



# Indian Journal of Forensic Medicine & Toxicology

Institute of Medico-Legal Publications

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No5758/IJFMT/2021

15-03-2021

To,

**Hendra Tarigan Sibero**  
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Dear author/s

I have pleasure to inform you that your following Original Article has been accepted for publication in Indian  
Journal of Forensic Medicine & Toxicology

**The Difference in Interleukin-8 (IL-8) on Degrees of Acne Vulgaris Severity**  
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It will be published in Vol no. 15 issue no. 3 July-September 2021. It is further mentioned for your information that our journal is a double-blind peer reviewed indexed international journal. It is covered by Index Copernicus(Poland), Google Scholar, CINAHL, EBSCOhost (USA), EMBASE (Scopus) and many other international databases.. The Journal is index with Scopus and fulfills MCI Criteria as per MCI circular dated 12/02/2020

With regards

Yours sincerely

**Dr R K Sharma**

Editor

# The Difference in Interleukin-8 (IL-8) on Degrees of Acne Vulgaris Severity

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## Abstract

**Background:** Acne vulgaris (AV) is a follicular disease that occurs most often and affects the area containing sebaceous gland follicles, including the face, back, and body. This is a multifactorial condition. The prevalence of acne vulgaris (AV) is still high both in the world and in Indonesia. As many as 80% of AV is found at the age of 11-30 years and almost 100% in adolescents. Various factors can trigger the onset of AV which can lead to severe complications. **Aim:** This study looked for the difference in interleukin-8 (IL-8) on degrees of AV severity. **Materials and method:** This study was an observational analytic study with a cross-sectional approach. The research was conducted at the Diniyah Putri Islamic Boarding School, Lampung Province, Indonesia, in August 2020. The independent variable in this study was the AV degree, while the dependent variable was the IL-8 level. The sampling method in this study was consecutive sampling, as many as 63 AV patients. The research material is serum from venous blood. Examination of interleukin-8 levels using the ELISA method. Data analysis was univariate to find the mean and standard deviation of IL-8 levels, as well as the frequency distribution to determine the degree of AV. While the bivariate analysis was to determine the difference in the mean of IL-8 levels in AV patients. **Results:** The mean of IL-8 levels in AV patients was 38.53. Most of the AV patients are in a severe category. Further analysis found no difference in the mean of IL-8 levels between moderate and severe AV degrees. **Conclusion:** There was no difference in the mean of IL-8 levels in moderate and severe AV patients, but the IL-8 levels at severe AV degrees were higher than moderate AV degrees.

**Keywords:** degrees of acne vulgaris, IL-8 levels, severity, adolescent

## Introduction

Acne vulgaris (AV) is a follicular disease that occurs most often and affects the area containing sebaceous gland follicles, including the face, back, and body. This is a multifactorial condition.<sup>1,2</sup> AV is a problem in the health sector because it increases every year.<sup>3</sup> AV is still a global problem, most of the AV prevalence is in adolescents.<sup>4</sup> As many as 80% of AV is found at the age of 11-30 years and almost 100% in adolescents.<sup>5</sup> Adolescence is a period of transition from children to adults. In the transitional period, there will be hormonal, physical, psychological, and social changes. The physical changes that occur are the development of secondary sex signs, changes in behavior, and social relationships.<sup>6</sup>

Changes in adolescents can lead to certain disorders or diseases if no attention. In adolescent girls, there will be an increase in FSH at the age of 8 years, followed by an

increase in LH. FSH will stimulate granulosa cells to produce estrogen and inhibin. The hormone estrogen is one of the hormones that cause acne.<sup>7</sup>

Apart from the hormone estrogen, the androgen hormone can also trigger acne. Increased levels of the hormone androgen, namely testosterone, can trigger the oil glands to produce excess oil on the face. The effect is, the skin pores can become clogged and pimples appear. Fluctuations and imbalances in the levels of certain hormones in the body can cause the skin to become oily or dry. The effect is, the skin is more prone to breakouts. That is why these hormones are considered hormones that cause acne.<sup>8</sup>

AV is caused by various factors characterized by blackheads, papules, pustules, and nodules. AV lesions can include non-inflammatory lesions and inflammatory lesions. Various impacts can be caused by this disease.

The pathogenesis of AV involves inflammation by *Propionibacterium acnes* (*P. acnes*).<sup>9</sup>

Follicular epithelial irritation is the role of *P. acnes* in facilitating acne. Physical trauma in the form of friction or pressure can also stimulate acne vulgaris. This condition is known as mechanical acne, where the mechanical factors can include friction, pressure, stretching, scratching, and pinching the skin.<sup>10</sup>

Acne vulgaris is associated with excess sebum production, colonization of follicular infundibular with *P. acnes*, hyperkeratinization, and production of inflammatory mediators. Microcomedones, which result from the proliferation of ductal keratinocytes with infundibulum occlusion and sebum retention, have been postulated to be the primary lesion of acne. In adolescence, there is an increase in sebum production, thus inducing the growth of *P. acnes* and causing the clinical manifestations of AV.<sup>11</sup>

The significance of pro-inflammatory cytokines in the pathogenesis of acne is still the subject of research. The TLR2 receptors play a role in determining the etiology of acne. The stimulation of TLR2 by *P. acnes* increased the IL-8 concentration. Macrophages surrounding the pilosebaceous unit with TLR2 receptors are histologically described in the biopsy material of patients with acne.<sup>12</sup> The clinical manifestations of AV include a red rash on the face or back accompanied by local symptoms such as pain and redness. Meanwhile, systemic symptoms are almost non-existent. Another symptom that may be present is the presence of acne scars in the form of hollows on the skin so that the skin looks uneven.<sup>13</sup>

AV diagnosis can be made based on clinical symptoms. Laboratory tests were performed on AV patients with hyperandrogenism. Patients with virilization signs need a complete examination of testosterone levels such as free testosterone, luteinizing hormone, and follicle-stimulating hormone. Cultures of skin lesions can exclude

the possibility of gram-negative folliculitis, performed if the patient does not respond to treatment or improvement cannot be maintained.<sup>14</sup> Complications from AV include the appearance of scars, both complications from non-inflammatory and inflammatory acne. There are four types of scar due to acne, namely icepick scar, rolling, boxcar, and hypertrophic.<sup>15</sup> This study aimed to find the difference in interleukin-8 (IL-8) on degrees of AV severity.

**Materials And Methods**

This study was an observational analytic study with a cross-sectional approach. The research was conducted at the Diniyah Putri Islamic Boarding School, Lampung Province, Indonesia, in August 2020. The independent variable in this study was the AV degree, while the dependent variable was the IL-8 level. The sampling method in this study was consecutive sampling, as many as 63 AV patients. The research material is serum from venous blood. Blood sample centrifugation is carried out in the polyclinic, placed on a shelf, and put in a refrigerator. The blood containing 10 ml in the EDTA tube was taken to the Prodia Lampung Laboratory for IL-8 levels to be checked by the ELISA method using Human IL-8 Immunoassay Quantikine ELISA kit®. The reading of the results and interpretation is carried out by the Laboratory of Prodia Lampung. All processes for establishing quality assurance in this study will refer to procedures issued by the Center for Health Laboratories, Ministry of Health of the Republic of Indonesia. The data processing is done by editing, coding, processing, and cleaning the data processed by computerized. Data analysis was univariate to find the mean and standard deviation of IL-8 levels, as well as the frequency distribution to determine the degree of AV. While the bivariate analysis was to determine the difference in the mean of IL-8 levels in AV patients.

**Results And Discussion**

Table 1. Respondent Characteristics

Variable	Min	Max	Mean	Standard Deviation
Age	14	18	15,48	1,07

IL-8 Level	12,6	143,7	38,53	27,03
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Based on the results of data collection, it was found that the mean age was 15.48 years with a standard deviation of 1.07. The oldest age is 18 years, while the youngest age is 14 years. All respondents in this study were young women. Meanwhile, the mean of IL-8 levels in moderate and severe AV patients was 38.53 with a standard deviation of 27.03. The highest IL-8 value was 143.7 and the lowest was 12.6. Previous research has found that facial acne often affects adolescents. The prevalence of acne was 85.9%. This disease is more common in women (90%) than men (81.4%). However, the severe form is more common among men. Research has found that the prevalence of acne does not increase with age. There is a correlation between AV severity and quality of life.<sup>16</sup> The results of a similar study found that the highest AV incidence was between the ages of 17-18 years in women and between 19-21 years in men. The prevalence of AV increases at the age of 10-18 years and gradually decreases at the age of over 20 years.<sup>17</sup>

Table 2. Degrees of AV Severity

Degrees of AV Severity	Frequency	Percentage
Moderate	29	44,6
Severe	36	55,4
Total	65	100,0

The number of samples in this study was 65 people. The results showed that AV patients were in the moderate category as many as 24 people (38.1%) and in the severe category were 39 people (61.9%). This study found that there were more severe AV patients than moderate AV patients. The acne grade classification system is useful for patient care. This system can assist in AV classification, help determine suitable treatment options and monitor treatment progression. AV can be classified into three degrees, namely mild AV, moderate AV, and severe AV.<sup>21</sup> Previous studies found that the age distribution of study subjects was between 15-30 years. Adolescents tend to have a higher risk of developing AV to a more severe degree than adults.<sup>22</sup>

Table 3. The Difference in IL-8 on Degrees of AV Severity

Research in Indonesia, especially Medan City, got the characteristics of the majority of participants were women (81.9%) with the largest age group being the age group 17-25 years (81.9%). The degree of acne vulgaris in participants in this study was mostly in mild degrees (57.4%) and 2 people (2.1%) suffered from acne vulgaris in a very severe degree.<sup>18</sup> Research in Lampung Province found that women experienced more acne vulgaris (69.7%) compared to men (30.3%) and 53.2% experienced acne vulgaris at a young age (16-25 years).<sup>19</sup> The incidence of acne vulgaris at the General Hospital of Manado Province during the 2009-2011 period was 1.02%, 1.50%, and 1.07% of 10,003. AV is most common in the 15-24 year age group. The number of male patients was 46 (38.1%) and female patients were 75 (61.9%). This is associated with cosmetic use in women.<sup>20</sup>

A similar study on college students found that most respondents had mild AV severity (93%) and moderate AV severity (7%). Most of the degree of AV severity is mild, possibly due to facial care factors that have been done by female students.<sup>23</sup>

The determination of the degree of severity was assessed based on the number of blackheads, or inflammatory lesions, or total lesions by the Combined Acne Severity Classification (CASC) method. This method is objective and is quite practical and fast because the implementation procedure is easy. The calculation of the number of lesions in the CASC method combines inflammatory and non-inflammatory lesions, so it is difficult to determine the degree of AV severity based solely on inflammatory lesions.<sup>24</sup>

Degrees of AV Severity	Mean	Standard Deviation	p-value
Moderate	37,86	22,31	0,432
Severe	39,07	30,61	

Further analysis using an independent t-test showed that the mean of IL-8 levels in moderate AV patients was 37.86 with a standard deviation of 22.31. While the mean of IL-8 levels in severe AV patients was 39.07 with a standard deviation of 30.61. Analysis of the difference in the mean of IL-8 levels at the degree of AV severity obtained p-value = 0.432, which means that there is no difference in the mean of IL-8 levels between moderate and severe AV degrees. However, substantially, the mean of IL-8 levels in severe AV patients was higher than those in moderate AV patients.

In AV inflammatory lesions, the presence of *P. acnes* contributes to the initiation and maintenance of the inflammatory process by inducing proinflammatory cytokines and tissue-destroying enzymes such as proteases and hyaluronidases. The large population of *P. acnes* will activate the body's immune response, one of which is by stimulating keratinocytes to produce pro-inflammatory cytokines.<sup>25</sup>

Although the main cause of AV is unknown, various factors are thought to be involved in the pathogenesis of this disease, includes overproduction of the sebaceous glands, abnormal keratinization of follicles, inflammation, slow type of immune response, external factors including stress, smoking, drinking alcohol, food, genetics and the proliferation of *P. acnes* where all these factors influence each other.<sup>26</sup>

The cell wall of *P. acnes* contains carbohydrate antigens which stimulate the formation of antibodies. These anti propionibacterial antibodies trigger the inflammatory process by activating complement which then initiates a proinflammatory pathway. *P. acnes* also induces inflammation by eliciting a slow-type hypersensitivity response and by producing lipases, proteases, hyaluronidase, and chemotactic factors so it is a major source of follicular lipase, protease, and hyaluronidase enzymes. *P. acnes* also stimulates Toll-Like Receptor 2 (TLR 2) on monocytes and polymorphonuclear cells around sebaceous follicles. After TLR 2 binding,

proinflammatory cytokines such as IL-1, IL-8, IL-12, and tumor necrosis factor-alpha (TNF- $\alpha$ ) are released. Among these proinflammatory mediators, IL-8 was identified as a neutrophil that activates peptides together with *P. acnes* which induces factors that play a role in attracting neutrophils into the pilosebaceous unit. The production of IL-8 by *P. acnes* is through NF-kappa B.<sup>27</sup>

Based on the results of this study, it was found that IL-8 levels in the group of severe AV were higher than those in the group of moderate AV.

### Conclusion

Data collection showed that the mean age was 15.48 years and the mean of IL-8 levels in AV patients was 38.53. The number of moderate AV was 24 people (38.1%) and the severe AV was 39 people (61.9%). This study found that there were more severe AV patients than moderate AV patients. Further analysis using an independent t-test showed that IL-8 levels in moderate AV patients was 37.86 and IL-8 levels in severe AV patients was 39.07. Analysis of the difference in IL-8 levels at the degree of AV severity obtained p-value = 0.432, which means that there is no difference in IL-8 levels on degrees of AV degrees. However, substantially, IL-8 levels in severe AV were higher than moderate AV.

### Conflict Of Interest

None

### Source Of Funding

Self

### Ethical Clearance

This study has received ethical approval from the Faculty of Medicine, Universitas Lampung, Indonesia with registration number 3866/UN26.18/PP.05.02.00/2019.

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