGF-1 signalling may be increase by hydrophilic protein of cow's milk moreover, cow's milk contains active IGF-1 which its amino acid chain is similar to humans. It also increases IGF-1/IGFBP-3 ratio which cause increase bioavailability of IGF-1[23]. It found that, excessive usage of milk is linked to 10-20% higher serum IGF-1 in adults[24]. Knowing the above facts, we can understand that IGF-1 is crucial in increased sebum production and acne pathogenesis, interfering with the signals that come from IGF-1 inside sebaceous gland can be one of the mechanisms of decreasing sebum secretion and therapeutic for acne[25]. Pharmaceutical IGF-1 blockers might open a new window in acne therapeutics and further studies are mandatory in this field.

Conclusion

Insulin-like growth factor-1 (IGF-1) signaling during puberty may contribute in acne pathogenesis. There is a direct relationship between mean level of IGF-1 in patients with AV with degree of their acne severity. Increased IGF-1 levels in acne patients corresponding with increased acne severity, points that acne is a syndrome of insulin resistance

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Conflict of interests

There were no conflicts of interest.

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