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Research Article

The Role of Interleukin-1 Beta and Interleukin 8 in Acne Pathogenesis: A Serum-Based Severity Assessment

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Abstract

Background: Acne vulgaris (AV) is a skin disorder affecting both sexes, starting at adolescence, and might continue into late adulthood. It is represented by a flare-up of nodular and postural lesions. Acne vulgaris patients with severe presentation suffer the consequences of skin scarring and disfigurement. Both Interleukin 1 beta (IL-1β) and Interleukin 8 (IL-8) are pro-inflammatory cytokines that play a significant role in acne pathogenesis and disease progression.

Objectives: To assess the serum level of interleukin 1 beta and interleukin 8 in acne patients and see how it correlates with the severity of the disease.

Methods: It was a case–control study conducted from October 2024 to March 2025, with 60 acne vulgaris patients divided into two groups, mild and severe, with ages ranging from 14 to 25 years. The patients were seen in the Dermatology Center, Baghdad Teaching Hospital, The Medical City Complex, Baghdad, Iraq. Thirty healthy individuals of both sexes of similar age groups to the patients were recruited as controls in this study. A detailed history was taken, and clinical examination was performed on all the participants. For each participant, IL-1β and IL-8 were measured using the Enzyme-Linked Immunosorbent Assay method and the results were statistically analyzed and tabulated.

Results: The difference between the control and patient groups in regard to IL-1β and the difference between the patient groups themselves were not significant. Regarding IL-8, there was a significant difference between the control and patient groups and between the control and severe groups, while the difference between patient groups was highly significant.

Conclusion: Blood quantification of Interleukin 8 proved useful in trying to assess the severity of acne vulgaris, while serum Interleukin 1 beta levels proved to be of no value in assessing the severity of Acne vulgaris.

Keywords: Acne Vulgaris; Biomarkers; Interleukin-1 beta; Interleukin-8; Prognosis.

Introduction

Acne vulgaris (AV) is a chronic inflammatory skin disease occurring in the sebaceous glands within the hair follicles (1). Acne vulgaris is still a global problem, where most of the AV patients are adolescents (2). It affects about 80% of people at some point in their lives, with 90% prevalence on the face (3).

Some hormonal changes seen in adolescence can lead to moderate/ severe presentations, ending in disfiguring skin lesions and post-inflammatory hyperpigmentation, which requires various courses of treatment (4). Apart from the role of the hormone estrogen, the androgens, namely testosterone, can also trigger acne. Increased levels of androgen hormones can trigger the sebaceous glands to produce excess oil. The pathogenesis of AV is attributed to sebum overproduction, follicular proliferation, and to a microbe named *Cutibacterium acnes* (*C. acnes*), to end up in a subsequent inflammation (5).

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Inflammation plays a role in the occurrence of AV at both the early and late stages. The role of inflammatory cytokines is important as an effector mechanism of inflammation, causing the formation of many AV lesions (6). Some suggested a role of *C. acnes* in the stimulation of a group of cells, like keratinocytes and monocytes, through the toll-like receptors (TLRs) (7). The cytokines related to the AV include interleukin IL-1, IL-6, IL-8, and IL-22 (8, 9).

Furthermore, both IL-6 and IL-8 affect neutrophil chemotaxis, lysosomal enzyme release, and follicular epithelium damage (10). A previous study by Marcinkiewicz confirmed that the production of antimicrobial peptides (AMPs) induced by IL-1 was up-regulated in AV and positively correlated with the incidence and severity of AV (11). IL-8 plays a chemotactic role in attracting both specific and non-specific immune cells, particularly granulocytes such as neutrophils and basophils, as well as lymphocytes (12). The levels of IL-8 increase significantly at inflammatory sites, in the serum and bodily fluids; therefore, the measurement of IL-8

levels has been used for the diagnosis and prognosis of inflammatory diseases (13). Hence, most inflammatory cytokines can have a role in the pathogenic process of mild-to-severe presentation.
This study aimed to evaluate the serum level of IL-1 beta and IL-8 between healthy individuals and patients diagnosed with AV and their correlation to AV severity.

Patients and Methods
Sixty patients with AV and 30 controls without AV were recruited for the case-control study. They were selected from the Dermatology Center of the Medical City Hospital in Baghdad. The selection process took place from October 2024 to March 2025. Acne grading was performed according to the Global Acne Grading System (GAGS). The study included three groups divided according to the physical and dermatologic examinations. The first group included 30 patients with mild-to-moderate acne, 30 patients with severe acne and 30 individuals without AV. The age range for the cases was 14 – 25 years, and for the controls was 18 – 25 years.
The study was approved by the ethical committee of the College of Medicine, University of Baghdad, under the code (0250). All participants gave formal informed consent after a full explanation was given to them on the aim of the study.
Exclusion criteria
- Patients undergoing topical or systemic acne therapy, or both;
- Previously treated patients had to have a minimum withdrawal time of at least one month from any prescribed acne medication;
- Patients suffering from hyperproliferative dermatological conditions, including psoriasis and lichen planus;
- Patients with bullous disorders, cutaneous fibrosis, neoplasms, and metastases.

The participants underwent full history taking, dermatological examination, and complete general examination.
Three milliliters of venous blood were withdrawn from each participant under complete aseptic conditions from the cubital vein. The samples were placed in gel tubes at room temperature and thereafter centrifuged at 3000 rpm for 15 minutes. Then, all the sera were stored frozen at −20°C until analysis.
Measurements of serum IL-1β and IL-8 levels were done by the Enzyme-linked Immunosorbent Assay technique (14). The kit for IL-1β and IL-8 was provided by Cloud Clone Corp., USA (15).

Statistical Analysis The unpaired Student's t-test was utilized to compare the quantitative data of the two groups. Analysis of variance (ANOVA) tests were conducted using Microsoft Excel software. The ANOVA test was utilized to compare groups using the quantitative data. Tukey's test was used to identify which means within a group of means are significantly different from others, where a *p*-value ≤ 0.05 is considered statistically significant.

Results
Among the cases included in the current study, there were 22 (36.7%) males and 38 (63.3%) females, with a mean age of 18.3 ± 2.67 years. Among the controls, there were 15 (50.0%) males and 15 (50.0%) females, with a mean age of 21.1 ± 1.68 years. The acne patients were divided into two groups: The mild/ moderate and the severe, each group with 30 patients.
The mean value of the IL-1 beta was (0.0297±0.0006) in the acne patients and (0.0296±0.0001) in the controls, with no statistical significance. The mean IL-8 level value was (0.1337± 0.0004) in the acne patients and (0.1335± 0.0001) in the controls, which was statistically significant (*P* value <0.01), (Table 1).

Table 1: Mean ± standard deviation of IL1 beta and IL 8 in controls and patients

Chemokine	Mean ± SD		P Value
	Controls	Patients	
IL-1 beta	0.0296 ± 0.0001	0.0297 ± 0.0006	*P* > 0.05
IL-8	0.1335 ± 0.0001	0.1337 ± 0.0004	*P* < 0.01*

**** Statistically significant***

Using the ANOVA test, the mean value of IL_1 beta level in the mild/moderate acne group was (0.0297 ± 0.0003) and (0.0299 ± 0.0008) in the severe acne group, the difference between these groups was not significant. The mean IL-8 level in the mild/moderate acne group was (0.1335 ± 0.0001) and (0.1338 ± 0.0005) in the severe acne group; the *P* value of the test was statistically significant, (Table 2).

Table 2: Mean and standard deviation of IL-8 and IL 1 beta in mild and severe patients

Chemokine	Mean ± SD		*p*-value of ANOVA
	Mild	Severe	
IL-1 beta	0.0297 ± 0.0003	0.0299 ± 0.0008	*p* > 0.05
IL-8	0.1335 ± 0.0001	0.1338 ± 0.0005	*p* < 0.01 *

ANOVA, analysis of variance, * statistically significant

As regards IL-1 beta, the difference between the three groups was not significant (*P* > 0.05). The difference between the severe and the control groups was not significant (*P* value > 0.05), between the control and mild groups was not significant (*P* value > 0.05) and between the mild

and severe groups was not significant ($P > 0.05$). Tukey's test indicated no significant difference between the groups ($P > 0.05$).
The difference between the IL-8 severe and control groups was highly significant (P value < 0.002), between mild and severe was significant (P value < 0.01), and between the control and mild groups was not significant (P value > 0.05). Tukey's test indicated a significant difference between the control and severe groups ($p < 0.01$) and between the mild and severe groups ($P < 0.01$), (Table 3).

Table 3: Comparison between the IL-8 levels in the study groups by Tukey's test

Group pairs	Tukey HSD *P*-value	Tukey HSD inference
Controls and mild	$P > 0.05$	Non-significant
Controls and severe	$P < 0.001$ **	$P < 0.01$ *
Mild and severe	$P < 0.007$ **	$P < 0.01$ *

*** Statistically significant, * * statistically highly significant**

Discussion

Acne vulgaris is a multifactorial disease of the pilosebaceous unit of the skin. Although AV was perceived as a chronic disease, recent studies have shown that both innate and adaptive immunity play a role in the inflammation of acne (16).
C. acnes and innate immunity play a major role in progressive chronic inflammation (16). They activate innate immunity via Protease-Activated Receptors **(**PARs) and TLRs, to help in the production of IL-1, IL-8, and IL-22 (17), from the local keratinocytes, in the skin biopsy (18).
In this study, the level of IL-8 showed a significant difference in patients, when compared to the controls, because of its pro-inflammatory role starting in innate immunity and ending up in active T-cell-mediated immune response in severe cases. the role of IL-8 as a biomarker for AV severity was backed by the results obtained in the current study, especially the significant difference between the severe cases and both the controls and mild cases, which was in line with the findings of these studies (11,19, 20). The difference between the mild cases and control was not significant according to Tukey's test, which can be attributed to the low number of lesions in most of these cases, as the serum concentration increased with the number of inflamed and postulated lesions because of the spillover effect on IL-8. Mild cases have an increase in IL-8 locally in the vicinity of preexisting lesions. When the severity increases, and more lesions start appearing, overproduction of IL-8 will occur, thus the excess of the produced IL-8 will enter the circulation making its level increasingly higher in more severe cases, which is suggested by the study of Dinarello *et al* (21).
The levels of IL-1β in our cases were close to normal in both mild and severe cases, which can be explained on the basis of circumstantial and trivial secretion in the serum. IL-1 β has more tightly regulated secretion mechanics, as it has potent pyrogenic and systemic effects, as suggested by Narros-Fernández *et al* (22). IL-1β levels in the serum may not fully reflect local inflammatory activity in the pilosebaceous units, where acne pathogenesis originates, as AV is a local skin issue. The serum levels were lower than those detected in the immunohistochemical analysis of skin biopsies obtained from scarry lesions in AV patients as shown in these studies done by Anh *et al* and by ElAttar *et al* (23, 24).

Limitations

The limitations of the current study include the small sample size, which affected the generalizability of the results, and the unequal gender proportions with female predominance, which may have affected the findings in regard to male patients. Serum levels of IL-1β and IL-8 were evaluated at a single time point, capturing only a snapshot of inflammatory activity. Future studies could elaborate more on the dynamic changes during acne progression or treatment.

Conclusion

Blood quantification of Interleukin 8 proved useful in trying to assess the severity of acne vulgaris, while serum Interleukin 1 beta levels proved to be of no value in assessing the severity of Acne vulgaris.

Authors' declaration

We attest that every table and figure in the article is part of the ongoing investigation. Additionally, the text includes figures and photographs that have been approved for republication even though they are not part of the current study. The authors attest their support of ethical considerations. Ethical Clearance: On February 1, 2025, the project was authorized by the local ethical committee at the Department of Microbiology, College of Medicine, University of Baghdad, under code number (0250).

Conflict of Interest: Prof Dr Adil A. Noaimi is an Editorial Board Member in the journal, but did not participate in the peer review process other than in his role as an author.

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Data availability: Upon reasonable request, the corresponding author will make the data sets generated and/or analyzed during the current work available.

Authors' contributions

Study conception and design: (Ihsan W. Al-Husseinawi, Hayfaa S. Alhadithi, Adil A. Noaimi). Literature search: (Ihsan W. Al-Husseinawi). Data acquisition: (Ihsan W. Al-Husseinawi, Adil A. Noaimi). Data analysis & interpretation: (Ihsan W. Al-Husseinawi). Manuscript preparation: (Ihsan W. Al-Husseinawi). Manuscript editing & review: (Ihsan W. Al-Husseinawi, Hayfaa S. Alhadithi, and Adil A. Noaimi).

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دور إنترلوكين 1 بيتا وإنترلوكين 8 في التسبب في حب الشباب: تقييم شدة المرض على أساس المصل

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الخلاصة:

خلفية البحث: حب الشباب الشائع هو اضطراب جلدي يصيب كلا الجنسين، ويبدأ في مرحلة المراهقة وقد يستمر حتى أواخر مرحلة البلوغ. يتمثل في تفاقم الآفات العقدية والوضعية. يعاني مرضى حب الشباب الشائع، الذين يعانون من أعراض حادة، من ندبات جلدية وتشوهات. يُعد كل من IL-8 و IL-1 بيتا من السيتوكينات المسببة للالتهابات، والتي تلعب دورًا هامًا في نشوء حب الشباب وتطوره.

الاهداف: تقييم مستوى الإنترلوكين 8 والإنترلوكين 1 بيتا في مصل مرضى حب الشباب وكيفية ارتباطه بشدة المرض.

المنهجية: أُجريت هذه الدراسة المقارنة على ٦٠ مريضًا يعانون من حب الشباب من تشرين الأول ٢٠٢٤ إلى آذار ٢٠٢٥، جُمعوا من مركز الأمراض الجلدية في مستشفى مدينة الطب في بغداد، وتتراوح أعمارهم بين ١٤ و٢٥ عامًا. ٣٠ شخصًا سليمًا تم توضيفهم كمجموعة ضابطة في هذة الدراسة. أُجري تاريخ مرضي مفصل وفحص سريري لجميع المشاركين. تم قياس مستويات IL-1β و IL-8 باستخدام طريقة مقايسة الممتز المناعي المرتبط بالإنزيم للمرضى والمجموعة الضابطة، وحُللت النتائج إحصائيًا ورُسمت على شكل جدول.

النتائج: لم يكن الفرق بين مرضى IL-1β ومجموعات التحكم معنويا ، كما لم يكن الفرق بين المجموعة الشديدة والمجموعة الضابطة معنويا وكذلك بين مجموعات المرضى. وفيما يتعلق بـ IL-8، كان هناك فرق كبير بين المجموعة الضابطة والمرضى ، وكان الفرق بين المجموعة الشديدة والمجموعة الضابطة مهمًا ، وكان الفرق بين مجموعات المرضى مهمًا للغاية.

الإستنتاج: لقد ثبت أن تحديد كمية الإنترلوكين 8 في الدم مفيد في محاولة تقييم شدة حب الشباب، في حين ثبت أن مستويات الإنترلوكين 1 بيتا في المصل ليس لها أي قيمة في تقييم شدة حب الشباب.

مفتاح الكلمات: حب الشباب، العلامات الحيوية، إنترلوكين-1 بيتا، إنترلوكين-8،توقع سير المرض ..