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Assessing the serum levels of interleukins (IL-6,8,17, and 22) in subjects with acne vulgaris

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ABSTRACT

Background: The skin is affected by acne vulgaris, a chronic, complex, inflammatory illness. Data from recent literature have examined the function that inflammatory pathways play in the very early stages of the aetiology of acne vulgaris. Th17 cells, their cell line, and the cytokines that are its downstream effectors are essential for both causing and sustaining the illness.

Objective: This study evaluated the interleukins (IL-6,8,17, and 22) in serum from individuals with acne vulgaris and examined their involvement in the pathophysiology of the condition.

Methods: This study evaluated 60 age- and gender-matched controls and 120 individuals with a confirmed diagnosis of acne vulgaris. Using an enzyme-linked immunosorbent assay (ELISA), the blood levels of interleukins 6, 8, 17, and 22 were measured in each of the included patients, and these levels were connected with the severity of acne vulgaris.

Results: The findings indicate that the study subjects had serum levels of interleukins 6, 8, 17, and 22 of 0.13±0.0152 pg/ml, 0.36±0.078 pg/ml, 0.17±0.0073 pg/ml, and 0.21±0.0131 pg/ml, respectively. In contrast, the levels in the control group were 0.11±0.0073 pg/ml, 0.12±0.032 pg/ml, 0.11±0.0031 pg/ml, and 0.19±0.0097 pg/ml, respectively. In terms of serum interleukin levels, there was no statistically significant difference between the two groups. There was a strong and statistically significant positive connection seen between the blood levels of IL-8 interleukin and the severity of the condition. There was also a notable positive association seen between the levels of IL-8 and IL-17.

Conclusion: The current study comes to the conclusion that interleukins 8 and 17 have a crucial effector function in the pathophysiology of acne vulgaris. It has been demonstrated that Th17 cells, the primary generator of interleukin-8 in acne vulgaris lesions, are stimulated by interleukin 6.

Keywords: Interleukins, inflammatory mediators, IL-6, IL-17, IL-8, IL-22, acne vulgaris

INTRODUCTION

The dermatological clinical entity known as acne vulgaris manifests as a multifactorial, inflammatory, pleomorphic condition throughout time. Numerous causes, including inflammation of the pilosebaceous ducts, hypercornification, colonisation of Cutibacterium acnes (formerly known as Propionibacterium acnes), and increased sebum production, have been implicated in the pathophysiology of acne vulgaris.1

The precise order of these previously described events and the relationships between the aforementioned components are unclear when it comes to the pathophysiology of acne vulgaris. According to reports, sebocytes in acne vulgaris exhibit an amplification of their reaction to androgens, resulting in sebaceous gland hyperplasia and elevated sebum production.2

The follicular duct in acne vulgaris is where C. Acnes colonises and converts sebum triglycerides to free fatty acids. These free fatty acids trigger the nuclear translocation of nuclear factor kappa-B (NF-κB) in keratinocytes, resulting in the production of interleukins 6 and 1β as well as TNF-α (tumour necrosis factor-α).3 IL-6 is a pro-inflammatory cytokine that causes the pilosebaceous duct to become hyperkeratotic. Furthermore, C. acnes causes the innate immune system to become activated by binding to TLRs 2 and 4, which are found on monocytes and keratinocytes. This activation results in the production of additional MMPs (matrix metalloproteinases), TNF-α, IL-1, IL-6, IL-8, and IL-12.

Apart from innate immunity, the pathophysiology and mechanism of acne vulgaris are significantly influenced by the pathways of adaptive immunities, namely Th1 and Th17. Before naïve CD4+ cells reach their functional activity and release numerous inflammatory mediators including interleukins 17 and 22 and interferon-gamma (IF-γ), they differentiate into T helper cells such as Th1 and Th17 depending on the cytokine milieu.5, 6. The current study postulates that individuals with acne vulgaris have changes in the blood levels of many interleukins, including IL-6, 8, 17, and 22. The severity of acne vulgaris is connected with the serum levels of interleukins-6,-8,-17, and 22 in the current investigation.

The current investigation sought to determine the interleukins' (IL-6,8,17, and 22) serum levels in acne vulgaris patients as well as their potential involvement in the aetiology of the condition.

MATERIALS AND METHODS

The current cross-sectional clinical investigation sought to determine the interleukins' (IL-6,8,17, and 22) blood levels in acne vulgaris patients as well as their potential involvement in the aetiology of the condition. The study was conducted after approval from the relevant institutional ethical committee. The study's participants were from the Institute's Department of Dermatology. Prior to research participation, informed permission was obtained from all individuals, both verbally and in writing.

120 participants, both male and female, with a verified clinical diagnosis of acne vulgaris were enrolled in the study. The study's inclusion criteria were participants with untreated acne vulgaris between the ages of 15 and 45, with washout periods of two and four weeks, respectively, for topical and systemic medication. The study's exclusion criteria included subjects with hyperandrogenism, autoimmune diseases, PAPA (pyogenic arthritis, pyoderma gangrenosum and acne) syndrome, pyogenic arthritis, insulin resistance syndrome, metabolic syndrome, PCOS (polycystic ovarian syndrome), pregnant women, and nursing women, as well as those with acne that was secondary to any of these conditions. The study also eliminated participants with thyroid abnormalities, type 1 diabetes mellitus, acneiform eruptions caused by medication, and body mass index (BMI) more than 25. Sixty volunteers whose age and gender matched were made up the control group.

Using a history and clinical evaluation, the symptoms of PCOS, metabolic syndrome, and insulin resistance were evaluated. The following conditions were noted on a premade structured proforma: menstrual history in female patients; blood pressure; waist circumference; BMI (body mass index); hirsutism; xanthelasma palpebraum; numerous acrochordons; presence of acanthosis nigricans; and seborrhoeic dermatitis. Following final inclusion, each subject had a thorough history taken, which was followed by a clinical assessment.

Based on the severity of acne vulgaris as determined by the GAGS (Global Acne Grading System)7, participants were then split into two groups of sixty each. The grading system was as follows: 0 for none, 1-18 for mild, 19-30 for moderate, 31-38 for severe, and >39 for extremely severe. In both cases and control participants, 10 millilitres of blood were drawn in a fasting state from the antecubital veins in simple vacutainer tubes under stringent aseptic and sterile circumstances. The blood sample was centrifuged for five minutes at 2800 rpm after being let to rest for thirty minutes at room temperature. After that, the serum was divided and kept at -20°C. Enzyme-linked immunosorbent assay, or sandwich ELISA, was utilised to identify interleukins in the blood, such as IL-6, IL-8, IL-17, and IL-22, utilising

various commercial kits and adhering to manufacturer guidelines. The absorbance was measured using a spectrophotometer at the main wavelength of 450 nm.

The collected data were statistically analysed using the unpaired t-test, chi-square test, ANOVA, and Mann-Whitney U test using the SPSS software version 21.0 (IBM Corp., Armonk, NY, USA). The statistics were presented as percentage, frequency, mean, and standard deviation. An acceptable p-value for statistical significance was <0.05.

RESULTS

The current cross-sectional clinical investigation sought to determine the interleukins' (IL-6,8,17, and 22) blood levels in acne vulgaris patients as well as their potential involvement in the aetiology of the condition. This study evaluated 60 age- and gender-matched controls and 120 patients with verified diagnoses of acne vulgaris.

Using an enzyme-linked immunosorbent assay (ELISA), the blood levels of interleukins 6, 8, 17, and 22 were measured in each of the included patients, and these levels were connected with the severity of acne vulgaris. In the study group, the average age of the study participants was 22.33±5.29 years, whereas in the control group, it was 21.84±3.76 years. The study group consisted of 35% (n=42) and 65% (n=78) male study participants; in contrast, the control group's distribution of study subjects' age and gender was similar (p=0.896 and 0.873, respectively). There were 33.33% (n=20) and 66.67% (n=40) male and female individuals in the control group, respectively.

The research participants' mean illness duration for acne vulgaris was 6.36±1.24 years, with a range of 1 to 16 years. Of the research participants, 40% (n = 48), 51.67% (n = 62), and 8.33% (n = 10) had mild, moderate, or severe acne, respectively.

The study's findings demonstrated that, when the blood levels of different interleukins were compared between the two groups of participants, the mean levels of IL-6 in the cases and controls were 0.13±0.0172 and 0.11±0.0093 pg/ml and 0.11±0.0093 pg/ml, respectively, indicating a non-significant difference (p=0.822). The mean serum levels of IL-8 were 0.36±0.078 and 0.12±0.32 pg/ml, respectively, in the patients and controls, indicating statistically significant differences with p<0.001. The mean blood levels of IL-17 in the study individuals were 0.17±0.0073 pg/ml, which was substantially higher than the 0.11±0.0031 pg/ml in the controls (p<0.001).

Table 1 indicates that IL-22 levels were statistically non-significantly higher in study individuals (0.21±0.0154 pg/ml) as compared to 0.19±0.0097 pg/ml in controls (p=0.704). Additionally, it was observed that when different interleukin levels were compared to the severity of acne vulgaris, subjects with mild, moderate, and severe acne vulgaris had IL-6 levels of 0.11±0.0292, 0.14±0.237, and 0.15±0.0475 pg/ml. Severe acne was significantly higher than moderate and mild acne (p=0.03).

For mild, moderate, and severe acne vulgaris, IL-8 levels showed similar results with 0.15±0.321, 0.1±0.0774, and 1.79±0.5084 pg/ml and a p-value of 0.03. The levels of IL-17 for mild, moderate, and severe illness were similar, with p-values of 0.804 and corresponding values of 0.17±0.0113, 0.17±0.0112, and 0.2±0.0204 pg/ml. Table 2 illustrates similar non-significant results for IL-22 levels (p=0.573).

DISCUSSION

This study evaluated 60 age- and gender-matched controls and 120 patients with verified diagnoses of acne vulgaris. Using an enzyme-linked immunosorbent assay (ELISA), the blood levels of interleukins 6, 8, 17, and 22 were measured in each of the included patients, and these levels were connected with the severity of acne vulgaris.

The study design bore similarities to the research conducted by Kistowska M. et al. (2015) and Yang L. et al. (2021), wherein the authors employed a study design akin to the current study in their respective investigations. In terms of demographics, it was observed that the average age of the research subjects in the study group was 22.33±5.29 years, whereas the average age of the study subjects in the control group was 21.84±3.76 years. The study group consisted of 35% (n=42) and 65% (n=78) male study participants; in contrast, the control group's distribution of study subjects' age and gender was similar (p=0.896 and 0.873, respectively). There were 33.33% (n=20) and 66.67% (n=40) male and female individuals in the control group, respectively.

The research participants' mean illness duration for acne vulgaris was 6.36±1.24 years, with a range of 1 to 16 years. Of the research participants, 40% (n = 48), 51.67% (n = 62), and 8.33% (n = 10) had mild, moderate, or severe acne, respectively. These results were in line with earlier research by Firlej E et al. 10 in 2022 and Anwar A et al. 11 in 2015, whose authors evaluated participants with acne vulgaris and similar demographic traits to those of the study's patients.

When the blood levels of different interleukins were compared between the two study subject groups, it was observed that the mean serum levels of IL-6 were 0.13±0.0172 and 0.11±0.0093 pg/ml and 0.11±0.0093 pg/ml, respectively, in the case and control groups, indicating a non-significant difference with p=0.822.

The mean serum levels of IL-8 were 0.36±0.078 and 0.12±0.32 pg/ml, respectively, in the patients and controls, indicating statistically significant differences with p<0.001. The mean blood levels of IL-17 in the study individuals were 0.17±0.0073 pg/ml, which was substantially higher than the 0.11±0.0031 pg/ml in the controls (p<0.001). Nevertheless, research participants had statistically non-significantly higher levels of IL-22 (serum value of 0.21±0.0154 pg/ml) compared to 0.19±0.0097 pg/ml in controls (p=0.704). The present study's findings were in line with the research conducted by Singh A et al. (2021) and Murlistyarini S et al. (2018), who found that participants with acne vulgaris had considerably higher levels of pro-inflammatory cytokines and interleukins.

There were statistically significant differences with p<0.001 in the mean blood levels of IL-8 between the patients and controls, which were 0.36±0.078 and 0.12±0.32 pg/ml, respectively. The research participants had mean blood levels of IL-17 of 0.17±0.0073 pg/ml, significantly greater than the 0.11±0.0031 pg/ml in the controls (p<0.001). However, the levels of IL-22 in study participants were statistically non-significantly higher (serum value of 0.21±0.0154 pg/ml) than in controls (019±0.0097 pg/ml; p=0.704). The results of this study were consistent with those of Singh A et al. (2021) and Murlistyarini S et al. (2018), who discovered that individuals with acne vulgaris had significantly higher concentrations of interleukins and pro-inflammatory cytokines.

These findings were in agreement with Abd-Elmaged WM et al[14] in 2019 and Wang Z et al[15] in 2011 where significantly higher levels of IL-6 and IL-8 in subjects with acne vulgaris.

CONCLUSIONS

Considering its limitations, the present study concludes that interleukins 8 and 17 have a crucial effector function in the pathophysiology of acne vulgaris. It has been demonstrated that Th17 cells, the primary generator of interleukin-8 in acne vulgaris lesions, are stimulated by interleukin 6.

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TABLES

S. No	Interleukins	Cases (n=120) Mean ± S. D	Controls (n=60) Mean ± S. D	p-value
1.	**IL=6**	0.13±0.0172	0.11±0.0093	0.822
2.	**IL-8**	0.36±0.078	0.12±0.32	**<0.0001**
3.	**IL-17**	0.17±0.0073	0.11±0.0031	**<0.0001**
4.	**IL-22**	0.21±0.0154	0.19±0.0097	0.704

Table 1: Comparison of serum levels of various interleukins in two groups of study subjects

S. No	Interleukins	Acne grades			p-value
		Mild	Moderate	Severe	
1.	**IL=6**	0.11±0.0292	0.14±0.237	0.15±0.0475	**0.03**
2.	**IL-8**	0.15±0.321	0.1±0.0774	1.79±0.5084	**0.03**
3.	**IL-17**	0.17±0.0113	0.17±0.0112	0.2±0.0204	0.804
4.	**IL-22**	0.19±0.0151	0.22±0.0264	0.2±0.0183	0.573

Table 2: Comparison of various interleukin levels with the severity of acne vulgaris