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Association of serum interleukin-10 (IL-10) with the severity of acne vulgaris



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ABSTRACT

Background: Acne vulgaris is a common inflammatory disorder in pilosebaceous gland units, which affected more than 90% of teenagers, and half of them settled until adulthood. Inflammation is one of the four critical factors in the pathogenesis of acne vulgaris, and it could be a primary process or secondary to *Propionibacterium acnes*. The immune system has a various anti-inflammatory mechanism to counter-balance inflammatory mediators. One of the potent cytokines that play a role in regulating the inflammatory state is Interleukin-10 (IL-10). This study conducted to determine the association of serum IL-10 with the severity of acne vulgaris.

Methods: This is a cross-sectional analytic study involving 33 subjects with acne vulgaris and 31 normal-healthy volunteers as a control. Both groups had their serum IL-10 measured. Acne vulgaris severity was

assessed with Lehmann criteria. Anova was used to determine the statistical difference of IL-10 among different groups of acne severity. This study has been approved by the Ethical Committee Faculty of Medicine, Universitas Sumatera Utara.

Results: The mean serum IL-10 of normal-healthy and acne vulgaris subjects were $5,79 \pm 1,23$ pg/ml and $5,25 \pm 1,55$ pg/ml, respectively. Mann-Whitney test showed a significant difference ($p=0,029$). The mean IL-10 serum levels according to acne vulgaris severity were $6,63 \pm 1,94$ pg/ml in the mild category; $4,89 \pm 0,95$ pg/ml in the moderate category and $4,38 \pm 0,61$ pg/ml in the severe group. ANOVA showed significant difference with $p=0,001$.

Conclusion: There was an association between serum levels of IL-10 with the severity of acne vulgaris.

Keywords: acne vulgaris, serum Interleukin 10, anti-inflammatory mediator

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INTRODUCTION

Acne vulgaris is an inflammatory condition of the skin affecting the pilosebaceous units. It is a self-limiting disease and often found in adolescence period. Acne vulgaris is characterized by polymorphic lesions such as blackheads, papules, pustules, nodules and cysts at predilection area.¹⁻³ Although acne vulgaris is a self-limiting disease, it can cause sequels such as scar tissue and pigmentary changes that can persist for a lifetime.^{1,2,4} More than 90% of adolescents suffer from acne vulgaris, and it is estimated that the prevalence of acne vulgaris in the global population is 9.4%, making acne the 8th most prevalent disease worldwide.^{1,5,6}

Inflammation is one among four key factors in the pathogenesis of acne vulgaris. Other factors involved are epidermal follicular hyperproliferation, increased sebum production, and increased *Propionibacterium acnes* activity. Inflammation can occur as a primary or secondary phenomenon.^{1,2,7,8} Inflammation as a primary phenomenon is shown by the evidence that IL-1a was found as the key to initial inflammatory mediators and comedogenesis.^{9,10} Inflammation as a secondary phenomenon is an immunological reaction to *P. acnes* which causes the formation of pro-inflammatory cytokines and may be induced by free fatty acids produced

through the hydrolysis of triglycerides contained in sebum by the lipase enzyme secreted by *P. acnes*.⁷ These findings bring the perception that acne may be associated with an imbalance of the pro-inflammatory response to *P. acnes*.

The immune response to pathogens involves the activation of rapid pro-inflammatory cytokines to initiate the body's defense against microbial invasion. In line with that, the immune system has an anti-inflammatory mechanism that can suppress the production of pro-inflammatory molecules to limit tissue damage and maintain or restore tissue homeostasis.^{11,12} One potential counter-regulatory cytokine is Interleukin (IL)-10 which inhibits macrophage, and dendritic cells function by suppresses antigen presentation and inhibit the production of cytokine, chemokines, nitric oxide, reactive oxygen species, and costimulatory molecules.¹²

In several previous studies, different results were found regarding IL-10 levels in acne vulgaris. A study conducted by Kang et al. found that mRNA levels of several inflammatory cytokines, including IL-10 around acne lesions, were higher than those of the closest uninvolved normal skin.¹³ Meanwhile, in a study conducted by Caillon et al. showed a decrease

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in IL-10 produced by PMBC (peripheral mononuclear blood culture) in acne patients that statistically significant.¹⁴ Research that evaluates the role of IL-10 in acne vulgaris is still limited. This is what encourages authors to measure serum IL-10 and to study its association with the severity of acne vulgaris.

METHODS

This is a cross-sectional analytic study involving 33 subjects with acne vulgaris and 31 healthy volunteers as a control. Serum IL-10 of both groups were measured with Quantikine ELISA method, using the human IL-10 kit obtained from R&D Systems catalog D1000B. Acne vulgaris severity was assessed with Lehmann criteria. Data collected will be analyzed statistically with T-test or its non-parametric equivalent to evaluate the mean difference of serum IL-10 among subjects with acne vulgaris and normal-healthy volunteer as well as with ANOVA to assess the association between serum IL-10 and the severity of acne vulgaris. The degree of significance (α) used in this study was 0,05. The protocol of the research has been approved by the Ethical Committee Faculty of Medicine, Universitas Sumatera Utara with ethical clearance registry number: 333/TGL/KEPK FK USU-RSUP HAM/2018.

RESULTS

From a total of 33 subjects with acne vulgaris, female (57.6%) was more common than male (42.4%). The majority of acne subjects were within 17-25 years old (90.9%). Based on the severity of acne vulgaris, the highest number of subjects was moderate acne vulgaris (36.4%), followed by severe acne vulgaris (33.3%) and mild acne vulgaris (30.3%). This study also involving 31 normal-healthy volunteers as control. Their characteristic distribution was matched with the acne vulgaris subjects (table 1).

The mean serum IL-10 of normal-healthy and acne vulgaris subjects were $5,79 \pm 1,23$ pg/ml and $5,25 \pm 1,55$ pg/ml, respectively. Mann-Whitney test showed a significant difference between the mean IL-10 of the subjects with acne vulgaris and control ($p=0,029$). Within-subjects with acne vulgaris, the highest mean serum IL-10 levels were $6,63 \pm 1,94$ pg/ml found in mild acne, followed with $4,89 \pm 0,95$ pg/ml in moderate acne and $4,38 \pm 0,61$ pg/ml in severe acne ($p=0,001$). The statistical analysis showed a significant difference in serum IL-10 among the three groups of acne severity ($p=0,001$) (table 2).

DISCUSSION

The pathogenesis of acne vulgaris is complex and multifactorial. One of the four main factors that play a role in the pathogenesis of acne vulgaris is inflammation.^{1,2,7,8} Inflammation that occurs in acne vulgaris is mainly triggered by an immunological reaction to *P. acnes*, which causes the formation of pro-inflammatory cytokines.^{8,9} The chemotaxis substance produced by bacteria attract immune cells such as neutrophils, monocytes and lymphocytes.⁹ One potential anti-inflammatory cytokine with a strong suppressive effect to prevent autoimmune diseases is IL-10.¹² The ability of IL-10 to inhibit cytokine production by both T-cells and natural killer cells (NK) acting indirectly through macrophage/monocyte function. A further study also showed the pleiotropic activity of IL-10 against B-cells, T-cells and mast cells.^{12,15}

In this study, we found the mean serum IL-10 was lower in the acne vulgaris group compared with the control group (5.25 ± 1.55 pg/ml vs. 5.79 ± 1.23 pg/ml; $p=0.029$). This result shows a significant association between IL-10 serum levels and acne vulgaris. The mean values of IL-10 serum levels for each group of acne vulgaris severity were as follows: mild degree of acne 6.63 ± 1.94 pg/ml, moderate degree 4.89 ± 0.95 pg/ml and severe degree of acne 4.38 ± 0.61 pg/ml ($p=0.001$) showed that there was a significant relationship between IL-10 serum levels and the severity of acne vulgaris.

Table 1 Characteristics of the Subjects

Characteristics	Number of subjects (%)	
	Subjects with acne	Normal-healthy volunteers
Gender		
Male	14 (42,4)	13 (41,9)
Female	19 (57,6)	18 (58,1)
Age		
17-25 years old	30 (90,9)	30 (96,8)
26-35 years old	3 (9,1)	1 (3,2)
Acne severity		
mild	10 (30,3)	
moderate	12 (36,4)	
severe	11 (33,3)	
Total	33	31

Table 2 Serum IL-10 of Each Group of Acne Severity

Acne severity	Serum IL-10 (pg/ml) levels					
	n	Mean	SD	Min	Max	p-value
Mild	10	6,63	1,94	4,15	11,30	
Moderate	12	4,89	0,95	2,94	5,94	0,001*
Severe	11	4,38	0,61	3,41	5,39	

*Significant difference (ANOVA)

The results in this study are different from the study conducted by Demina et al. which looked for the role of cytokines in the pathogenesis of acne in 276 acne patients aged 16-44 years. They found that IL-10 serum levels were increased in mild acne compared to controls with a mean difference ± 22 pg/ml and moderate acne compared to controls with a mean difference IL-10 serum levels was ± 30 pg/ml. Nevertheless, we found the weakness in this study because it does not clearly state the mean serum of IL-10 and the significance value is not statistically known.¹⁶

Different results were also found in the following studies, albeit they used a different research method. Research conducted by Kang et al. found that the mRNA levels of the cytokine IL-10 gene increased by 46-fold ($p < 0.001$) compared to the closest uninvolved healthy skin. This study was in vivo study using skin samples of 16 acne patients aged 13-39 years using a 3 mm biopsy device. The mRNA levels of several different cytokine genes, including IL-10, were measured. According to their result, the increased synthesis of IL-10 was a feedback mechanism to reduce the state of inflammation that occurs.¹³

The study by Caillon et al. found a decrease in IL-10 secretion from peripheral blood mononuclear cells as an anti-inflammatory cytokine in acne vulgaris (976 ± 102 pg/ml) compared to control group (766 ± 122 pg/ml in; $p < 0,05$). In this study, the measurements of IL-10 levels by peripheral blood mononuclear cells were measured after stimulation with *P. acnes* with a concentration of 100 μ g/ml. The study also identified possible associations of acne severity and IL-10 secretion after administration of *P. acnes*, but the results showed no difference in IL-10 secretion in mild or moderate to severe acne, although data were not shown in the literature. The low secretion of IL-10 from peripheral blood mononuclear cells of acne patients compared to controls might indicate an imbalance in the production of pro-inflammatory cytokines and anti-inflammatory cytokines against stimuli (*P. acnes*) given.¹⁴

The research conducted by Al-Shobaili et al. investigate the relationship of TNF- α and IL-10 gene polymorphisms with susceptibility to acne vulgaris and the association of the gene polymorphism to its severity. This study involved 166 patients with acne vulgaris in Saudi. The results found no statistically significant differences in the IL-10 genotypic variant (-1082 gene) between cases and controls. Nevertheless, in this study, it was stated that the IL-10 genotype frequency of the -1082 variant was relatively high in acne compared to controls but required a larger sample to be statistically significant.¹⁷

CONCLUSION

Interleukin-10 act as an anti-inflammatory cytokine that plays a role in the pathogenesis of acne vulgaris. Decreased serum IL-10 serum associated with the severity of acne vulgaris. However, it should be noted that the pathogenesis of acne vulgaris is multifactorial and must be reviewed as a whole package.

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AUTHOR CONTRIBUTION

All authors have contributed to all process in this research, including preparation, data gathering and analysis, drafting and approval for publication of this manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest regarding the publication of this article.

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