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Evaluation of Serum Soluble Intercellular Adhesion Molecule 1 (sICAM1) as A Biomarker in Acne Vulgaris

Salma Samir Bahzat[*1], Abeer M. Elkoly [1], Gehad Mohsen Elmazny[2], Manar Ali[1]
1*Department of Dermatology, Andrology & STDs
2 Clinical Pathology, Faculty of Medicine, Mansoura University, Egypt
[*]**Corresponding Author**: Salma Samir Bahzat, **Mobile**: (+20) 1070174082, **Email**: Saloma123cx@gmail.com

ABSTRACT

Background: Acne vulgaris (AV) is an inflammatory disorder of the pilosebaceous unit, characterized by the development of papules, pustules, and nodules. Intercellular adhesion molecule-1 (ICAM1) is a transmembrane glycoprotein belonging to the immunoglobulin (Ig) superfamily normally expressed at minimal levels in numerous cells but upregulated in response to several inflammatory agents.

Objectives: This study aimed to assess and compare the serum levels of soluble ICAM1 in patients with AV to those in healthy controls (HC) and to correlate the level of ICAM-1 with disease activity.

Patients and methods: The study included 40 patients with AV and 40 age- and sex-matched healthy volunteers as a control group. The assessment of disease severity was conducted using the Global acne grading system (GAGS). The serum concentrations of soluble intercellular adhesion molecule 1 were measured using enzyme-linked immunosorbent assay (ELISA).

Results: The mean sICAM-1 level was significantly increased among AV cases compared to healthy controls. Mild acne was present in 15 cases, moderate acne among 15 cases and severe acne was present among 10 cases. Cases with severe AV were statistically significantly younger than those with mild and moderate acne. A significant positive correlation was detected between disease duration and acne severity. There was a significant association between sICAM-1 and the degree of acne severity. Median sICAM-1 levels were highest among severe cases, followed by moderate cases, and then mild cases.

Conclusion: It could be concluded that serum sICAM-1 levels are higher in AV cases than in healthy controls and serve as an independent predictor of acne susceptibility and severity.

Keyword: Serum SICAM1, Acne Vulgaris.

INTRODUCTION

Acne vulgaris (AV) is a chronic inflammatory disorder of the pilosebaceous unit characterized by the presence of papules, pustules, or nodules on the face, trunk, or upper limbs. AV often begins in the preadolescent period and subsides in the third decade; however, it might remain into adulthood. While post-adolescent acne primarily affects women, adolescent AV is more common in men [1, 2].

Acne happens by oversensitivity of the sebaceous glands to plasma androgens, worsened by P. acnes and inflammation. Its pathogenesis includes a complicated interaction of host factors, and immune responses, and could also be affected by genetics and diet [3, 4].

Several studies have demonstrated that inflammatory reactions happen before hyperkeratinization. ICAM1 and different inflammatory agents are controlled by macrophages and cytokines in the vessels nearby the pilosebaceous follicle [5].

ICAM1 is a 90 kDa member of the Ig superfamily. It has an important function in the transfer of white blood cells from the plasma into tissues and is fundamentally present on endothelial cells (ECs) and increases in expression due to proinflammatory cytokines [6].

The interaction between 2-integrin counter-receptors CD11a/CD18 and CD11b/CD18 (on the immune cell surface) and ICAM1 developed on ECs throughout inflammation, permitting immune cell transendothelial migration to the inflammation area. It has been demonstrated that expression of epithelial ICAM1 could participate in epithelial damage by the contribution of inflammatory cells to the affected site [5, 7]. Increased values of sICAM1 were determined in various inflammatory and immunological disorders [8]. Some studies have shown a relationship between serum ICAM-1 levels and acne. This study aimed to assess and compare the serum levels of soluble ICAM1 in patients with AV to those in healthy controls. Additionally, the study aimed to correlate the level of ICAM-1 with disease activity.

PATIENTS AND METHODS

This case-control study included a total of 40 patients with AV and 40 age- and sex-matched healthy volunteers as the control group, who attended the Outpatient Clinic of the Department of Dermatology, Mansoura University Hospitals, Mansoura, Egypt. This study was conducted over one year between (mention period e.g., June 2024 and June 2025).

Inclusion criteria: patients of both sexes, aged over 18 years, with any degree of acne severity.

Exclusion criteria: Pregnant or lactating women, patients had other dermatological diseases, autoimmune disorders (AID), autoinflammatory diseases (e.g., FMF), endocrine disorders, psychiatric illnesses, hepatic or renal disease, a history of chemotherapy, or if they were receiving systemic medications for acne,

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including oral retinoids and antibiotics such as clindamycin or erythromycin.

All the cases were subjected to complete history taking including personal history (name, age, sex, pregnancy status, lactation status, and occupation), history of the current disease (onset, course, duration, triggering or relieving factors), history of medications (formulation, route, dosage, compliance, duration, mechanism of action and adverse events), family history of acne vulgaris or other Dermatoses and past history of any accompanying systemic, dermatologic disorders or major surgeries.

General examination was done to rule out systemic disorders, and to estimate BMI. Full dermatologic assessment was conducted comprising skin, hair, nails and mucous membranes to exclude inflammatory and AID. Local examination for acne lesion and distribution was done using GAGS [9]. Based on this approach, the face, chest, and upper back were divided into six areas. Each area's score was calculated by multiplying the area factor by the most severe lesion [Local score = location factor × Grade (zero four)]. The GAGS location factor was categorized as follows: nose factor was one, chin factor was one, chest & upper back factor was three, forehead factor was two, right cheek factor was two, left cheek factor was two. Based on severity, a grade was given to each type of lesion, no lesions classified as zero, comedones classified as I, papules classified as II, pustules classified as III and nodules classified as IV.

The severity of the AV was assessed based on the GAGS, where cases with scores less than or equal to 18 were classified as mild AV, cases with scores between 19-30 were classified as moderate AV and cases with scores ≥ 31 were classified as severe AV [10].

Biochemical Analysis: The serum concentrations of sICAM1 were measured using enzyme-linked immunosorbent assays (ELISA Kits).

Ethical Consideration

This study was ethically approved by Mansoura University's Research Ethics Committee. Written informed consent of all the participants was obtained. Confidentiality was respected. Patients had the right to leave the study at any time. The study protocol conformed to the Helsinki Declaration, the ethical norm of the World Medical Association for human subjects.

Statistical Analysis

After collecting data, SPSS program, version 25 (PASW, Chicago: SPSS Inc.) was used. Numbers and percentages were used to describe the qualitative data. After determining normality using the Kolmogrov-Smirnov test, quantitative data were presented using mean±SD for normally distributed data. The results were deemed significant at the (≤0.05) level. To compare qualitative data between groups, the Chi-Square test was employed. For normally distributed data, two independent groups were compared using the student t test. ROC curve was used to assess validity of continuous variables.

RESULTS

Table 1 shows that there was an insignificant difference between the studied groups regarding mean age and sex, as well as regarding all anthropometric measurements between cases. SICAM1 was significantly increased in AV cases compared to healthy controls (p=0.001). A higher median value of SICAM1 was recorded in AV cases compared to healthy controls.

Table (1): Age, sex characteristics, anthropometric measurements and SICAM1 of studied groups

	Cases N=40	**Control N=40**	**Test of significance**	**P value**
Age / years Mean ±SD	22.25±4.31	23.98±5.08	t=1.64	0.106
Sex Male Female	11(27.5) 29(72.5)	16(40.0) 24(60.0)	χ^2=1.39	0.237
Weight (kg) Mean ±SD	72.5±10.31	73.55±19.71	t=0.298	0.766
Height (m) Mean ±SD	1.70±0.09	1.66±0.085	t=1.91	0.06
BMI (kg/m^2) Mean ±SD	25.11±3.40	26.59±6.72	t=1.25	0.216
SICAM1 (ng/ml) Median (min-max)	493.1 (200.4-1880.60)	91.4 (70.8-128)	Z=7.68	0.001*

t: Student t test, χ^2= Chi-Square test, z: U test, *statistically significant

Table **(2)** shows that mild acne was present in 15 cases (37.5%), moderate acne among 15 cases (37.5%) and severe acne was present among 10 cases (25%). Mean score of acne was 14.27±2.08 for mild cases, 24.0±3.14 for moderate cases and 40.30±6.65 for severe cases with statistically significant difference.

Table (2): Acne severity score among studied cases

Score	Severity	Number	Percentage %
14.27±2.08[ab]	Mild	15	37.5%
24.0±3.14[ac]	Moderate	15	37.5%
40.30±6.6	Sever	10	25%
P value	0.001*		
Test of significance	F=126.14		

F: One Way ANOVA test, *statistically significant

Table (3) displays a significant difference regarding mean age of the cases studied with post Hoc Test comparing different degrees of acne. Severe acne was significantly common among younger cases with mean age 19.40±0.97 years versus 23.67±4.82 years for mild acne. There was insignificant relation between acne severity and anthropometric measurements of the studied cases including weight, height and body mass index (p=0.707, 0.229 &0.562). There was a statistically significant positive relation between disease duration and acne severity. Shorter median disease duration among cases with mild acne and higher duration among cases with severe acne. There was a statistically significant relation between Serum soluble intercellular adhesion molecule 1 (SICAM1) and acne severity degree (p<0.001). Median SICAM1 was higher among severe cases followed by moderate cases and the least for mild cases.

Table (3): Age, sex, anthropometric measurements, duration of disease and **SICAM1** according to acne severity

	Mild N=15	**Moderate N=15**	**Severe N=10**	**Test of significance**	**P value**
Age / years Mean ±SD	23.67±4.82[A]	22.73±4.43	19.40±0.97	F=3.49	0.04*
Sex Male Female	6(40) 9(60)	2(13.3) 13(86.7)	3(30.0) 7(70.0)	MC=2.72	0.257
Weight (kg)	72.80±9.90	73.73±12.45	70.20±7.64	F=0.350	0.707
Height (m)	1.72±0.09	1.69±0.09	1.66±0.08	F=1.54	0.229
BMI (kg/m^2)	24.35±2.13	25.61±4.57	25.49±3.03	F=0.585	0.562
Duration of disease (years) Median (min-max)	2(1-6)	2(1-10)	3(2-10)	KW=29.94	<0.001*
SICAM1 Median (min-max)	278.5 (200.4-299.8)	509.8 (233.2-670.1)	1665.6 (1356.5-188.6)	Kw=29.94	<0.001*

F: One Way ANOVA test, MC: Monte Carlo, KW: Kruskal Wallis test, *statistically significant

Table **(4)** shows area under curve for Serum soluble intercellular adhesion molecule 1 in the differentiation between case and control groups. It was excellent, with the best detected cut-off point was 216.8 yielding sensitivity (Sn) 97.5% and 100% specificity (Sp).

Table (4): Validity of SICAM1 in differentiating cases from control groups

	AUC (95%CI)	**P value**	**Cutoff point**	**Sensitivity %**	**Specificity %**
SICAM1	1.0 (1.0-1.0	<0.001*	216.8	97.5	100.0

AUC: Area under curve

Table **(5)** shows that area under curve for Serum soluble intercellular adhesion molecule 1 in differentiating mild from moderate cases was excellent (0.902) with the best detected cutoff point was 299 yielding Sn 86.7% and 93.3% Sp. Regarding area under curve for SICAM1in differentiating mild from severe cases was excellent (1.0) with the best detected cutoff point was 828.15 yielding Sn 100% and 100% Sp. Regarding area under curve for SICAM1 in differentiating moderate from severe cases was excellent (1.0) with the best detected cutoff point was 1013.3 yielding Sn 100% and 100% Sp.

Table (5): Validity of SICAM1 in differentiating mild from moderate cases, mild from severe cases and moderate from severe cases.

	AUC (95%CI)	P value	Cutoff point	Sensitivity %	Specificity %
SICAM1 in differentiating mild from moderate cases	0.902 (0.768-1.0)	<0.001*	≤299	86.7	93.3
SICAM1) in differentiating mild from severe cases	1.0 (1.0-1.0)	<0.001*	≥828.15	100.0	100.0
SICAM1 in differentiating moderate from severe cases	1.0 (1.0-1.0)	<0.001*	≥1013.3	100.0	100.0

DISCUSSION

Acne vulgaris (AV) is a chronic inflammatory skin disease of the pilosebaceous unit. Its pathogenesis includes the integration of several factors that eventually cause the development of comedo [11]. A lot of factors are concerned in AV pathogenesis; however, inflammation is the main factor [12].

ICAM1 is a transmembrane glycoprotein detected at minimal levels in numerous cells and increases due to several inflammatory agents. When inflammation occurs, ICAM1 expression on the ECs interacts with immune cells' surface counter receptors, to allow their transendothelial migration to the inflammatory site. Major values of sICAM1 were demonstrated in various inflammatory and immune-mediated disorders [13].

Our study aimed to assess and compare the serum levels of soluble ICAM1 in cases with AV compared to HC and to correlate the levels of soluble ICAM1 in relation to disease severity.

Regarding the demographics, the present study revealed no significant difference between the two groups in age or sex. The mean age of studied cases was 22.25±4.31 years versus 23.98±5.08 years for control group, with female predominance (72.5% were females versus 60% of control group) as they were age and sex matched. In addition, there was insignificant difference between both groups concerning mean weight, height and body mass index. **Mustafa *et al***. [5] also found insignificant difference between AV cases regarding age and sex (Mean± SD age was 21.9±4.6 for cases) with female predominance (56.7% in cases). On the other hand, **Mashi *et al***. [14] examined 419 participants with AV and revealed that their mean age was 25.52±7.216 years and more than half of them, 228 (54.4%) of the participants were males. The discrepancies in sex predominance between both studies may be due to the changes in the sample sizes and the age distribution of the subjects in both studies.

According to our study there was insignificant relation between acne severity and anthropometric measurements of the studied cases including weight, height and BMI (p=0.707, 0.229 & 0.562). **Abdou *et al***. [15] also stated that there was insignificant difference between both groups regarding mean weight, height and BMI. In disagreement with our results, **Gündüz & Ataş** [16] found a significant relationship between AV severity and the BMI, and percentile score. Thus, they suggested that encouraging proper weight maintenance may have a beneficial impact on adolescents' AV severity.

The current study stated that median serum sICAM1 level in AV cases was significantly higher than control group (493.1(200.4-1880.60) ng/ml in cases versus 91.4 (70.8-128) ng/ml in controls). Likewise, **Abdou *et al.*** [15] revealed that serum ICAM1 levels were demonstrated to be higher in AV cases compared with healthy controls (the mean was 750.1±120.9 in cases versus 204.6±8.9 in controls), and **Mustafa *et al***. [5] revealed a significant increase in serum sICAM1 level among AV cases compared to healthy controls (the median was 379 in cases versus 211.75 in controls).

Moreover, **Jeremy *et al.*** [17] displayed that ICAM1 expression in the skin appeared to rise in noninvolved skin without statistical significance, while a considerable increase was determined in papules of less than 6 hours. **Qin *et al***. [18] provided evidence of C. acnes participation in the inflammation process in AV by stimulating NLRP3 inflammasome in APCs and ultimately improved IL-1β formation.

It has been demonstrated that the discharge of cytokine IL-1 beta causes sICAM1 expression by the p38 MAPK signaling pathway. Those mechanisms cause inflammatory response in AV cases and raised gravidity of AV lesions [8].

The present study revealed that mild acne was present in 15 cases (37.5%), moderate acne among 15 cases (37.5%) and severe acne was present among 10 cases (25%). Mean score of acne was 14.27±2.08 for mild cases, 24.0±3.14 for moderate cases and 40.30±6.65 for severe cases with statistically significant difference. While **Alshammrie *et al.*** [19] had found that 38% of their cases had mild AV degree, 43% had moderate degree and 19 % had severe degree.

The present study showed a significant difference regarding the mean age of the studied cases with AV severity; severe acne was significantly more common among younger cases with a mean age of 19.40±0.97 years versus 23.67±4.82 years for mild acne. While a study conducted in South India displayed that the severity of AV was significantly increased among cases with age more than or equal to 20 years old, which agreed with our results. Additionally, male patients exhibited more severe AV than female patients. The mean duration of AV was 45.5 months, ranging from one month to 25 years. Cases with longer disease duration had more severe AV [20]. But in agreement with ours, a

study from Saudi Arabia found a significant negative relationship between age and acne severity, indicating that older patients tend to have less severe acne [21].

Our study revealed that median ICAM1 was higher among severe cases, followed by moderate cases, and the least for mild cases. In addition, **Mustafa *et al***. [5] displayed that there was a significant positive association between serum sICAM1 value and disease severity, which may be explained by evident proinflammatory response. In addition, ordinal regression analysis was carried out to predict AV severity. Increased serum sICAM1 value could be considered as an independent risk predictor for AV severity. The current study revealed that SICAM1 level was excellent in discrimination between AV cases from controls, with the best detected cutoff point was 216.8 yielding Sn 97.5% and 100% Sp. In addition, when ROC curve of serum sICAM1 level was carried out for AV diagnosis by cutoff value of 277.8ng/ml, Sn was 93.3%, Sp was 96.7%, PPV was 96.6%, NPV was 93.5%, and accuracy was 95% [5].

The present study revealed that the ICAM-1 level for differentiating mild from moderate cases was excellent **(**AUC = 0.902**)**, with a cutoff point of **299**, yielding a sensitivity of 86.7% and a specificity of 93.3%**.** For differentiating mild from severe cases, the performance was excellent (AUC **= 1.0**), with the best cutoff point of 828.15, yielding 100% sensitivity and 100% specificity. Similarly, for differentiating moderate from severe cases, the performance was excellent **(**AUC = 1.0**)**, with the best cutoff point of 1013.3, yielding 100% sensitivity and 100% specificity.

Limitations of the current study were the small sample size, and it is important to carry out more studies on many cases. In addition, enrolled cases weren't included pre- or post-treatment; as a result, upcoming studies assessing sICAM1 levels pre- and post-treatment may be useful in assessing the relationship between sICAM1 level variations and therapeutic efficacy.

CONCLUSION

It could be concluded that serum sICAM-1 levels are higher in AV cases than in healthy controls and serve as an independent predictor of acne susceptibility and severity.

As AV is a problem in adolescence, early evaluation of sICAM1 level could help with AV management. A better understanding of AV pathophysiology may help direct future therapeutic modalities.

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