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Measurement of serum levels of interleukin 17 in acne vulgaris Patients and its relation to severity of the disease

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Abstract

The purpose of this research was to examine the role of IL-17 in acne vulgaris (AV) patients especially in the development of scarring lesions, the severity of illness, and disease etiology. Fifty patients with AV of varied severity (Group A) were included in this case-control study from the Outpatient Clinic of the Dermatology Department at Beni Suef University Hospitals. Thirty healthy volunteers, matched for age and sex, made up the control group IL-17 serum levels were reviewed using ELIZA among study contributors. The age and sex distributions of the groups under study did not differ significantly. Mild acne accounted for 36% of the patients, moderate for 34%, and severe for 30%. Scarring was seen in 28% of the subjects in the present study. The levels of IL-17 were significantly higher in the case group when compared with the control group.

There are still gaps in our understanding of the pathophysiology of this common condition, and this study's results points to interrelationships between IL-17 and AV etiology

1. Introduction:

Comedones, papules, pustules, nodules, and scars are the hallmarks of acne vulgaris (AV), a common inflammatory skin disorder that affects pilosebaceous follicles. Its primary sites of impact are the head, neck, upper body, and upper extremities. Although the disorder commonly begins in youth and is considered an adolescent disease, it often persists into adulthood [1].

Hormonal effects, follicular hyperkeratinization, inflammation, environmental factors, genetic predisposition, and the development of Propionibacterium acnes are some of the many factors that contribute to AV. A major contributor to the development of AV is inflammation [2]. AV is becoming more and more linked to metabolic diseases including glucose intolerance and lipid abnormalities, which supports the idea that the illness affects more than simply the skin [3].

Interleukin-17 is a family of six cytokines that includes IL-17A through IL-17F. The most studied and most homologous cytokines for immune modulation are interleukin-17A (IL-17) and interleukin-17F (IL-17F). The Th17 subset of CD4+ helper T cells secretes IL-17RA and IL-17RC, two cytokines that communicate with one another [4].

The purpose of this research was to determine the prevalence of IL-17 in AV patients' serum and to draw connections between this cytokine and the etiology, progression, and scarring of the illness.

2. Patients and Methods:

This case-control study was conducted on 2 groups; Group A consisted of fifty patients diagnosed with AV, whereas Group B consisted of thirty healthy individuals who were age- and sex-matched. Participants came from Beni Suef University Hospitals's Dermatology Department's Outpatient Clinic during a six months period in 2021.

2.1 Inclusion criteria:

Patients aged 15 to 40 years with varying degrees of acne severity as

classified by the Global Acne Grading System (GAGS) **[5]**.

2.2 Exclusion criteria:

- Patients with AV on topical (less than 2 weeks before take a sample) or systemic therapy (less than 1 month before take a sample).
- Patients with history of cardiovascular or renal disease, diabetes mellitus, hypertension or hyperlipidemia.
- History of using any type of vasoactive drugs.

2.3 Methods:

All patients underwent the following procedures**:**

I. Comprehensive history acquisition;

including personal history, current medical status, familial history of AV and post-acne scarring, as well as previous drug use and systemic illnesses.

II. Clinical assessment:

1. Thorough general examination.

2. A thorough dermatological evaluation to determine clinical variation, severity of AV, and the presence of AV scars.

3. The diagnosis of AV was determined through a thorough examination of the patient's medical history and the distinct clinical features of non-inflammatory lesions, which include closed comedones (whiteheads) and open comedones (blackheads), alongside inflammatory lesions such as papules, pustules, nodules, and/or cysts found on the face, chest, and upper back.

III. Evaluation of AV severity:

Acne severity was evaluated using GAGS: To determine the extent and distribution of Acne, the GAGS uses a location-specific factor to multiply each rating from 0 (no lesions), 1 (one comedone), 2 (one papule), 3 (one pustule), and 4 (one nodule) across six sites: the face/forehead, left and right cheeks, nose, chin, chest, and upper back. After adding together all the local scores, you get the global score. No acne at all (0 points), mild acne (1–18), moderate acne (19–30), severe acne (31-38), or very severe acne (> 39) [5].

IV. Laboratory investigations:

All patients examined were assessed for serum levels of IL-17 using sandwich ELIZA technique according to manufacturer instructions.

Statistical methodology

Data were analyzed using Epi-Info version 6 and SPSS version 8. Data were summarized using the mean, standard deviation (SD), median, and interquartile range (IQR). The Mann-Whitney U test, the validity of the screening test, the Student's t-test, and the chi-square test were used. The

correlation between variables was assessed using the correlation coefficient "r". A p-value is considered significant if it is less than or equal to 0.05.

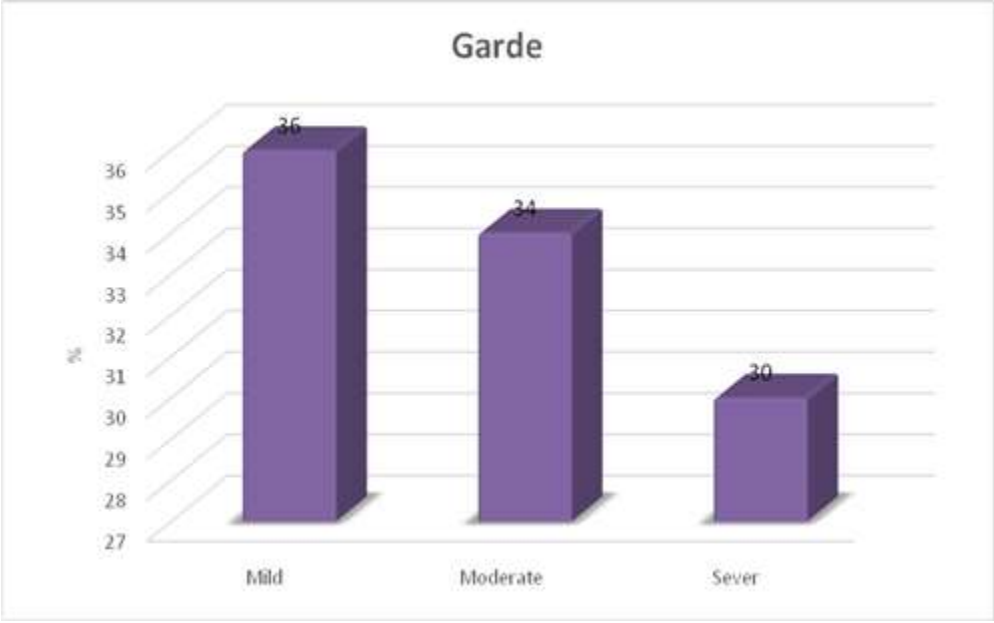
3. Results:

Table (1): Demographic data of the studied groups

Variable		**Cases (n=50)**		**Control (n=30)**		**t**	**P**
Age (years)	**Mean ±SD** **Range**	25.94±5.88 16-37		25.04±4.89 16-35		0.83	0.41
Sex (n, %) χ^2	**Male** **Female**	26 24	52 48	13 17	46 54	0.36	0.55

This table shows that there were no statistical significant differences between the studied groups in age or sex distribution.

Figure (1): Acne vulgaris grade among the studied cases group



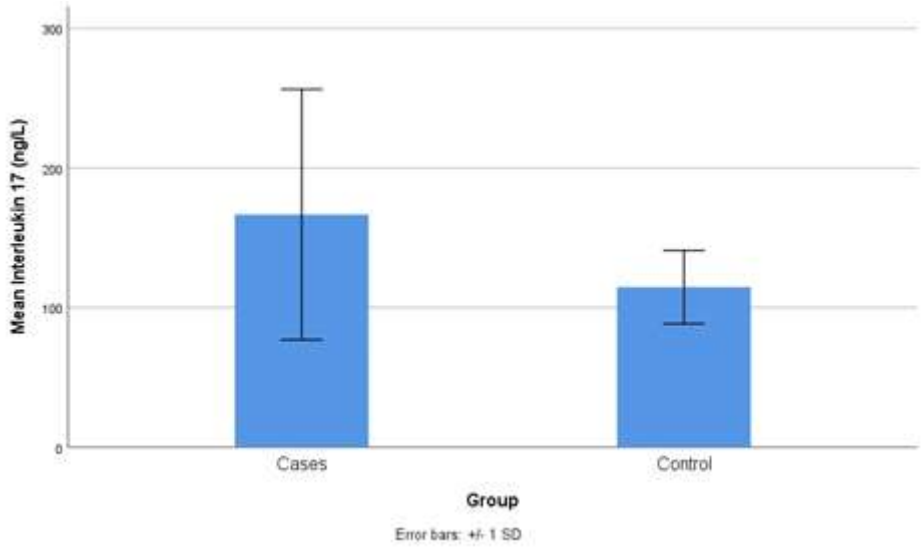
This figure shows that 36% of the cases had mild acne, 34% had moderate and 30% had sever.

Table (2): Interleukin-17 among the studied groups

Variable		Cases (n=50)	Control (n=30)	MW	P
IL-17	**Mean ± SD**	166.68 ± 89.77	114.62±26.26	8.32	<0.001**
	Median (IQR)	142(138-150)	122(110-130)		
	Range	136 - 652	11-158		

MW: Mann Whitney test **: Highly Significant (p<0.001)

Figure (2): Interleukin-17 among the studied groups



This table and figure shows that there was a statistical significant increase in IL-17 level among cases group compared to control group.

Table (3): Correlation between IL-17 and age and duration of the cases group

Variable		IL-17 (n=50)
	r	**P- value**
Age (years)	0.10	0.32
Duration (years)	0.11	0.47

r: Spearman's correlation coefficient

This table shows that there was no statistical significant correlation between IL-17 and age and duration of the cases group.

Table (4): Relation between IL-17 and grading and scarring in the cases group

Variable		N		IL-17		Test	P
			M±SD	Median	IQR		
Grade	**Mild**	18	138.61±2.09	138	137-140	KW	
	Moderate	17	145.29±5.17	145	141-149	21.01	<0.001**
	Sever	15	224.6±151.68	178	143.5-219.5		
Scar	**No**	36	159.75±86.53	141	138-145	MW	
	Yes	14	184.5±98.7	157.5	144-178	2.66	0.008*

MW: Mann Whitney test KW: Kruskal Wallis test *: Significant (p<0.05) , **: Highly significant (P<0.001)

This table shows that there were a statistical significant increases in IL-17 among severe cases compared to mild and moderate cases and also there was a statistical significant increase in IL-17 among cases had scar compared to cases had no scar.

Table (5): Validity of IL-17 in diagnosis of AV among the studied cases

Cut off	AUC (95% CI)	P	Validity				
			Sensitivity	Specificity	PPV	NPV	Accuracy
>136.5	0.98 (0.95-1)	<0.001**	88	98	97.8	89.1	93

AUC: Area under curve, CI: Confidence interval, PPV: +ve predictive value NPV: -ve predictive value,**Highly significant (p < 0.001)

This table shows that IL-17 at cut off >136.5 ng/l had sensitivity 88%, specificity 98% and accuracy 93% in diagnosis of AV.

4. Discussion:

Over the last fifty years, the incidence of AV, an inflammatory disorder of the pilosebaceous unit, has increased. It is believed that Propionibacterium acnes, via toll-like receptors (TLRs), triggers the inflammatory response in acne vulgaris, which may lead to increased immunological responses mediated by TLR2. When inflammation occurs, both the innate and adaptive immune systems play a role, with the Th17 pathways playing a particularly pivotal role [3].

Research has shown that Propionibacterium acnes may increase the production of inflammatory cytokines and trigger the synthesis of IL-17A and IFN-γ. Activated T cells release IL-17, which is thought to play a pivotal role in the pathogenesis of a number of skin diseases [6]. Transplant rejection, inflammatory bowel disease, multiple sclerosis, systemic sclerosis, psoriasis, rheumatoid arthritis, and systemic lupus erythematosus are among the chronic illnesses associated with high IL-17 production [7].

When it comes to AV lesions, our knowledge of the cytokine profile is limited. New studies have laid the groundwork for understanding the issue, but we still don't know how it affects the severity of AV at various degrees. To further understand its role in AV disease etiology, severity, this study intends to measure blood IL-17 levels in AV patients. Fifty patients attending the Outpatient Clinic of the Dermatology Department at Beni Suef University Hospitals with AV ranging in severity were part of Group A in this case-control study. Thirty healthy volunteers, evenly distributed across age and sex, made up Group B. This study adds to the limited body of literature that investigates the etiopathogenesis of AV by evaluating IL-17 levels in individuals with the illness. Individuals in the study underwent thorough medical history taking in addition to standard dermatological and general physical exams. Also measured were IL-17 concentrations in the blood. Mild acne accounted for 36% of cases, moderate for 34%, and severe for 30% of the cases in our study of acne severity. The results were in line with those of Bilgic et al. [8], who found that moderate acne affected 61% of patients, severe acne 31.1%, and mild acne 8% of the time. Out of the total number of acne lesions, 35% were mild, 35% were moderate, and 30% were severe,

according to Ebrahim et al. [9]. Dawson and Dellavalle [10] and Ebrahim et al. [9] both found that 22 patients (27.5%) had acne scarring, and the present study's 28% scarring rate is in line with their results. These studies highlight the chronic nature of AV. These results show that IL-17 levels were significantly higher in the case group than in the control group. This supports the previous findings of Kelhälä et al. [6], who discovered IL-17A(+) T cells and the activation of cytokines linked to the Th17/IL-17 pathway in clinically early inflammatory acne lesions. When comparing the patient group to the control group, Ebrahim et al. [9] found that blood IL-17 levels were much higher in the former. There was no statistically significant relationship between IL-17 levels and AV illness in the study by Topan et al. [11], which evaluated the effects of IL-17 on AV. Agak et al. [12] found that human peripheral blood mononuclear cells (PBMCs) were significantly ($p<0.001$) stimulated to produce IL-17, with an average concentration of 500-700 pg/mL, when inoculated with P. acnes from AV patients.

We found that IL17 levels were significantly higher in severe cases compared to mild and moderate cases, which is in line with what Kelhälä et al. [6], Agak et al. [12], and Kistowska et al. [13] found. Researchers Murlistyarini et al. [14] looked at IL-12, IL-17, and LL-37 blood concentrations in AV patients and found a correlation between these levels and the severity of the condition. According to GAGS, they found a statistically significant correlation between blood IL-17 levels and AV severity. Patients with severe AV lesions had significantly higher blood IL-17 levels than those with mild or moderate lesions, according to Ebrahim et al. [9].

Scars from acne occur when the skin surrounding the sebaceous glands is damaged, either by active lesions or by the gradual healing process that follows acne breakouts, which is common in severe to moderate acne. Acne scars may appear in anywhere from 43 percent to 95 percent of those who suffer from acne.

We compared serum IL-17 levels in acne patients with scarring and nonscarring acne to fill the gap in our understanding of the pathogenesis of acne scars. Our research showed that IL-17 levels were significantly higher in scarred individuals compared to scar-free individuals. In their study, Ebrahim et al. [9] found that serum IL17 levels were significantly higher in the group of

acne patients whose acne scarred as compared to the group whose acne did not scar.

According to the research of Rodero et al. [16], IL-17 has the potential to disrupt the first inflammatory stage of wound healing. It is possible that IL-17 affects many skin cell types due to the fact that keratinocytes, fibroblasts, and inflammatory cells all have IL-17 receptors.

Our study found that IL-17 had a sensitivity of 88%, specificity of 98%, and accuracy of 93% when used as a cutoff for the diagnosis of AV, with a threshold of >136.5 ng/l. The early prediction and identification of severe acne in the persons studied showed a strong relationship between serum IL-17 levels at cutoffs of ≥ 9.51 pg/mL and ≥ 12.59 pg/mL, according to Ebrahim et al. [9]. The results showed a sensitivity of 85%, specificity of 60%, and an accuracy rate of 72.5%. It also has the potential to be a predictor of AV prognosis. In addition to being a biomarker for the origin of the illness, they found that serum IL-17 may be a predictive signal for the severity and scarring caused by AV.

Among the few studies that compare IL-17 blood levels in AV patients to healthy controls, this one stands out. Hence, finally, we found that IL-17 might have a role in how AV develops. One limitation of the current study is its small sample size, which calls for further research on a wider scale. Additional studies comparing blood levels before and after therapy could provide light on the correlation between IL-17 and therapeutic efficacy, as we collected samples either before or after drug discontinuation. Ultimately, we did not evaluate cells that secrete IL-17 in our study; so, more investigation is necessary.

5. Conclusion and Recommendations:

Our investigation revealed a substantial statistical elevation in IL-17 levels in AV patients compared to controls. Moreover, there were statistically significant elevations in IL17 levels in severe instances relative to mild and moderate cases, as well as in cases with scars compared to those without scars. According to the findings of this research, it is advised to: undertake more research with a bigger cohort of patients and control subjects, evaluate the associations between IL17 and various dermatological diseases and to examine the impact of treating AV in relation to serum IL-17 levels.

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